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ABSTRACTS

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CHEMISTRY, PHARMACOLOGY AND TECHNOLOGY OF DITERPENOID ALKALOIDS AND CREATION OF MEDICINALS ON THEIR BASE

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Diterpenoid alkaloids (DA) are the most distributed class of natural substances. These bases were founded in 10 genii of plants belonging to 7 families, but *Aconitum* and *Delphinium* plants are the most important sources of them.

DA displayed a wide spectrum of pharmacological activity, including curare-like, neurocardiotoxic, antyarrhythmic, antimicrobial, local anesthetic, analgesic, antiviral etc. That′s why DA represented fundamental and practical interest for medicine and molecular biology as new drugs and bioreagents [1].

The complex investigations of DA isolated from *Aconitum, Delphinium*, *Consolida*, *Artemisia* plants had been carried out in ICPS AS RUz from 70-years of XX century. The alkaloid composition of 35 plants of *Aconitum* species, more 20 species of *Delphinium*, 2 species of *Consolida* and one species of *Artemisia* had been investigated at the moment. More 200 DA isolated, a half of them were new [2, 3]. Pharmacological activity of available DA was investigated.

The high lability is attributed to DA due to the presence of ester groups in their structures that easily destroyed in strong basic and acidic environment even in weak heating. Taking into consideration these properties the manufacture technologies keeping the native structure of DA had been elaborated. They are based on the methods of water-spirit extraction and acid water extraction – ultrafiltration of the raw material. In the technological cycles the weak basic agents, weak mineral or organic acids solutions were used, the temperature of technological processes was not more 30°C. The pilot device for manufacture of DA drug substances by the method of water-spirit extraction of plant raw materials had been installed in ICPS AS RUz.

According these technologies the following drug preparations obtained, introduced or introducing into the practice: allapinin (antyarrhythmic, local anestetic, analgesic, neuroprotective); axaritmin (antyarrhythmic, analgesic); aklesin, antiarythmin and dihydroatisine hydrochloride (antyarrhythmic); 1-*O*-benzoylnapelline hydrochloride (antyarrhythmic, local anesthetic).

DA are the very effective bioreagents used as neurochemical tools in different kinds of medical and biological investigations. There are activators of tetrodotoxin-sensitive sodium channels (aconitine, mesaconitine etc.), *n*-cholinoblockers (lycaconitine, corifine etc.), blockers of potential-gated sodium channels (lappaconitine, zeravshanizine, tajaconine etc.).

In spite of good results achieved in chemistry, pharmacology and technology of DA the potential of this group is not limited. Scientific reasonable approach to evaluation of raw materials and technological processes, deep chemical and pharmacological investigations, applying the modern equipment and new technologies for processing of alkaloid-containing plants will lead to creation of new high effective drug preparations and bioreagents.

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HUMAN PROTEOME PROJECT FOR MEDICINE

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The Human Proteome Project (HPP) started in 2007 and officially launched in 2010 as the long-term collaboration of research groups in the field of cataloging all of the proteins coded by the human genome (Legrain et al., MCP, 2011). There was a shift from the analysis of information material (human genome) to the analysis and inventory of proteins – molecular machines operating in the human body. Chromosome-centric HPP (C-HPP) was established as a wing of HPP implementing the chromosome-centric principle (Paik et al., Nat.Biotechnology, 2012, 221–3) prescribes the identification of the protein product encoded by each gene of the given chromosome. Russia has selected Chr 18, inspired by the intensive discussion occurring at the Moscow meeting in 2009, while considering the criteria for ranking human chromosomes according to their feasibility for the C-HPP: (a) minimum of protein-coding genes; (b) abundance of genes relevant to the diseases according to the available literary data; (c) lack of immunoglobulin-coding genes. Chr 18 contains totally 492 annotated genes and 276 protein-coding genes – so, about 276 master-proteins must be detected during the Russian part of pilot phase of C-HPP. Total number of protein species, coded by Chr 18, could be estimated as 20 000 included protein species, arising from nsSNP (SAP), alternative splicing and PTM.

Indicatively, the success of C-HPP depends on the new type of deliverables, which will be of use in the clinical diagnostics. Tocreate the medical background for single chromosome, for example Chr18, we have compiled information about 92 genes, reported in association with 105 diseases either in databases (GeneCards and OMIM (www.omim.org) or in the relevant literature. According data about protein variances, we could expect the number of disease-related protein forms for Chr 18 is about 1 000. Within the framework of the C-HPP approach to the human proteome the top priority should be given to highly sensitive and specific (up to 10–18 M) detection of those proteins in injured tissues and plasma, which are absent in healthy human body (“0”) and typical exclusively for diseases (“1”). Alternatively, a “digital” signature would be consist of a protein present in a healthy human body and absent at some pathology. The digital response capturing can be featured by protein modification events, including SAP, AS, PTM and also fused oncogenes due to chromosome aberrations. That is fundamentally different approach: detection of protein modification events instead master protein as biomarker.

FLORA OF TURKEY AS A SOURCE OF ESSENTIAL OILS

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Essential oils are valuable materials for perfumery, cosmetic, food, pharmaceutical, veterinary, household products, biocides industries and are heavily used in the field of aromatherapy.

Flora of Turkey is rich and diverse with over 12.000 flowering plant taxa belonging to >9000 species. Over 33% of the flora consists of endemic species and 1/3 of the flora comprises aromatic plants. Flora of Turkey is well documented in 11 volumes of the Flora of Turkey and the East Aegean Islands (1965–2001).

Annually, Turkey exports over $100 million worth of medicinal and aromatic plants. In 2011, total exports of oregano, laurel and sage amounted to $62 million. In 2011, Turkey exported $21 million worth of essential oils, hydrosols and related products including rose oil (+ concrete) ($20 million), oregano oil ($ 1 million).

Main aromatic plants of Turkey which are and could be used for essential oil production include the cultivated *Rosa damascena* (Oil rose, Isparta gulu), oregano (Kekik) (from *Origanum*, *Thymus*, *Coridothymus, Satureja* and *Thymbra*), Sage (Adacayi) (*Salvia fruticosa, S. officinalis* (cultivated)), mint (Nane) (*Mentha spicata*, and *M. piperita* from cultivated plants), laurel (Defne) (*Laurus nobilis*), Anis (Anason) (from cultivated *Pimpinella anisum*), cedrus (Sedir) (*Cedrus libani*), birch (Hus, 5 Betula species: *B. medwediewii, B. pendula, B. litwinowii, B. browicziana, B. recurvata*), *Juniperus foetidissima* (Kokar ardic), cumin (cultivated *Cuminum cyminum*, kimyon), coriander (cultivated *Coriandrum sativum*, kisnis), rosemary (*Rosmarinus officinalis*, biberiye), black cumin (cultivated *Nigella sativa*, corekotu), linden (*Tilia* species, ıhlamur).

MODERN APPROACHES FOR PHARMACOLOGICAL INTERVENTION OF ALZHEIMER′S DISEASE AND OTHER NEURODEGENERATIVE DISORDERS

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Alzheimer′s Disease (AD) is the most prevalent form of age-related dementia, which affects about 5% of individuals over the age of 65 and more than 20% over the age of 80. The annual burden of expenditures related to AD in 2010 was estimated as US $ 604 billion [World Alzheimer report 2010]. At the present time only few medicines have been approved for AD treatment though the market for AD agent estimated about 8 billions US $.

The analysis of contemporary approaches for discovery of novel efficient agents for AD treatment permits to outline the following main trends:

1. The development of therapeutic agents acting on the main stages in pathogenesis of AD. These agents are called "disease modifying drugs (DMD)". Such agents should slow the progression of structural damages and produce the improvement of cognition functions in AD patients that persists even after abolishment of the agent. The main strategies in the development of DMD focused on blockade of pathogenic β-amyloid oligomers formation, in particular, β- and γ-secretases inhibition, α-secretase activation, and β-amyloid deposition. The alternative is the prevention of neurofibrillary tangles formation related to abnormal phosphorilation of τ-proteins. Some other approaches such as stimulation of clearance of β-amyloid or modulation of ApoE pathway are also under investigation.

2. The multifactorial nature of AD determines strong interest for the developing novel multi-targeted drugs for AD. Among them special attention is focused on compounds acting simultaneously on acetylcholinesterase and monoaminoaxidase, different subtypes of glutamate receptors, pharmacophores which possess additionally NO-generating and antioxidant activities, multi-target biologically active compounds from plants.

3. Search and study of novel potential biotargets related to the pathogeneses of AD. Recent years number of new promising mechanisms for treating of AD pathology has been proposed. In particular, stabilization of mitochondrial functioning, prevention of pathological protein aggregation in brain (proteinopathy), activation of endogenous mechanism of nervous cell protection, stimulation of neurogenesis and autophagy. Some original agents, which utilize such mechanisms as novel efficient neuroprotectors and pro-neurogenic compounds have been reported.

4. During the last 10 years more than 20 compounds passed phase 2 clinical trails but none of them passed phase 3. As a result of very low outcome from clinical trails of innovative drugs and correspondingly high risk for investments the already known drug repositioning for AD treatment is discussed now as a very attractive area for fast development of AD-therapeutics [Corbet at al., Nature Rev.Drug Disc., 2012].

NOVEL REARRANGEMENTS IN TARGETED SYNTHESIS OF NATURAL COMPOUND ANALOGS

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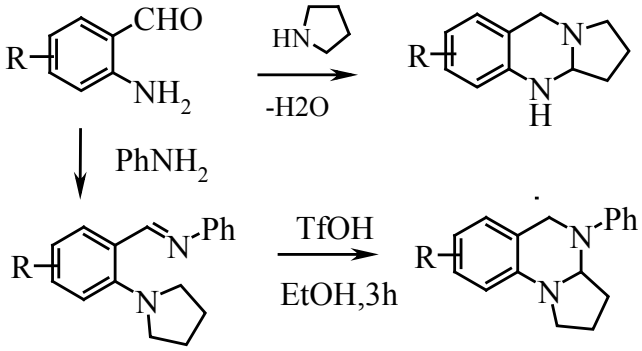
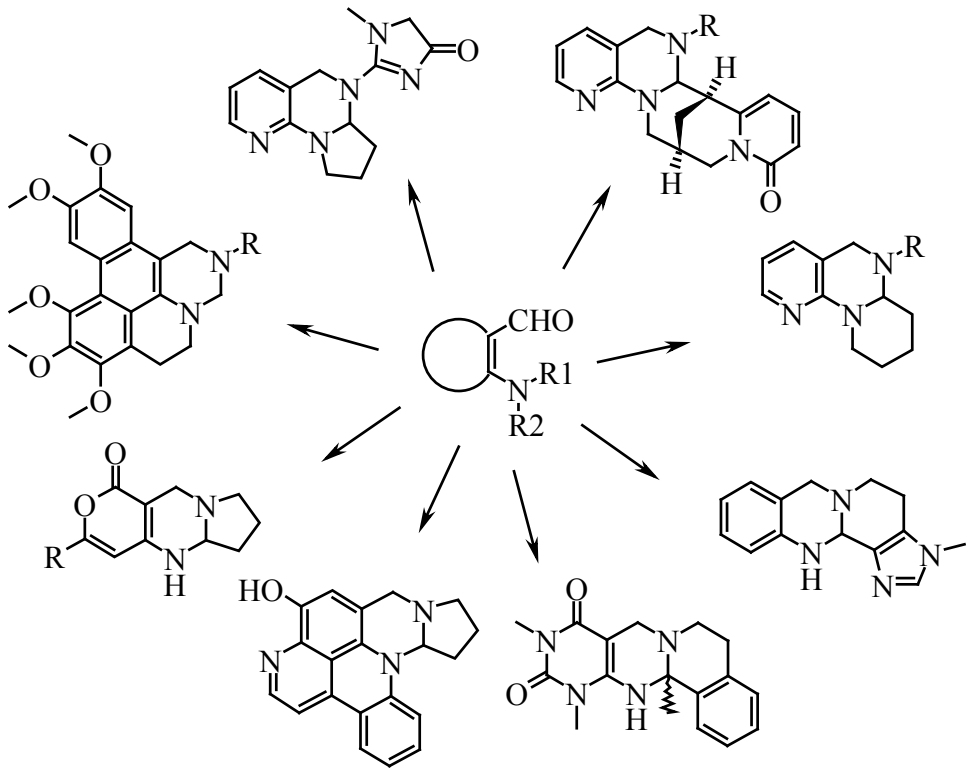
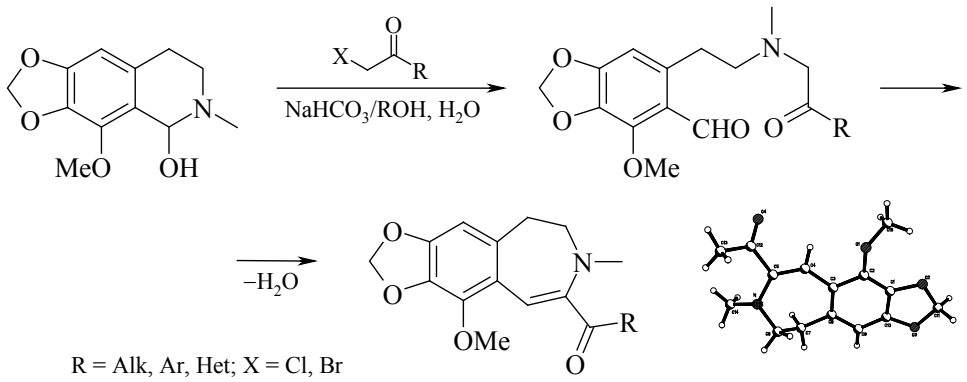
In their 2008 paper, Daniel Seidel et al. [1] described the reaction of *o*-aminobenzaldehyde derivatives with secondary and primary amines which leads to the formation of cyclic aminals. The reaction has been a versatile tool for the synthesis of condensed heterocyclic systems:



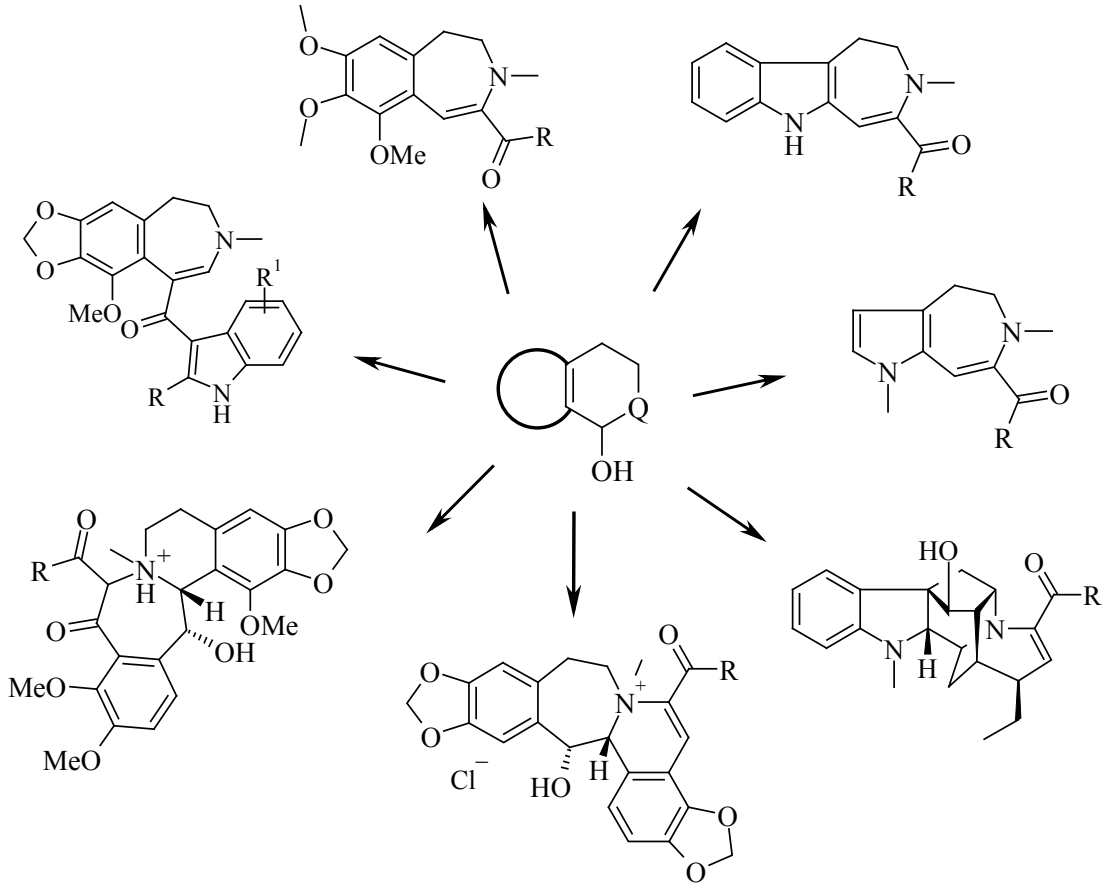
We have extended such reactions to the synthesis of new complex heterocyclic systems on the basis of synthetic and natural *o*-aminobenzaldehydes [2]:



In the course of the study of alkaloid Cotarnine transformations [3] we have found that in the interaction of the Cotarnine base and its natural analogs there take place rearrangements with the formation of benzazepine systems [4]:



Taking various hemiaminals as an example it has been shown that the rearrangement proceeds by the general pattern which makes it possible to carry out directional synthesis of the most diverse heterocycles representing mimetics and analogs of rare alkaloids with a high bioactivity:



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CONTRIBUTION OF SCIENTISTS OF BUKHARA ENGINEERING INSTITUTE OF TECHNOLOGY TO DEVELOPMENT OF BASIC RESEARCHES IN THE DIRECTION OF CHEMISTRY OF NATURAL CONNECTIONS

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The Bukhara engineering institute of technology created on April 15, 2013 in compliance to decrees of the President of Uzbekistan, is one of prestigious Higher education institutions of system of the higher education of the republic. At institute along with preparation of highly qualified personnel in the directions of a bachelor degree and specialties of a magistracy research works on wide the directions of development of production and pedagogical education are conducted. Preparation of scientific and pedagogical shots is carried out by institute of preparation of the senior research associates. Specialized chairs of the chemical, petrochemical and food directions are equipped with modern laboratories, devices and oborudovaniye of physical and chemical research. The main orientation of scientific researches are devoted to research and improvement of technological processes and the equipment of branches of production. Research works on the International and State grants, hozdogovorny subjects prestigious manufacturing enterprises of the republic and the region are in recent years performed. Results of scientific and technological development are approved and introduced under production conditions with big economic effect. 5 monographs are in recent years published, over 350 scientific works in the International and republican editions are published. Are defended 3 doctor′s and 12 master′s dissertations by institute 6 contracts on international cooperation are signed. As a whole scientists and specialists of institute are actively included in development of domestic science and equipment.

CREATION OF NEW MULTIFUNCTIONAL MATERIALS ON THE BASIS OF NATURAL MONOTERPENOIDS AND POLYMERS

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In Russia it is concentrated about 40% of world resources of coniferous breeds. Along with turpentine and rosin, these plants are the richest source of other chemical compounds possessing a wide spectrum of properties and prospects of application.

In Institute of chemistry of Komi SC the emulsion technology of processing of plant raw material without application of organic solvents is developed. In this way it is possible to isolate the monoterpenoids, polyprenols, carotinoids and other biologically active substances. Recently in Institute researches on development of emulsion technology of polysaccharides isolation from Abies wood greenery is conducted. High-molecular polysaccharides of coniferous wood greenery – water-soluble pectines and hemicelluloses – can be used as food fibres, enterosorbents, biologically active polymeric matrix for biogenic metals immobilisation, for medicines capsulation.

Various oxygen containing monoterpenoids represent significant interest for medicine as structure part of various medical products. As a result of oxidizing transformation of α-pinene a lot of valuable oxygencontaining derivatives are received. The synthesized products can be used for manufacture of pheromone preparations for monitoring and struggle against insects-wreckers, and also vitamins and medical products. At introduction of nitrogen containing functional groups in terpene molecules the medicinal substances with potential antiviral, antibacterial, antiparasitic activities turn out.

On the basis of natural monoterpenoids we develop a way of selective synthesis of terpenophenols with various structural type of terpenic substituent. Low toxicity of terpenophenols and their functional derivatives causes an opportunity of their application at reception of highly effective medical products.

Perspectivity of modern medical products with the set properties is defined by high solubility in physiological solutions. Ways of obtaining of water-soluble conjugates of pharmacologically active terpenophenols and their derivatives with polysaccharides are developed and researches of their physiological activity are carried out.

Work is executed at financial support of the project 12-T-3-1004 «Use of wood greenery of coniferous breeds for creation of a complex of highly active preparations» of fundamental investigation program of branch of chemistry and sciences about materials of the Russian Academy of Science «Creation of new kinds of production from mineral and organic raw material».

DETERMINATION OF ANTI-DIABETIC POLYSACCHARIDES OF *Ocimum basilicum* SEEDS INDIGENOUS TO XINJIANG OF CHINA BY HPTLC-UV/VIS-MS

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The seeds of *Ocimum basilicum* have traditionally been used for prevention and treatment of a number of diseases in Xinjiang of China. In this study, six polysaccharide extracts were isolated from the seeds of *Ocimum basilicum* by sequential extraction and purified. After methanolysis, the monosaccharide compositions of the six polysaccharide extracts were analyzed by HPTLC on HPTLC plate′s silica gel 60 with a mixture of isopropyl acetate–ethyl acetate–methanol–water. Densitometric quantitation was performed by absorbance measurement at 370 or 630 nm. The results revealed that the polysaccharides in *Ocimum basilicum* seeds consisted primarily of fructose (hRF 80), glucuronic acid (hRF 58), galacturonic acid (hRF 51), rhamnose (hRF 40), xylose (hRF 25), arabinose (hRF 18) and galactose (hRF 9). Xylose, glucuronic acid and fructose were the three major components found and account for 45, 31 and 21%, respectively. All extracts contained uronic acids, ranged 3 to 24%. An unknown monomeric unit above glucuronic acid was characterized by HPTLC-MS to be a hexuronic acid, and HPTLC-MS proved to be a well suited method for characterization of polysaccharide-based biopolymers and assignment of its monomers. The polysaccharide extracts (aqueous cold, aqueous hot, acidic, alkaline) showed inhibitor activities of protein tyrosine phosphatase 1B *in vitro* with IC_{50} values of 8.2, 2.2, 70.9 and 0.8 μg/mL, respectively. For the first time, a molecular basis was provided to explain the hypoglycemic effect of the seeds of *Ocimum basilicum* that has been used as antidiabetic adjuvant in traditional Chinese medicine.

Acknowledgment. Thanks for financial support of Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

CONJUGATES OF NATURAL COMPOUNDS WITH NYTROXYL RADICALS AS A BASIS FOR CREATION OF FARMACOLOGICAL AGENTS OF NEW GENERATION

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The literature review on spin-labeled biologically active natural compounds has shown that various classes of natural compounds such as anthracycline antibiotics, lignans, triterpene acids, chromanes, flavonoids, stilbenoids, alkaloids, amino-acids, *etc*. can be used for the creation of conjugates with nitroxyl radicals [1]. Numerous *in vitro* and *in vivo* studies have shown that these conjugates reveal increased resistance to reduction of nitroxyl group, improved membrane penetrability, as well as strengthened antioxidant, anticancer and antivirus activity in comparison with the parent compounds.

The series of spin-labeled derivatives of podophyllotoxin, rotenone, stilbenes *etc*. have revealed significant anticancer and antioxidant activity with a notable reduction of general toxicity, which makes them rather perspective for the creation of new drugs. Cytotoxicity of these spin-labeled derivatives in some cases exceeds the one of anticancer agents etoposide and paclitaxel. Moreover, in most of the cases, selectivity index tends to increase.

As shown by the example of conjugates of nitroxyl radicals with “molecular compasses” (folic acid, fragments of gramicidin, heparin), the creation of targeted delivery systems for diagnostic and medicinal agents to be delivered to pathological areas of the body on the basis of such compounds seems rather feasible. Comparative study of the influence nitroxyl radical structure on the properties of spin-labeled conjugates shows the advantages of six membered piperidine nitroxides. Also, many investigations highlighted that the identity of the amino acid spacers had a major impact on cytotoxic activity of such conjugates.

Thus, modification of biologically active natural compounds with the help of nitroxyl radicals appeared to be one of the most perspective approaches of medicinal chemistry for the creation of novel pharmacologically active compounds which can become the basis of new diagnostic and therapeutic agents for most dangerous diseases. The use of individual biologically active natural compounds is characterized by low toxicity and the possibility of their durable application, which corresponds to the modern tendencies in the creation of pharmacological agents of new generation. Introduction of nitroxyl radicals into biologically active molecules contributes to their potential possibility to be used in pharmacokinetic and pharmacodynamic studies by EPR and MRT methods.

The work is funded by the federal program №16/12-Gen-M of Moscow Administration and Grant RFBR N 12-03-00718a.

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DEVELOPMENT OF THE CHEMISTRY AND BIOLOGY OF TRICYCLIC QUINAZOLINES AND THEIR SYNTHETIC ANALOGUES

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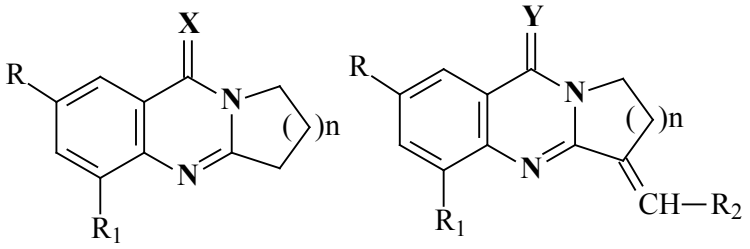
There are many efficient biologically active compounds among alkaloids of the plants *Peganum harmala* and *Mackinlaya subulata* Philipson and their synthetic analogues [1–3].

Chemical modification of natural compounds and their synthetic analogues are a perspective direction for creation of new preparation for agriculture and drugs with various activities [3–5].

In this work we generalized the obtained results on synthesis, transformations and biological activity of a series of tricyclic quinazolines and their synthetic homologues and derivatives:



R, R_1=H, Br, NO_2, NH_2
R_2=OH, $N(CH_3)_2$, alkyl, aryl
X=H_2, O, S; Y=O, S
n=1-3

The purpose of this work is comparative analysis of reactivity of the tricyclic quinazolines and their analogues in electrophylic and nucleophylic substitution/addition reactions and searching for the potentially active compounds.

Modification of tricyclic quinazolines and their synthetic homologues may open very interesting direction in the field of fundamental science as well as for development of efficient preparations for agriculture and medicine. Problems of development of the alkaloids chemistry and perspectives of creation biologically active substances will be considered.

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PECULIARITIES OF ISOPRENOID BIOSYNTHESIS AND BIOTECHNOLOGICAL USAGE OF PLANT CELLS *in vitro*

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A plant cell is considered to be a result of the hypothetic "host" organism symbiosis with two ancient bacteria – the precursors of plastids and mitohondria. That left its imprint upon the metabolism of contemporary cells: "procaryotic" and eucaryotic systems of metabolism often work simultaneously. For instance, there are two pathways of isoprenoid biosynthesis working in a plant cell only. They are: "eucaryotic" (mevalonate) take place in the cytosol and "procaryotic" (through the deoxy-xylulose) in the plastids.

It is found out that sesqui- and triterpenoids are synthesized through the mevalonate pathway, whereas, some di- and tetraterpenoids are synthesized through the "procaryotic" one in the chloroplasts. However, it is practically unknown as far as it is true for the secondary metabolites of the isoprenoid row. So, the investigation of isoprenoid biosynthesis in cell cultures of higher plants turns out to be a convenient system to solve this problem.

Biosynthesis both of tri- and diterpenoid compounds was investigated in different plant cell cultures such as: *Panax ginseng, P. japonicus* (ginsenosides); several strains of *Dioscorea deltoidea* (steroid glycosides); *Ajuga reptans, Serratula coronata, Rhaponticum carthamoides* (ecdisteroids); *Polyscias filicifolia* (triterpene glycosides), *Taxus s*pp. (taxoids) and *Stevia rebaudiana* (diterpene steviol-glycosides).

It is known that cell culture is not analogous to an intact plant. It is a special biological system: that is a population of somatic cells, and the secondary metabolism in cultivated cells differs from that in intact plant cells. It was demonstrated that both proper choice of the strain and optimization of cultural conditions (or each of them separately) could lead to the high levels of different triterpene compound synthesis and productivity. *Dioscorea deltoidea* plant cell culture synthesize both steroid glycosides which are located in leaves (protodioscine) and rhizome (deltoside) of the intact plants. It should be note, that cultivated cells contain 26-S isomers which are not found in the intact plants. Furostanole glycoside productivity of *Dioscorea* strain DM-0.5 was up to 6–12% by dry biomass. *Panax ginseng* and *Panax japonicus* plant cell cultures synthesize as minimum seven ginsenosides, the productivity of these compounds was up to 6.0–8.0% on dry biomass. The presence of large amounts of malonyl esters of ginsenosides Rb-group in suspension culture of *Panax japonicus* var. *repens* was demonstrated. The content of ecdisteroids in plant cell biomass is up to 1.0%. By contrast, the detectable synthesis of diterpene steviol-glycosides only initiated in the mixotrophic cultures during chloroplast formation.

Production of plant cell biomass was carried out in 0.63 m^3 bioreactors in semi-continuous conditions. The pharmaceutical products "Vitagmal", "Vitagmalin", "Triphytol" from *Polyscias filicifolia* plant cell cultures were obtained with NPF "Biopharmtox" collaboration.

DEVELOPMENT OF ORIGINAL PHARMACEUTICAL FORMULATIONS BASED ON AGSULAR® SUBSTANCE

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The original pharmaceutical Agsular® substance, having a wide range of pharmaceutical activity, derived from Siberian larch polysaccharide arabinogalactan (with its chemical modification), have been developed in the Irkutsk Institute of Chemistry SB RAS.

According to its preclinical tests (2009–2011) Agsular® (as the drug substance itself and as oral medications) has almost the same efficacy as anticoagulant and antithrombotic Vessel Due F® (sulodexide, Alfa-Wassermann S.p.A, Italy) and as hypolipidemic and antiatherogenic Zocor® (simvastatin, Merck Sharp & Dohme, the Netherlands). Agsular® is assigned to the Toxicity Class III. In this connection, the oral medications of Agsular® are recommended for clinical tests to be included into register of the RF Ministry of Health as a hypolipidemic agent.

The explorations of the pharmaceutical activity of the unique modified polysaccharide Agsular® find out a polyvalent mechanism of its action, including not only the ability to control the lipid metabolism and hemorheological blood parameters, but also to strengthen the vascular walls and improve microcirculation, that is the very problem at chronic venous insufficiency.

In addition to that, the external use of Agsular® drugs has been investigated for the cases of vascular pathology and they manifest their apparent venous protective effect. The comparison of the activities of the original pharmaceutical compositions developed on the basis of Agsular® substance with such commonly used anti phlebological drugs as Lioton® (Berlin-Chemie/Menarini Pharma GmbH, Germany), Troxevasin® (Balkanpharma-Troyan AD, Bulgaria), Nigepan® (JSC "Nizhpharm", Russia) shows the high efficiency of the former, comparable, and in some cases even surpassing the above preparations.

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CHEMISTRY, BIOLOGY AND PHARMACOLOGY OF THE SESQUITERPENES ISOLATED FROM *Ferula* SPECIES GROWING IN ANATOLIA*

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Genus *Ferula* (*Apiaceae*) comprises ca. 180–185 species and is the largest *Apiaceae* family in Asia. There are 24 species of *Ferula* grow in Turkey, 15 of these species are endemic to Anatolia. Phytochemical investigations of the indigenous *Ferula* species growing in Anatolia have yielded numerous novel sesquiterpene compounds including esters, alcohols, ketones, keto-alcohols, coumarins as well as phenylpropanoids and phenolic compounds.

Preliminary pharmacological studies performed in the early 1980s had shown stereoid-like biological activities for some of these compounds. Further studies have shown many more biological activities of these compounds such as anticancer, antibacterial, anti-fungal, anti-viral, anti-inflammatory and immunomodulator activities.

Taxonomical classification of the *Ferula* species growing in Anatolia is a challenging task for many botanical experts, yet structures of the unique sesquiterpene compounds isolated from these plants provide critical information for the classification of closely related *Ferula* species at subgenus, species, subspecies and variety/form level. Phytochemical investigations has also yielded novel class of sesquiterpene compounds specific to this genera, furthermore, isolation of the key intermediate metabolites provided pivotal information for the elucidation of the biosynthetic pathways of these sesquiterpene compounds.

As part of the structure–activity relation chemical studies, major sesquiterpenes of *Ferula* species were subjected to the various chemical transformation reactions. Some of these reactions were produced anticipated compounds, however, some have yielded unexpected products that were not described hitherto in the literature. These novel chemical transformation products provide meaningful explanation for the presence of their precursors in *Ferula* species as a unique chemical defense compounds.

*This presentation is dedicated to Prof. Dr. Ashraf I. Saidhkhodzhaev honoring his pioneering studies in the chemistry of Genus *Ferula*.

LOW DOSE BIOACTIVE DRUGS FOR AGRICULTURE FROM SIBERIAN CONIFEROUS PLANTS BIOMASS

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Siberian coniferous plant material is an inexhaustible source of bioactive compounds that are used for manufacturing of physiologically active drugs applied in medicine and agriculture. The raw material for extraction of these compounds may be wood, bark, woody greenery and waste products of wood processing industry. The use of natural plant protection products gives the opportunity to produce high volume of environmentally friendly crops, reduces the damage caused by extreme natural factors and adverse ecological conditions.

Based on the sum of triterpene acids isolated from Siberian fir woody greenery (*Abies Sibirica*) such well-known drugs as NOVOSIL, SILK and ECOSIL were produced. These drugs serve as high – performance natural growth regulators and immunity inducers for the plants with fungicidal effect to a range of fungal, bacterial and viral diseases. Further processing of the raw materials resulted in phenolic mixture of biologically active compounds on the basis of which, a new low dose drug for agriculture ABISTIM was received [1]. Similarly, phenolic complexes were isolated from the wood and bark of larch (*Larix Sibirica*). Siberian fir essential oil was used for creation of PIHTOROS emulsion [2, 3]. The system of lipid and phenolic compounds extracted from larch wood, served as the basis for development of BIOFUNGISTIM drug [4]. Bioactive carbohydrate complexes were isolated from the fir woody greenery, larch wood and bark. On the basis of NOVOSIL, ECOSIL and ABISTIM the blend compositions with PIHTOROS were developed and tested. Many years of laboratory and field tests of the drugs in both open and protected grounds on a wide range of cereals, legumes, forage, vegetable and flower crops in the SPCSI SB RAAS showed their high efficiency. All these drugs are considered to be low dose plant protection means and are designed for pre-processing and spraying during the vegetation period; they stimulate the root formation, growth and evolution of plants, contribute to early and high yield, improve the quality of agricultural products and significantly reduce the damage of plants from various diseases.

Thus, the common scheme for complex Siberian coniferous biomass processing that significantly improves isolation degree of practically important extractives and expands the range of biologically active products for agriculture was developed.

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PHYSICAL ACTIVATION OF EXTRACTION BIOLOGICALLY ACTIVE SUBSTANCES DERIVED FROM NATURAL SOURCES: MICROWAVE, MCA AND ULTRASOUND

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The problem of creating new high-ways of biologically active substances (BAS) is a priority for the development of the science of chemistry and chemical technology. Improvement of these methods is, inter alia, through the use of various physical impacts in chemical reactions and processes, including microwave, mechanochemical and ultrasound.

Accompanied by physical impact, along with the destruction of the cell wall components of change in the chemical composition of plant material due to rupture of a number of chemical bonds.

The successful implementation of the various options for physical activation process is to increase the extraction of biologically active substances in the product over the full range of bioactive compounds in a biologically available (water-soluble) forms.

The report describes the features and mechanisms to increase the efficiency of the extraction of bioactive compounds from natural raw materials by microwave, mechanochemical and ultrasound activation.

Microwave extraction, unlike a conventional liquid extraction, significantly reduces the time of extraction due to the rapid heating of the solvent. Moreover, the microwave exposure can be reduced to minimize the temperature gradient and accelerate heat transfer. In addition, microwave extraction substantially reduces the consumption of solvents and energy costs and significantly increases yield of the desired product. The microwaves act directly on the water molecules inside the plant cell, which leads to a rapid rise in temperature inside the cell. Cellular water evaporates quickly, the pressure within the cell rises sharply, leading to the destruction of cell membranes and cell walls forming a "hole." This facilitates intracellular fluid flow, and the solvent to penetrate into the cell which leads to an increase in extraction efficiency.

Previously obtained preliminary evidence that intensive mechanical activation of plant material, which increases the degree of dispersion is accompanied by an increase in output and a variety of biologically active substances and their activation.

Ultrasonic waves can accelerate chemical reactions by emulsification of liquid components, dispersing the solid components, their erosion surface degassing prevent precipitation or coagulation products, intensive mixing, etc.

The report presents the results of the use of microwave systems CEM Corporation (USA), a planetary ball mill Retcsh PM100CM and ultrasonic homogenizer Bandelin the HD2200 model (Germany) for efficient extraction of biologically active substances from medicinal plants.

NEW ANTIVIRAL AGENTS INSPIRED BY THE CHEMICAL DEFENSE OF PLANTS

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Yunnan Province of China is called "Plant Kingdom" due to its plant biodiversity in the world. Plants have evolved multiple mechanisms to selectively suppress pathogens by production of secondary metabolites with antimicrobial and antiviral activities. Therefore, direct selections for antiviral compounds from plants can be used to identify new agents with potent antiviral activity but not toxic to hosts. We are interested in biological and ecological significances of secondary metabolites of plants, and hope to approach on the special mechanism of anti-TMV agent derived from plants.

Three different types of anti-TMV (anti tobacco mosaic virus) agents were discoveried from *Strobilanthes cusia* (Nees) Ktze and *Cynanchum paniculatum* (Bge.) Kitag., which showed different action mechanisms of anti-TMV. Seco-pregnane sterides are effective and selective inhibitors targeting to subgenomic RNA of α-like positive-strand RNA virus (*Togaviridae* family) including plant-infecting TMV, and animal-infecting SINV, EEE and Getah virus [1]. New chemical inducer 3-acetonyl-3-hydroxyoxindole (AHO) induced the systemic acquired resistance in plants *via* the salicylic acid-mediated signal transduction pathway [2]. Cinchonaglycoside C can induce a ribosome-inactivating protein (RIP), which possess anti-TMV function [3]. β-Carboline compounds isolated from *Picrasma quassioides* and quassinoids from the fruit of *Brucia javanica* also showed good anti-TMV activities, and synergistic effect against TMV when β-carboline combined with quassinoid isolated from same plant [4]. Quassinoids from the fruit of *Brucia javanica* also showed good anti-TMV activities, which not only inhibit the accumulation of TMV coat protein but also enhance the host plant′s resistance to TMV infection [5]. Some limonoids isolated from *Meliaceae* family also showed good anti-TMV activity [6], despite of their significant other ecological effects such as insecticidal and antifeedant activities.

Benzylphenethylamine alkaloids showed stronger anti-TMV activity [7], which can suppressed heat shock cognate 70 protein (Hsc 70) expression of the host cells but not affected the viral enzymes, which perhaps is a one of the main reason for their antiviral activity with a wide spectrum. Thus simplified derivatives of Benzylphenethylamine alkaloids showed significant activities against HBV and HCV. It is very interested that a novel activator of the Wnt/β-catenin signaling pathway has been found from this kind of derivatives [8].

There has been limited report about inhibitor of plant virus up to now, even for the anti-TMV agent. Although TMV widely infects many plants of different families, and its biological behavior has been studied very deeply, investigation of effective anti-TMV agents from plants is still a new research field.

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COTTON-SOYBEAN PALMITIN FOR MARGARINE PRODUCTION

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It is known, that the cotton palmitin is value raw materials for margarine production. Its content in cotton and soy oils is exceeded 24%–10%, respectively.

Efficiency of the mixing of cotton and soy oils with the subsequent fractionation of palmitic fraction by low-temperature crystallization from fusion is established. Thus, the so-called cotton and soy palmitin, which according to the photocolorimetric analysis is characterized by higher contents of phospholipids (0.3% in terms of stearoleolecithin), that predetermines its functional application in production of fatty products of emulsion character. And higher exit (to 80%) of cotton and soy salad oil causes economic efficiency of its production in comparison with the cotton.

Influence of cotton and soy palmitin on firmness of margarine emulsions with various fat contents is investigated. The fatty bases for margarine emulsions chosen for experiments consisted of prescription fatty components of widespread feeding margarine with replacement of 10% of prescription amount of vegetable oil with the cotton and soy palmitin containing from 0.1 to 0.4% phospholipids. Oil-water-milk emulsion of margarine was prepared according to the technological instructions. Thus, fat content of margarine emulsions of various options were 60, 72 and 82%. Values of margarine emulsion firmness served as a criterion for assessment of quality of the obtained emulsion systems were defined.

Results of experiments shown, that the inclusion in margarine of 10% cotton and soy palmitin, containing 0.2–0.4% phospholipids, may promote substantial increase of margarine emulsion firmness and reduction of emulsifier amounts, especially for margarine emulsion with 72 and 82% of fat contents. It means, that the cotton and soy palmitin can have synergy impact on effect of the emulsifier provided by a compounding (frequently they are monoglycerides distilled). As showed laboratory and production researches in the conditions of JSC “Toshkent yog-moy kombinati”, in such systems the amount of emulsifier can be reduced almost twice at preservation of demanded firmness of emulsion.

MODIFICATION OF BIOLOGICALLY ACTIVE PLANT METABOLITES *via* THE TRANSITION METAL CATALYZED REACTIONS

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Methods of functionalization of some plant metabolites or their derivatives, *viz*., the eudesmane-type ethylidenelactones, diterpenic and morphinane alkaloids using the transition metal catalyzed reactions are discussed.

Reaction of sesquiterpene methylidenelactones isoalantolactone **1**, alantolactone **2** and tournaforine **3** (isolated from *Inula helenium* or *Artemisia tournefortiana*) with aryl iodides and aryl bromides catalyzed by the system $Pd(OAc)_2$–(*o*-Tol)$_3$P–Et_3N in DMF proceeded with the formation of 13-arylsubstituted exo- and endocyclic lactones (total yield up to 94%). The ratio of isomers depended on the lactone nature, base and additives, as well as on the structure of aryl halide. Reactions of isoalantolactone **1** with 5-bromo- or 5-iodouracyls proceed with the formation of 13-(*E*)-(2,4-dioxotetrahydropyrimidin-5-yl)eudesma-4(15),11(13)-dien-8β,12-olides as the main products. We shown the activity of the 4,15-double bond of isoalantolactone **1** in the Heck reaction.

The diterpene and morphinane alkaloids were studied in the bromination and iodination reactions for the further introduction of the halides obtained into the Heck reaction with terminal alkenes. Iodo derivatives of lappaconitine reacted with ethyl acrylate with the formation of cinnamic esters. The reaction of 5′-iodolappaconitine with styrene, 2-methyl-5-vinylpyridine, *N*-vinyl-1,2,4-triazole led to the coupling compounds in 51–86% yields. The reaction with ethyl vinyl ether is a method for the introduction of the acetyl group in the own compound with the formation of a 5′-acetyllappaconitine.

The reaction of 5′-iodolappaconitine with trimethylsilylacetylene catalyzed by the system $Pd(PPh_3)_2Cl_2$–PPh_3–CuI–Et_3N led to a alkyne derivative of diterpene alkaloids in 77% yield. The latter was converted to 5′-ethynyllappaconitine, which was involved into the Sonogashira reaction with 5′-iodolappaconitine to give a dimeric alkaloid in 75–80% yields. The oxidative dimerization of terminal acetylene by the Glaser reaction allowed us to obtain dimeric alkaloid with a diinyl spacer.

The Sonogashira reaction was used for the synthesis of the morphinane-type acetylene derivatives. The reaction of 1-iododihydrothebainehydroquinone with terminal alkynes catalyzed by the system $Pd(PPh_3)_2Cl_2$–PPh_3–CuI–Et_3N led to cross-coupling products in 44–90% yield. In the same reaction, 1-iodo-(2,5-dioxo-*N*-*R*-pyrrolidino)[3,4-*h*]-*endo*-ethenotetrahydrothebaines were converted into the corresponding 1-ethynyl derivatives of alkaloids (56–62% yield). The desilylation allowed us to obtain 1-ethynyl derivatives of morphinane alkaloids. The products of the Cu(I)-catalyzed Mannich reaction of 1-ethynyldihydrothebainehydroquinone or 1-ethynyl-(2,5-dioxo-*N*-*R*-pyrrolidino)[3,4-*h*]-*endo*-ethenotetrahydrothebaines with formaldehyde and *N*-monosubstituted piperazines or anabasine are obtained.

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STEROIDAL ALKALOIDS: CONTRIBUTIOM OF THE INSTITUTE OF CHEMISTRY OF PLANTS SUBSTANCES INTO THE FOUNDAMENTAL PHARMACOLOGY

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Steroidal alkaloids presented by more than 800 units have divided for 8 chemical classes. The main sources of these compounds are plants of following families: *Liliaceae*, *Solanaceae*, *Buxaceae*, *Apocinaceae*, *Eclipta*, as well tropical frogs *Phyllobates*, birds: *Pitohui*, *Ifrita* and marine invertebrates: *Corticium*, *Terpios*, *Zoanthus*. In the ICPS by pharmacological methods have been studied 5 groups from 8 and 3 of them – for the first time.

Veratrum alkaloids of verazine type reveal such psychopharmacological activities as: nootropic, proaggressive, antidepressant. Some of them increased contraction force of skeletal muscles. All representatives, especially veralosine, excitate sex behaviour of male and female rats. With the purpose of create the analoug of minor alkaloid veralosine semi-synthetic derivatives of approachable alkaloid solasodine were synthesised. It was showed, that some representatives administered in low doses per os reveal aphrodisiac activity. Some of them gradually in high degree increased level of arterial pressure for several hours. This compound may be qualified as new stimulant of sympatho-adrenal system.

Besides, in ICPS for the first time was discovered selectivity of Fritillaria alkaloids to M_2-subtype of muscarinic receptors. It′s showed, on the base of M_2-blockers there are principal possibility to create, at least 4 directions of medicinal drugs branches: antiarrhythmic preparations for cardiology, new class of cholinopositive drugs; psychotropic preparations with atypical anxyolytic, nootropic and antidepressant activities.

Pharmacological studies of Korolkowia alkaloids conducted in ICPS for the first time revealed complete spectrum of antiarrhythmic compounds. There are representatives of 1-st, III-rd and IY-th classes of antiarrhythmic drugs, as well alkaloids of combined 1 + III, 1 + III + 1Y classes. Combined drugs are demanded in clinical medicine. Korolkowia plant may be declared as genuine source of antiarrhythmic compounds.

Investigation of pharmacology of ceveratrun ester alkaloids permit reveal representatives with significantly more expressed pharmacological width, compared with known hypotensive drug “Protoveratrine”. Studies of mechanism of action of these compounds on arterial pressure have showed, that hypotensive action concomitant with hidden activation of simpatho-adrenal system and it abolition lead to increase of hypotensive action. For the first time it was eliminated nausea side effect of these compounds. It was noticed, that ceveratrum ester alkaloids increase effect of neurotropic and hormonal drugs. These findings precede to latter appeared concept “resistance to drugs” By other words these compounds may be used in studies of multiresistance mechanism. In future methods of struggle with development of multiresistency will be extended.

In conclusion it may be stated, that steroidal alkaloids studied in unsufficient degree. Conducted in ICPS pharmacological studies of steroidal alkaloids have showed, that these compounds have notable interest. They are representatives of different classes of pharmacological agents with polymorphic pharmacological activities. Sometimes they have significant preferences compared with known drug preparations. They enrich foundamental pharmacology by principal new representatives of pharmacological agents of different directions with new, sometimes unknown mechanisms of action.

THE DRUGS ON THE BASIS OF FLAVONOIDS AND POLYSACCHARIDES LARCH SIBERIAN AND GMELIN

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For the first time in Russia carried out commercially, deep processing of all components of wood raw material with the release of a wide range of medical products for the environmentally safe technologies.

The methods of separating the individual components of extractives – dihydroquercetin and arabinogalactan have been developed and created the technological schemes of their industrial production.

A method of analysis of the components of the biomass of larch, satisfying the requirements of certification of drugs has been worked out. The medical practice has shown that biologically active preparations of larch are essential for the prevention and treatment of social diseases such as influenza, SARS, heart attack, stroke, diabetes, malignant neoplasm.

Using natural compounds in the treatment of colds and flu - is a worldwide trend. Natural biologically active substances, and especially flavonoids, gradually take a leading position in the market of antiviral and anti-inflammatory drugs. An example would be the successful investigation of protective activity of flavonoid dihydroquercetin and polysaccharide arabinogalactan at experimental influenza infection caused by viruses of different types: A (H1N1), A (H5N2) and B. As a result of many years of research "Araglin D" has been designed. It is the drug in the form of nanobiocomplex obtained by mechanochemical synthesis. The new product provides primarily the protection of the organism from the infections during a flu epidemic and SARS.

In the field of neurology for the treatment of early forms of cerebrovascular diseases it is advisable to make extensive use of the drug Diquertin created on the basis of dihydroquercetin on the unique technology of the authors. Diquertin possessing antiaggregant, hypolipidemic, vasoactive and neuroprotective effects, has a significant influence on the mechanisms of cerebral ischemia. The drug can be used in the treatment of acute cerebral vascular disease, as well as for secondary prevention.

The studies on polysaccharides within the development of technology of 100% processing of larch wood and bark as forestry wastes to afford new medicines, veterinary drugs, dietary supplements, and valuable materials for cosmetic and agricultural industry. There are data on larch wood and bark extraction by two-phase solvent system, namely kinetic study of extraction process, diffusion constants, mass-transfer coefficients, mechanism and physicochemical characterization of the transfer process, its mathematical model, and structural characteristics of the samples isolated. The work is aimed for the development of economically and ecologically wise production technology for demanded products on the basis of renewable raw materials with 15–20% increase of forestry efficiency due to waste processing. The technology is to give new medicines and food supplements as well as 40–50% cheaper analogs to the known ones.

ABIOLOGY OF *Indigofera tinctoria* L. ON THE SALINE LAND OF ARAL SEA BASIN AND PRODUCING OF THE NATURAL PLANT INDIGO PIGMENTS FOR THE INDUSTRY

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In consideration of the increasingly growing demand fornatural pigments of the world industry (the worldwide sales are said to increase up to US $ 24.5 billion in 2015, and reach US $ 27.5 billion in 2018), and medications, as well as for the rehabilitation of ecology of saline land of Aral Sea, agro-technology of cultivation and biotechnology of production of plant indigo to produce natural indigo dye from biomass to be used in the textile, pharmaceutical, decorative, perfumes, cosmetics and other industries were developed.

Until now it was thought that it is impossible to cultivate such tropical culture as *Indigofera tinctoria* L. grow in arid conditions and saline soils of the Aral Sea. Nowadays for wide adoption of such economically useful and ecologically sound dyeing and medicine plant as Indigofera (which is widely used in Tibetan traditional medicine since ancient times used to get the antibacterial and antifungal agents, salves for bites of snakes, dogs, drugs for the treatment of epilepsy, skin ulcers and liver toxicity, typhoid, anti-depressant, and even against cancer) the following steps were accomplishedon the frame of the project:

– the biotechnology of manufacturing of the natural plant dye indigo both in laboratory (1.5% product yield from the green biomass) and in the tonnage volume of the field has been developed. The marketing researches abut indigo in different world countries and on the European markets showed that 1 kg of plant indigo costs from 80 to 240 Euro and the price of the chemically sintethaed one is not more than 20 Euro) [2];

– the ongoing research on biology peculiarities, HPLC spectrum and PH of the natural and synthetic pigment of indigo under the conditions *in vitro* and *in vivo* [3];

– for the first time a new salt tolerant variety of Indigofera plant "Feruz-1» with high symbiotic association with nitrogen-fixing root nodule bacteria was created by the methods of classical genetic engineering and plant breeding in combination with the methods of biotechnology and soil microbiology, also a seed production farm of this variety was established [4].

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AIR FLOW-ASSISTED IONIZATION MASS SPECTROMETRIC IMAGING METHOD FOR WHOLE-BODY MOLECULAR IMAGING ANALYSIS OF NATURAL MEDICINES

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It is important to determine how a drug candidate is distributed and metabolized during the preclinical steps of drug development and discovery. Mass spectrometric imaging (MSI), a label-free molecular imaging method, can be used to image multiple molecules in a single measurement with high specificity [1]. Besides the focus on the drug tissue distribution, detecting endogenous metabolites changes throughout the whole-body animal on a time scale will give a full view of the correlation between drug distribution and therapeutic or toxicological responses and help to understand the mechanism of drug action.

Herein, a novel easy-to-implement, whole-body MSI method was developed with ambient air flow-assisted ionization (AFAI). AFAI-MSI method can effectively image molecules in a large whole-body section in open air without sample pretreatment, and directly map spatial distribution of molecules and monitor its biotransformation. This approach was applied to analyze the potential anticancer agent 3,6,7-trimethoxyphenanthroindolizidine (CAT), a phenanthroindolizidinealkaloid with strong antitumor activity isolated from *Tylophoraatrofolliculata* and an adenosine analog drug candidate N^6-(4-hydroxybenzyl) adenine riboside (NHBA), isolated from *Gastrodia elata blume*.

In this study, a global view of the differential distribution of CAT and its metabolites was simultaneously acquired in whole-body rat and model mouse bearing neuroglioma along the administration time. The obtained drug distribution provided rich information for identifying the targeted organs, and predicting possible tumor spectrum, pharmacological activity and potential toxicity of drug candidates [2].

Based on the AFAI-MSI method, NHBA and various endogenous metabolites were simultaneously and spatially detected with high sensitivity. Changed metabolites in response to drug administration were found through hyperspectralvisualization. From the comprehensive information, some clues about the correlations between NHBA distribution and therapeutic or toxicological effects were found.

The results demonstrate the AFAI-MSI method can be used to simultaneously and spatially detect the drug molecule and changed endogenous metabolite. Combined pharmaco-metabolomics analysis, a spatiotemporal behavior of drug and endogenous metabolites can be visualized to indicate the action mechanism of drug candidate.

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REDUCTION OF α-METHYLENINDOLENINE TYPE ALKALOIDS

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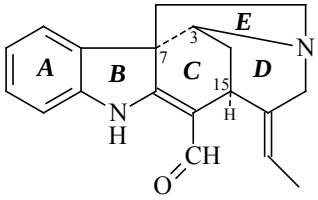
Vinca erecta Rgl. et Schmach is rich for indol alkaloids. Over 70 compounds had been isolated from this plant. Preparations from *V. erecta* based on indol alkaloids: barvinkane, ervinine, vinkamine, metvine used in medicine [1]. The main alkaloid of *V.erecta* is norfluorocurarine (vincanine) (**1**), which can be initial substance for the synthesis of new bioactive derivatives.



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The present report is devoted to summarize results of norfluorocurarine and α-methylenindolenine type alkaloids representatives reduction, the composition of their end-products depends on reaction environment (neutral, acid or alkaline). The structure, stereochemistry and absolute configuration of reduction products were determined by NMP-spectroscopy and X-rays structure analysis [2–5].

It was observed that reduction of norfluorocurarine and α-methylenindolenine type alkaloids depends on medium nature. Indoline derivatives formed in acid and neutral medium, while indole derivatives in the alkaline medium, so this fact is attributed to the alteration of electronic structure of initial alkaloid depending on the environment.

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REACTIVITY, DEUTERIUM EXCHANGE RATE OF THE α-METHYLENE GROUP PROTONS OF DESOXYVASICINONE AND ITS HOMOLOGUES

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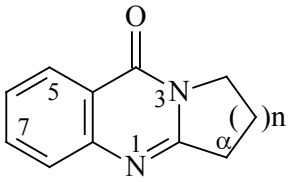
Previously we demonstrated an opportunity of substitution of α-methylene group protons of alkaloids deoxyvasicinone (**1**), mackinazolinone (**2**), which were isolated from plants [1, 2] and their homologues on electrophilic groups [3–5]. At performance of this work the remarkable feature of reaction – the dependence of substitution ability from the size of the polymethylene group of a molecule has been observed. In synthetic homologues - 2,3-penta- (**3**) and 2,3-hexamethylene-3,4-dihydroquinazolin-4-one (**4**) no similar substitution obtained [3]. To clarify the reasons of this phenomenon the availability of α-methylene protons for chemical interactions, more simple chemical transformation – substitution of α-methylene protons by deuterium in series of compounds **1–4** has been investigated:



1 n=1, **2** n=2, **3** n=3, **4** n=4

Deuterium exchange rate of compounds **1–4** was determined in the neutral, alkaline and acid conditions. Good correlation of deuterium exchange rate with results of early researches on electrophylic substitution [3–5] is obtained. In both cases the reaction occurred faster for mackinazolinone **2** and more slowly or even does not occur for **3** and **4**. Reaction rate increases with increase of basicity and acidity of environment. In neutral (CD_3OD) condition it was possible to observe deuterium exchange only for mackinazolinone **2** (a half substitution time is about 1000 hours).

The obtained data concurred with our previous works on interaction of homologues **1–4** with bromine, aromatic, heterocyclic aldehydes and acid chlorides [3].

In this work some possible mechanisms of deuterium exchange and their connection to the structures of desoxyvasicinone and its homologues and environment conditions had been simulated and evaluated.

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ALKYLATION OF PHENOLS BY POLYPRENOLS

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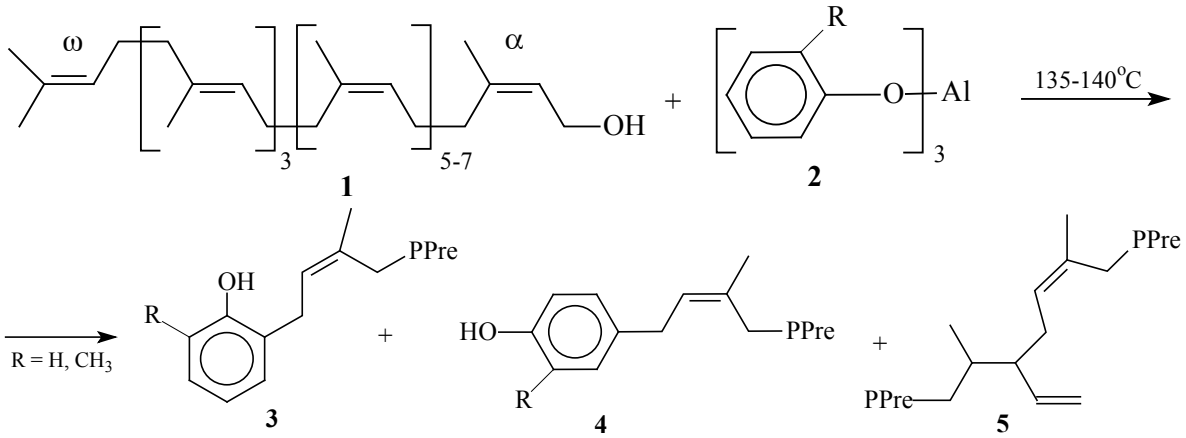
Recently transformations of polyisoprenoid alcohols (PP) are intensively investigated along with other classes of natural compounds [1, 2], which are perspective syntons for obtaining of physiological active substances. Their interaction with cell membrane and less toxicity made them perspective agents for development drug preparations and plant security features. Each of plant is characterized by a set of isoprenoids, which act as individual substances in chemical transformations. Besides, introduction of the substituent to isoprenoid molecule is improving the biological activity. So, study of polyprenols modification in grade leaves attracted the special interest to. They represent by prenols with n = 10–13 and have following homologues content: deca-, undeca-, dodeca- and threedecaprenols 6.9, 36.2, 46.8 and 9.6% correspondently.

We have studied alkylation of phenols by polyprenols C_{50}-C_{60}. Obtained results show, that 2-polyprenolphenols (alkyls) formed as main products.



Share of 4-polyprenylphenols were some times less. It can be note, that along with *para*- and *ortho*-alkylproducts the formation of polymerization of polyprenols is observed.

Structures of obtained products demonstrated by physical-chemical methods: IR-, 1H and ^{13}C NMR, ESI-mass-spectrums.

Results of aromatic compounds alkylation by polyprenols will be discussed and compared in presented work.

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SESQUTERPENS, COUMARINS OF PLANTS OF *Ferula* L. FROM FLORA OF CENTRAL ASIA AND THEIR BIOLOGICAL ACTIVITY

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The Flora of Central Asia is rich with medical plants. There are among them also the plants of *Ferula* genus.

Perennial herbs the *Ferula* L. (*Apiaceae* family), including 150 species, are widely distributed in the world. The Flora of the Central Asia includes about 100 species and is widely used in the folk medicine as anticancer, antimicrobic, various diseases treating and estrogen remedies.

The coumarins, flavonoids and sesquterpenoids were isolated from genus *Ferula*.

The results of chemical studies of *Ferula* species – *Ferula jaeschkeana* Vatke, *Ferula samarcandica*, *Ferula tenuisecta* Eug. Kor, *Ferula kuhistanica* Korov, *Ferula involucrata*, *Ferula feruloides* and *Ferula ovina* from the flora of Central Asia: various chemical compositions at these plants, the structures of isolated compounds (including new compounds) and also their biological activity will be presented in the report.

SUBMERGED CULTIVATION OF A MICROSCOPIC FUNGUS OF THE GENUS *Stachybotrys* AND STUDY ITS CHEMICAL COMPOSITION

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Microscopic fungi are the source of a wide variety of compounds. As a result of fermentative culture development they are used in practice for the preparation of important drugs. The search for new sources of biologically active compounds is an important task, both in terms of practice and from a theoretical point of view. The aim of this study was to develop the culture conditions of the microscopic fungus of the genus *Stachybotrys* and the establishment of secondary compounds of dry mycelium. The starting material was provided by the laboratory of the Institute of Microbiology, Collections of microorganisms of Uzbek Academy of Sciences. Growing fungus cultures was carried out on a synthetic medium of Chapik. To improve the efficiency of the submerged cultivation of the fungus the necessity of carbohydrate diet source was studied. Culturing in medium supplemented with glucose, fructose and sucrose at concentrations of 20 gpl, 30 gpl and 40 gpl shown, that a high yield of wet and dry weight was observed on medium supplemented with sucrose, at 30 gpl the yield was 246, 6 and 6.7 gpl, respectively. The effect of age and the amount of inoculum, introduced to the culture medium, was also studied. Plating spore suspensions ranging from 5 and finishing with 20 daily material shown, that the optimum for biomass yield are 7 to 10 daily; the yield of dry biomass was 8.2 and 7.8 gpl, respectively. The optimal initial concentration of spores was 2×10^7 spores per mL.

For chemical analysis the mycelium was separated from the culture liquid and dried at 60°C. As a result of multiple methanol extraction of dry mycelium (89 g) 40 g of the mixture was obtained. To study the obtained composition HPLC analysis method was developed. This analysis shown the presence of 45 components. Column chromatography of the sample of extractive sum has resulted in several fractions, requiring further re-chromatography. Among the obtained fractions there are the fractions, containing lipids and essential oils, polysaccharide compounds, sterols, and glycosides. The crystal compound, obtained by chromatography, was determined on TLC as β-sitosterol.

HPLC AND LC-MS INVESTIGATION OF CYSTEINE SULFOXIDES AND AMINO ACIDS IN SOME *Allium* SPECIES

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Many important crop plants belong to the genus *Allium* L., which contains more than 700 species worldwide. They occur mainly in the semiarid regions of Europe, North America, North Africa and Asia. Species like garlic (*A. sativum* L.) and onion (*A. cepa* L.) are commonly used since ancient times as a spice and vegetable, and also as a medicinal plant. Onions, their extracts or isolated compounds, are able to modulate mammalian enzyme systems, may cause apoptosis and show antiinflammatory, antioxidant, antimicrobial, antifungal, antithrombotic, antihyperglycemic and antiparasitic properties.

The typical odour of onion is developed as soon as its tissue is damaged, because this damage leads to the release of volatile substances by enzymatic hydrolysis of non-volatile sulphur-containing storage compounds. These flavour precursors in onion are the odorless *S*-alk(en)yl-cysteine sulphoxides, which are typical for the *Allium* genus.

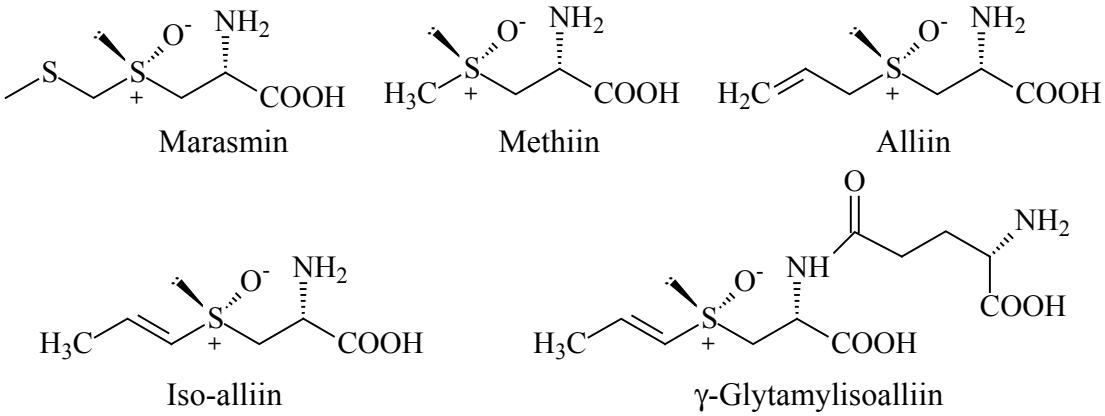
In present study the cysteine sulphoxides and amino acids in some *Allium* species *(A. caspium* ssp. *baissunense* (L), *A. longicuspis* (L), *A. sp. sect.* (L)) investigated qualitatively and quantitatively by HPLC and LC-MS.

The results of the investigation of *Allium caspium* ssp. *baissunense* revealed, that cysteine sulphoxide – marasmin were found 0.32% relatively to fresh weight of the bulbs and were greatest amount of alanine 0.22%, valine 0.12% than other amino acids.

The arginine and alliin exhibited the highest concentrations (2.73 and 2.46% respectively) in *Allium longicuspis*. The amount of glutamic acid, γ-glytamylisoalliin and iso-alliin were found approximate results – 0.416, 0.496 and 0.468% respectively.

In the sample *Allium* sp. *sect.* dominating substances were asparagine, glutamine, and arginine – 0.37, 0.53, 0.81%, respectively.

The amount of cysteine sulphoxides – methiin and alliin in *Allium* sp. *sect***.** were found relatively low concentration – 0.036 and 0.012%, respectively.



The chemical structures of cysteine sulphoxides.

COMPARISON OF DIFFERENT METHODS FOR DNA EXTRACTION FROM SOME HUMAN INFECTIOUS AGENTS

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There are certain requirements to the quality of DNA for successful polymerase chain reaction (PCR). We are presenting an inexpensive and effective method of extracting DNA from some infectious agents, as ureaplasma, mycoplasma, chlamydia, and others.

DNA extraction was evaluated by three methods: Phenol/Chloroform, CTAB and sorbent. The yield of DNA was measured by spectrophotometer.

The average concentration of DNA isolated by CTAB method was 9.62 ng/mL, by sorbent and phenol–chloroform methods was 63.7 ng/mL and above subsequently. It was observed, that sorbent and phenol–chloroform method allows collect high yield of DNA.The modified Boom method for DNA extracting with sorbent proved to be the most efficient, with subsequent PCR analysis.

OLIGOMER PROANTHOCYANIDIN FROM *Rhodiola litvinovii* ROOTS

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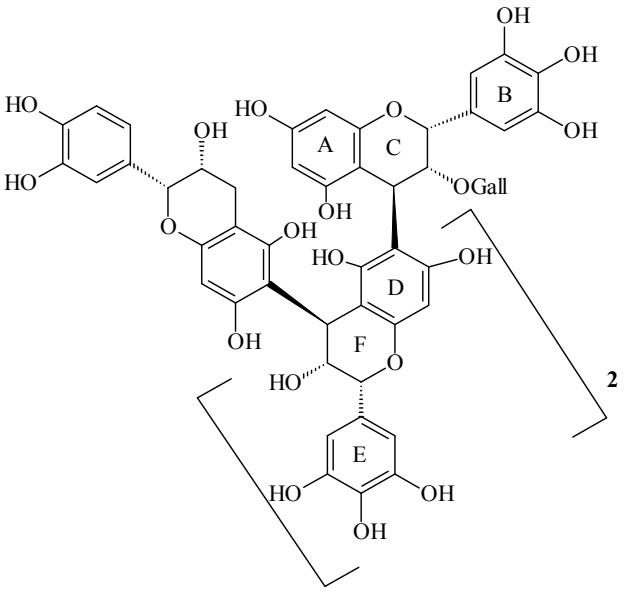
Previously we have isolated and elucidated the structures of a number of phenolic compounds of *Rhodiola litvinovii* (*Crassulaceae*) plant [1].

Continuing our investigations in this direction, we isolated and elucidated the structure of new natural oligomeric proanthocyanidin named litvinocin-A (**1**).

The message is devoted to the structure elucidation of litvinocin-A by the analysis of spectral data: UV-, IR-, ^{13}C NMR spectroscopy and by chemical transformations.

The structure of litvinocin-A was identified as (–)-epigallocatechin-3-*O*-gallat-(4β-6)-[(–)-epigallocatechin]$_2$-(4β-6)-(–)-epicatechin.



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THE STUDY OF THE GASTROPROTECTOR PROPERTY OF PLANT PREPARATION «GLYCYTHRINAT»

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It is known, that problems of gastro–enter disease, especially gastro duodenal ulcerate the present time they completely keep their actuality, as a theoretical and as a practical attitude. In spide of there are majority of antiulcer drugs, they are not to give satisfiaction demand of clinisist often and often. That′s why investigations of new high effective home made drugs, which is be used in this illnesses become actual problem.

In this work we investigated influence three sodium salt of glycerrhizic acid – glycythrinat on the acid and volume of gastro juice.

There were organized studies influence of glycythrinat comparing with omeprazol on acid and volume of gastro juice and on matters of general protein.

Put two series of experiement. On the first series studied influence of glycythrinat on producting function of gastrucs and acidity of gastro juice on rats, with the mass 150–200 g. On the second series studied influence of glycythrinat comparing with omeprazol on acidity gastro juice and synthesis general proteinum coming in components of glycoproteinum. Omeprazol put into with a dose 50 mg/kg, glycythrinat with a dose 100 mg/kg during 6 days. After the last put in the preparations to animals decopetereted, opened gastricus and measured volume of gastro juice. Then measured pH with a help of pH metro. General protein identified with a methods of O. H. Lowry.

The results of investigation show that, in control group of rats so volume of gastro juice contours 2.05 mL, ph = 1.33, common acidity 0.5 mL, titral unity is 100 TU. Under the influence of glycythrinat volume of gastro juice increased till 39%, pH = 3.25, total acidity 0.37 mL, titral unity contained 73 TU.

According to activity preparation pH moves alkaline side with 1.4 times, volume gastro juice increased 51% and general acidity 26%.

Another series of experiment was studied influence of glycythrinat comparing with omeprazol for acidity gastro juice and for synthesis of common proteinum. Gastro mucous membrane consist of glycoprotein, it′s mean part is acidy sialitsy, fructose and protein. Clarifying this compounds gives enough information about mucous membrane condition.

The results of investigation showed that intact group pH is 3.8, total protein contains 0.34 gr/mL. In group which rat get omeprazol notes with move pH into weak acidy side and contains 5.85, total protein is 0.51g/mL. In group of rat which getting glycythrinat also pH moves weak acidity side and contains 5.46, total protein 0.52 g/mL.

Thus new native «Glycythrinat» has antiulcers effect, moves pH acidity of gastro juice into alkaline side, decrease synthesis of general protein. Glycythrinat and omeprazol shows samediricted action for mucous membrane of gastro nd also activeness of Glycythrinat do not yield to omeprazol.

PERSPECTIVES OF THE NATURAL COMPOUNDS APPLICATION IN AGRICULTURE

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The formation and development of the chemistry of natural compounds in our country has a long history. Thus, Avicenna (10^{th} century) was dealing with certain chemical reactions while preparing complex medicines from natural compounds. In "Canon of Medicine" there are a lot of data on the use of fig leaves and fruits against skin diseases, on valuable properties of some parts of barberries and on curative effects of some minerals such as mummy and others.

Currently, inorganic substances such as minerals, ores and salts are also considered as natural compounds, whereas the subject of the chemistry of natural compounds is organic molecules that are present in organs and cells of plants and animals. These compounds have such advantages as initial biological activity and synthetic transformability.

Here we briefly report on modern tendencies in the development of one of the most important parts of the chemistry of natural compounds serving as a fundamental basis of using compounds of plant, animal, microbial and mineral origin in agriculture. There will be discussed the current state and perspectives of this scientific direction mostly in Uzbekistan. The main attention will be paid to the application of natural compounds based on their types (low molecular and macromolecular) and classes: alkaloids, carbohydrates, terpenoids, proteins etc.

Some data will be reported to characterize these compounds and spheres of their practical application in cotton-growing, gardening, poultry, as fertilizers, growth stimulants, fungicides, insectoacaricides, defoliants, herbicides and others.

PEDICINE – A NEW ALKALOID FROM *Haplophyllum pedicellatum*

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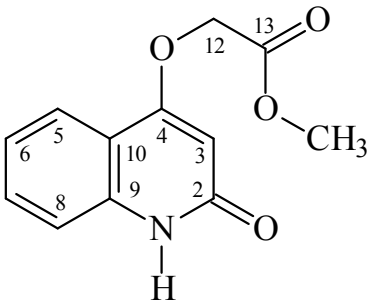
Haplophyllum pedicellatum Bge. (fam. *Rutaceae*) is herbaceous, densely fibrous plant found in Central Asia (Pamir-Altai, Kopendag, Parapamiz), Northern Iran and Northern Afghanistan.

The plant *Haplophyllum pedicellatum* collected from Surkhandarya region of Uzbekistan is interesting by contents of alkaloids. From the aerial parts of the plant we isolated 6 known bases – skimmianine, glycoperine, dictamnine, evoxine, haplophine, perfamine, and a new base (1) with m.p. 221–223°C (acetone), which was named pedicine.

The known alkaloids were identified by comparison with authentic samples. The structure of a new alkaloid pedicine (**1**) was elucidated by study spectral data (^{1}H and ^{13}C NMR spectra), as well as DEPT and HETCOR experiments.

Pedicine (**1**) is a new alkaloid isolated from this plant.



$C_{12}H_{11}NO_4$

1,1-BISPHOSPHONIC CONJUGATES OF URSOLIC, BETULONIC, BETULINIC, FOLIC ACIDS AND TROLOX

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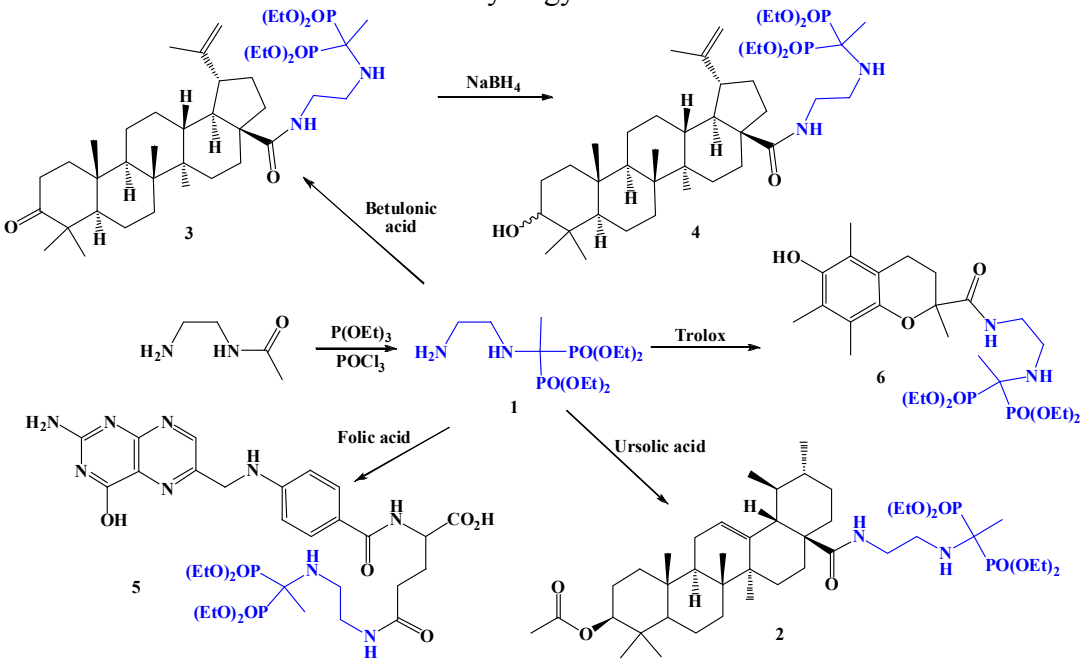
Due to the combination of the unique physical, chemical and biological properties, 1,1-bisphosphonates have become important in different fields of chemistry and medicine. The combination of this properties opens wide possibilities for the design and synthesis of biologically active compounds, that can be used as immunomodulators, agents to treat bone disorders related to calcium metabolism, anti-cancer agents etc [1]. One of the perspective research directions is the synthesis of new conjugates with biologically active compounds and drugs. A convenient method of modifying highly functional compounds is to use an available building block containing reactionary functional group for an easy covalent binding of pharmacologically active molecule with bisphosphonate. Potentially, the synthesized compounds can possess the combination of several necessary properties typical of the substrate and structural block as a result of synergy effect.



Authors have synthesized a new building block – tetraethyl 1-(2-aminoethylamino)ethane-1,1-diyldiphosphonate **1,** and successfully applied it in the synthesis of conjugates with natural biologically active compounds such as Ursolic **2**, Betulonic **3**, Betulinic **4** and Folic acids **5** and Trolox **6**.

Toxicologycal tests on anticancer activity of synthesized conjugates have showed the promising results.

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PHENOLIC COMPOUNDS FROM *Thymelaea microphylla*

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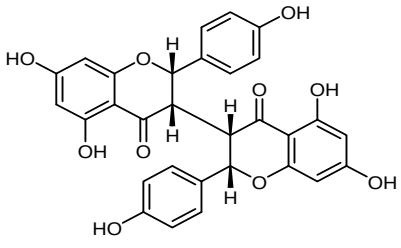
We are interested in the phytochemical study of *Thymelaea microphylla* which belongs to the *Thymelaeaceae* family, and its biological evaluation. Thefamily *Thymelaeaceae* includes about 67 genera and 1200 species. The plants of this family widespread in tropical and temperate zones of the globe particularly in Africa, and are absent in regions with colder climate and are represented in Algeria by the genera *Thymelaea* and *Daphne.*

The *Thymelaeaceae* are considered toxic by their content diterpene esters of the type tigliane or daphnane**.** The genus *Thymelaea* includes 31 spieces and represented in the North of Africa by diziane species. These species including *Thymelaea microphylla* used in traditional medicine of Algeria, have been the subject of various phytochimical studies showing thier richness in secondary metabolites with intersting biological activities such as flavonoïds, biflavonoids, coumarins, bis-coumarins, lignans, and diterpens.

The phytochemical investigation of ethyl acetat extract of the roots of *T. microphylla* led to the isolation and identification of five polyphenol compounds; three biflavonoids, one bicoumarin and one lignan named neochamaejasmin A (**1**) and B (**2**), daphnoretin (**3**), matairisinol (**4**), pinoresinol (**5**), daphnodorin B (**6**), genkwanol A (**7**), tiliroside (**8**), β-sitosterol (**9**) and β-sitosterol glycoside (**10**). The structures of these compounds **1–5** were determined using spectroscopic techniques: ^{13}C NMR and ^{1}H NMR, 2D NMR (COSY, HMBC, HSQC, NOESY), UV and ESI mass spectrometry and the comparaison with the data of literature. In the biological part, we have evaluated the anti-bacterial activity of EtOAc extract of this species. This evaluation was made on three bacterial strains Gram negative *Pseudomonas aeruginosa, Escherichia coli* and *Staphylococcus aureus*, by the diffusion method on agar medium. The obtained results showing strong zones of inhibition indicate that this species could be used as a source of antibacterial activity.



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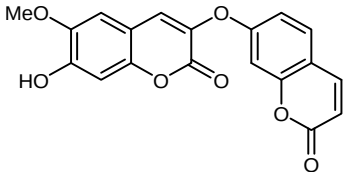

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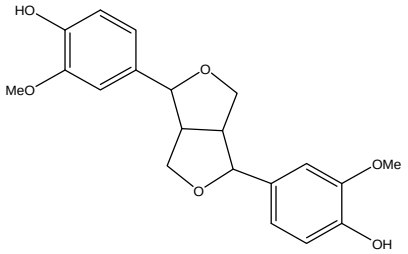

5

MODIFICATION OF CELLULOSE AS A PROMISING DIRECTION IN THE DESIGN OF NEW MATERIALS FOR MEDICINE

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Creation and research of biodegradable biomedical polymeric materials is one of most intensively developing area of chemistry of polymers and medical chemistry.

In this respect, special attention has been drawn to natural biopolymers from renewable feedstocks, such as cellulose, starch, and chitin. Such biopolymers form the basis for biodegradable and biocompatible materials.

Interest to the study of cellulose as a perspective object for creation of new materials is caused its unique properties and availability of raw materials. The high strength, biocompatibility and nontoxicity of cellulose promotes its use for design of materials with different properties for medicine.

In this report primary directions of the chemical modification of cellulose and its derivatives aimed at the design of new functional materials have been summarized. Investigations into the chemical modification of cellulose via nucleophilic substitution, regioselective insertion of functional groups, graft copolymerization, oxidation, and esterification are covered. The importance of studies dealing with the search for new solvents of cellulose aimed at extension of the potential inherent in its modification and processing and in the design of nanocellulose-based materials is emphasized.

It is shown that use of various approaches of the chemical and physical modification of cellulose allows to create medical materials with antibacterial, antimicrobic and antioxidant properties; hemostatic materials; biomaterials for tissue and cell engineering; medical materials with prolonged drug effects; systems for diagnostics and therapy of dangerous diseases.

The huge number of publications devoted to investigations of cellulose-based biomaterials indicates that the interest in this unique natural biopolymer is steadily increasing. The production of a wide range of new promising biomaterials demonstrates its tremendous importance for medicine.

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SYNTHESIS HETEROCYCLIC AND SULFUR-CONTAINING DERIVATIVES OF USNIC ACID

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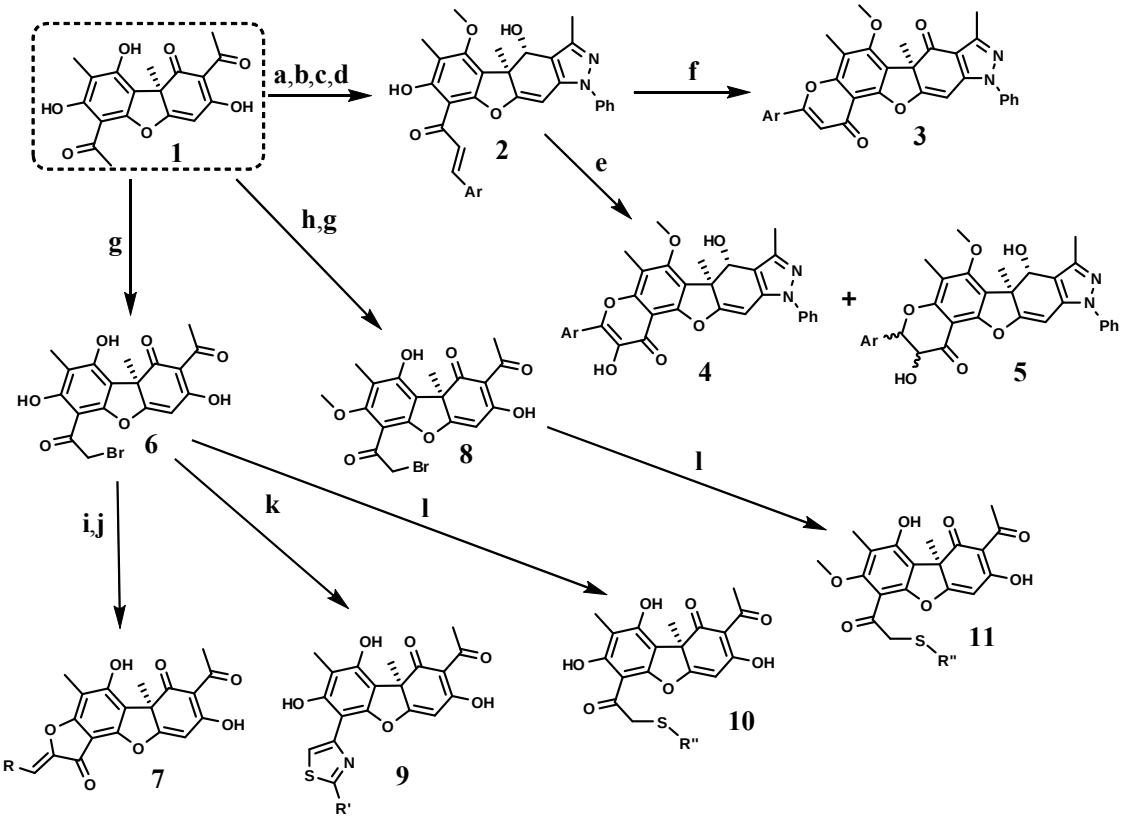
Actual direction of medicinal chemistry is the use of synthetic transformations of plant metabolites, which allows obtaining new effective drugs. Usnic acid (**1**) is a unique and affordable metabolite of lichens. Various species of lichens produce left and dextrorotatory enantiomers of usnic acid with high optical purity. Both enantiomers exhibit notable biological activity. Carrying out chemical transformations of usnic acid may lead to new compounds with outstanding biological activity.

Range of existing derivatives of usnic acid was significantly expanded in present study. New flavones **3**, flavonols **4**, dihydroflavonols **5**, aurone-like compounds **7**, thiazole derivatives **9** and sulfides **10–11** obtained on the basis of usnic acid.



a: $PhNHNH_2$, EtOH, boiling, **b**: $NaBH_4$, THF, –20°C, **c**: CH_2N_2, Et_2O, r.t., **d**: ArCHO, NaOH, MeOH, 60°C, **e**: H_2O_2, NaOH, MeOH, r.t., **f**: DDQ, dioxane, boiling, **g**: Br_2/HBr, dioxane, r.t., **h**: MeI, K_2CO_3, DMF, r.t., **i**: KOH, MeOH, r.t., **j**: RCHO, NaOH, MeOH, **k**: R′C(S)NH_2, EtOH, boiling, **l**: R″SH, KOH, MeOH, r.t.

THE RESULTS OF INVESTIGATIONS OF RUSSIAN FLORA PROMISING PLANTS AND WAYS THEIR USE

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We have investigated the plants genus *Rhodiola* (*Crassulaceae*), *Empetrum* (*Empetraceae*), *Carduus, Centaurea, Saussurea* (*Asteraceae*), *Agrimonia* (*Rosaceae*). In the result of investigations of 20 species of the genus *Rhodiola* it has been developed the drug of psychostimulant action and established the molecular carriers of therapeutic effect. Among them it must be specially noted the phenol alcohols – salidroside and *p*-tyrosol. Rhodiola Extract and *p*-tyrosol have indicated a significant antioxidant activity in combination with anti-stress and anti-metastatic activity. The use of an extract of *Rhodiola* in oncology is promising: having immuno-modulator effect, it reduces the toxicity of cytotoxic drugs and enhances their effect. Allocated flavonolglycosides have found in the experiment expressed antileukemic effect.

The result of deep chemical-pharmacological research was to determine the composition of BAS *Empetrum* and *Carduus crispus*, and a comprehensive study of their anticonvulsant activity. Further research of *Empetrum* as a source of high-active and low-toxic anticonvulsant drugs is very promising.

The actual problem in medicine is parasitic diseases. Our studies have shown that the most promising for practical application is *Populus tremula*, *Centaurea scabiosa* and *C. pseudomaculosa,* extracts of which have anti-opistorhiasis, anti-giardiasis, hepatoprotective and antioxidant effect. However, their chemical composition is very different: if active ingredients of *Populus tremula* are salicylic alcohol glycosides (salicin, tremulacin, salikortin, etc.), the antiparasitic activity of *Centaurea* is due to sesquiterpene lactones (SL) – grosshemine, cynaropicrin, repin. Flavonoids (hyspidulin, apigenin, chrisoaeriol, luteolin, scutellarein), phenolcarboxylic acid (caffeic, ferulic, cinnamic, chlorogenic, *p*-coumaric) and polysaccharide complex with high uronic acids were allocated from the aerial parts of *Centaurea scabiosa*. As a result, we have developed a "centabiosin" for treatment of helminth infestations of the hepatobiliary system.

Of the many species of the genus *Saussurea* the main interest is *S. controversa*, sharply distinguished from other species by their chemical composition (eg, the complete absence of SL), and very low toxicity. Flavonolglycosides series were isolated by means of chromatography, whose structure were established by spectral and chemical as quercetin (Q)-3-*O*-β-*D*-Glc-*O*-α-*L*-Rha, Q-3,5-*O*-Glc-Ara, Q-3,5-*O*-Glc-Xyl, Q-3-*O*-β-*D*-Gal, myricetin (My)-3-*O*-β-*D*-Glc, My-3-*O*-α-*L*-Rha, Ke-3,5,7-*O*-threeGlc. Received findings on the chemical composition and biological effects give the reason to believe that the *S. controversa* is a perspective as an anti-inflammatory, immunomodulatory and regenerating bone tissue (osteomyelitis) remedy. Chemical and pharmacological research of *Agrimonia pillosa* has shown the presence in above-ground parts of the plant 7-*O*-glucosides luteolin (cinaroside), quercetin and apigenin, as well as the ability of extracts to strengthen regenerative processes in the liver. Moreover rhitmomodulate properties of aqueous extract of *A. pillosa* have been revealed that gives the possibility to create the drug of new type.

CHEMICAL COMPOSITION OF THE VOLATILES OF *Ribes biebersteinii* FROM TURKEY

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The currant and gooseberry genus *Ribes* includes about 150 species of deciduous, evergreen, shrubs that grow in the colder and temperate parts of North America, Europe, Asia, and South America. In Flora of Turkey the genus *Ribes* (*Grossulariaceae*) is represented by eight species [1–5].

The volatile metabolites obtained from aerial parts of *Ribes biebersteinii* Berl. ex DC, were analyzed by GC-FID and GC/MS techniques. Plant was collected in August 2008 from Camlihemsin (Rize) region of Turkey. Air dried plant material was subjected to hydrodistillation for 3 h in Clevenger type apparatus to obtain essential oil.

The main constituents detected in the oil of *R. biebersteinii* were found to be as hexadecanoic acid (13.8%), 1-octen-3-ol (13.3%), (*Z*)-3-hexenal (11.6%) and phytol (5.3%).

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INNOVATIVE TECHNOLOGY OF CONIFEROUS WOOD GREENERY PROCESSING

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Perspective direction of use of coniferous wood greenery – a large-capacity logging slash – is its chemical processing for purposes of biologically active compounds isolation.

One of directions of innovative activity of Institute of chemistry of UD KSC of the Russian Academy of Science is creation of technology of plant raw materials processing by new, ecologically safe emulsion way without application of organic solvents. As objects of research the *Abies*, *Picea*, *Pinus* and *Cedar* wood greenery are used.

Investigations are spent in laboratory conditions and on a skilled technological line with use of the rotary extraction devices. Dependences of an output of low-molecular compounds on extraction solvent, the hydro-modulus, temperature, time of raw material processing are studied. Physical and chemical investigations of extractive compounds by chromatographic methods, IR- and a NMR -spectroscopy are carried out. It is found, that emulsion extraction method does not concede to traditional methods of extraction of low-molecular components from plant raw materials and allows isolate effectively as hydrophilic and hydrophobic compounds without use of organic solvents.

Long-term tests confirm the biological activity of extracts in plant-growing and livestock-raising. Pharmacological tests of individual components of the extracts, separate fractions and individual compounds have shown low toxicity of the tested samples.

As a result of our researches the way of obtaining of a complex of natural biological products is developed. The plants growth regulator «Verva» with fungicidal action is create on the bases of *Abies* wood greenery. The natural compounds which are a part of a preparation raise stability of plants to extreme influences of an environment. Operating substance of a preparation are triterpenic acids with lanostane structures which are not present in other coniferous tree species. Fungicide with a wide spectrum of action it is obtained from *Picea* wood greenery. Operating substance of a preparation are natural phenolic compounds.

Physiological researches of coniferous fodder additives for animals and birds are carried out. It is shown the stimulating influence of these fodder additives on animal organism. This fact allows increase efficiency of livestock-raising. For example, industrial tests in the agricultural enterprises have shown, that introduction in diets of milk cows of fodder additives from a *Abies* raises daily yields of milk of milk and renders positive influence on milk fatly.

Work is executed at financial support of the project 12-T-3-1018 of program of basic researches of branch of chemistry and sciences about materials of the Russian Academy of Science “Creation of scientific bases of ecologically safe and resources-economy chemistry-technological processes. Perfecting of processes for obtaining of experimental batches of substances and materials”.

THE COMPOSITION AND BIOLOGICAL ACTIVITY OF ESSENTIAL OILS OF ENDEMIC *Thyme* ssp. FROM FAR EAST

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For the first time the component composition of essential oils of endemic species of *Thymus* from Far East (Russia) was investigated by GC/MS method. Essential oils were obtained by standard method on Clevendger type apparatus by water distillation during 2 hours using pentane as trap.

The GC/MS system consisted of an Agilent 7890A gas chromatograph and an Agilent 5975C mass selective detector. The injections were made with an Agilent 7693 auto-sampler. The system was controlled by ChemStation software (Version E.02). A 30 m × 0.25 mm fused silica capillary GC column coated with a 0.25 мм film of 5% – phenylmethylpolysiloxane (HP-5MS) from J&W Scientific was used for the oil analysis.

Place and date of collection: *Thymus komarovii* – Primorye territory, Partisan district, limestone massif, near the village Ekaterinovka, on 07/02/2012; *Thymus nakhodkensis* – Primorye territory, Nakhodka city, Musatov shore of the bay, on limestone outputs, on 07/09/2012; *Thymus przewalskii* – Primorye territory, Khankaisky district, shore of Lake Hanka, near the village of Turij rig on sand dunes, on 07/06/2012.

Main components of essential oils: *Thymus komarovii* – camphor – 23.8%, caryophyllene oxide – 19.5%, camphene – 8.3%, α-cadinol – 7.%, 7-acetyl-2-hydroxy-2-methyl-5-isopropylbicyclo[4.3.0]nonane – 4.3%; *Thymus nakhodkensis* – camphor – 15.3%, 4-terpineol – 8.7%, caryophyllene – 6.6%, camphene – 6.6%, β-myrcene – 6.3%, β-ocimene – 4.6%, 1,8-cineole – 4.3%, α-pinene – 4.1%, *p*-cymene – 4.1%, *t*-muurolol – 3.5%, and *trans*-sabinene hydrate – 3.1%; *Thymus przewalskii* – camphor – 16.5%, geranyl acetate – 9.8%, camphene – 8,4%, borneol – 7.1%, caryophyllene oxide – 6.8%, geranial – 6.0%, bornyl acetate – 5.0%, *trans*-sabinene hydrate – 5.3%, α-pinene – 4.8%, limonene – 4.6%, *trans*-geraniol – 4.4%, and β-citral – 4.2%.

Biological activity of essential oils: antimicrobial – against *C. albicans*, *C. glabrata*, *C. krusei*, *A. fumigates*, *C. neoformans*, *S. aureus*, *MRS*, *E. coli*, *P. aeruginosa*, *M. intracellulare* microorganisms; antimalarial – against *Plasmodium falciparum* D6 and antileishmanial – against *Leishmania donovani* were investigated.

INVESTIGATION OF CYTOTOXIC ACTIVITY OF SOME ESSENTIAL OILS

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It is known that essential oils have antifungal, antimicrobial, antiviral, anti-inflammatory, anti-tuberculosis, anti-bacterial, and many other types of activity.

We have studied some of the essential oils from Kazakhstan and the Russian Far East on the cytotoxic activity against the larvae of marine crustacean *Artemia salina*.

The results showed that the investigated essential oils of *Artemisia austriaca* Jacq., *Juniperus sabina* L., *Juniperus sibirica* Burgsd., *Salvia stepposa* Des.-Shost., *Peucedanum alsaticum* Linn., *Artemisia terrae-albae* Krash, *Achillea nobilis* L., *Achillea micrantha* Willd., *Libanotis buchtarmensis* (Fish.) DC., *Angelica cincta* N. Boissieu., *Angelica glossorate*, *Angelica viridiflarum*, *Artemisia messersshmidtiana* Bess., *Coclopleurum deltoioleum*, *Dracocephalum argunensis*, *Glehnia littoralis* F. Schmidt., *Heracleum voroschilovii* Gorovoj., *Peucedanum elegans* Kom., *Spuriopimpinella calycina* (Maxim.) Kitag., *Thymus nakhodkensis* Gorovoj., Thymus *przewalskii* Nakai. exhibit acute lethal toxicity, and essential oils of *Ashyrophorus ciliatus*, *Stachys chinensis* Bunge ex Benth. don′t exhibit neurotoxicity.

Thus, the evaluation of cytotoxic activity of essential oils leads to the conclusion about strong activity of many essential oils against larvae of marine crustaceans *Artemia salina*.

EFFECT OF HIGH-ALTITUDE GRADIENT ON VARIABILITY OF COMPONENT OF ESSENTIAL OILS IN NATURAL POPULATIONS OF *Mentha longifollia* L. (HUDS) FLORA DAGESTAN

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Mentha longifolia (L.) Huds.) – perennial plant species in the genus *Mentha* family *Lamiaceae*, spread across the world, is found along the banks of rivers, ditches, lakes and marshes. There are 25 species and 100 subspecies of *Mentha*. In Dagestan meets two types: *Mentha longifolia* L. (Huds.) and *Mentha aquatica* L.

Mentha – one of the most important medicinal, aromatic plants. The most valuable is essential oil, which is widely used in food, perfume and cosmetic industry, in aromatherapy. The quality of essential oil of *Mentha* determined by the composition of components, among which the most important for medicine is menthol. Pharmacological properties of plants associated with choleretic, diuretic, hemostatic, sedative, anticonvulsant and diaphoretic actions.

For the first time in Dagestan study the effect of altitude on the raw material collection site variability of secondary metabolites in medicinal raw material *M. longifolia*.To study the variability in the content and composition of essential oil in 2006 during flowering were collected raw material from 8 natural populations of Dagestan from 1000 to 2450 m above sea level. Raw material is divided into fractions and dried to air-dry weight. The content of essential oil was obtained by method of parodistillyatsii. The analysis of the quantitative and qualitative composition of the essential oil of *M. longifolia* was carried out by gas chromatography-mass spectrometry.

Thus, according to the results it is clear that most of the essential oil deposited in the leaves and inflorescences. According to our data, the essential oil in the plant material *M. longifolia* ranges from 0.4% to 1.18%, is a free-flowing liquid of light yellow color, with pleasant characteristic odor. The production of essential oil plants, and oil composition depend on the genotype grade, age, and long-line position of leaves, growing conditions, the phases of growth. According to our data, the content of essential oil (in leaves and inflorescences) is not associated with height above sea level gathering place of raw materials. A higher accumulation of essential oils found in raw materials, assembled from more arid habitats.

In the samples studied were found mono-, sesqui- and diterpenes. The basic components of the essential oil of the studied samples are: pulegone (1.03–53.0%), menthone (0.5–70.5%), linalool (0.16–67.9%), eucalyptol (0.7–10.3%), terpinen-4-ol (0.0–33.6%), carvone-isomer (0.0–27.3%). Height above sea level seats of gathering in general affects the content of the individual components. For example, the content of menthone increases with height, and the content of pulegone seat height collection of raw materials had no significant influence.

CHARACTERIZATION OF LIPID COMPOSITION OF BOREAL CORALS AND COMPARISON OF THEM WITH TROPICAL CORALS

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Lipids form up to 40% of coral dry biomass and involved in a majority of biochemical and physiological processes in corals. Fatty acids (FA) as the main constituents of lipids are most probably indicative of external food sources, the composition of symbionts and associated organisms, and are applied for coral chemotaxonomy.

Zooxanthellae strongly influence on a proportion between reserved and structural lipid classes in tropical coral tissues. In nature, zooxanthellae can not live at water temperature lower than 12°C. Thus, no zooxanthellae present in the cold-water soft coral species studied. The autotrophic mode of feeding isn′t exist in these corals and all energy requirements coved by using of heterotrophic feeding only.

To determine the features of the lipid composition of coral and hydrocorals inhabited in North Pacific cold waters, eleven soft coral species and five hydrocoral species from the Okhotsk Sea were studied in comparison with tropical species from the South China Sea. These tropical specimens comprised reef-building corals, zooxanthellate and azooxanthellate soft corals. A variety of lipid classes (polar lipids (PL), sterols (ST), free fatty acids (FFA), triacylglycerols (TG), monoalkyldiacylglycerols (MADAG), and wax esters (WE) were presented in total lipids of all cold-water species studied.

Our study showed that lipid class composition of cold-water corals strongly differ from that of tropical zooxanthellate corals because of the absence of the symbionts, but there are no significant differences in lipid class composition of all azooxanthellate soft corals irrespective of environment conditions. At the same time, lipid class composition of azooxanthellate cold-water corals, which inhabit on the large depth (up to 400 m) and have no phototrophic food sources, strongly differed from that of tropical zooxanthellate corals. On the contrary, FA composition of the cold-water coral species strongly differed from that of tropical azooxanthellate soft corals. The most contribution to this difference were made by PUFA of n-6 and n-3 series, which were biomarkers of phyto- and zooplankton – important food source of corals. Probably, differences of plankton species composition from cold and warm waters with different FA compositions lead to the changes of FA profiles of azooxanthellate soft corals. The low content of 20:4n-6 in Primnoidae in comparison with other cold-water coral families indicate the increasing of phytoplankton portion in Primnoidae nutrition. High level of PUFA in both cold-water and tropical soft corals does not come to an agreement with the hypothesis about increasing of PUFA content in cold-water animals. Thus, lipid and their FA composition are useful indicators of the influence of environment conditions on biochemical diversity of North Pacific cnidarians and depend on their taxonomic position, nutrition, environment, and presence of symbionts.

BIOACTIVE METABOLITES FROM THE ALGAE-DERIVED FUNGI *Penicillium* GENERA

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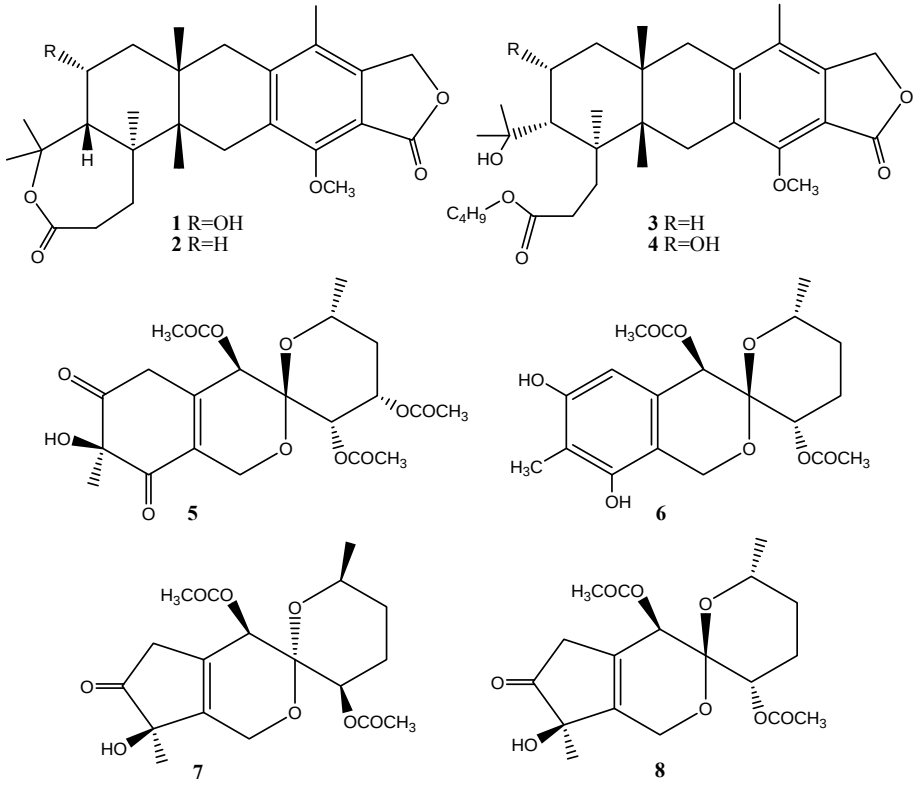
In our search for secondary metabolites from fungi with cytotoxity and/or novel chemical structure we have investigated two strains *Penicillium thomii* Maire and *Penicillium lividum* Westling obtained from the marine brown alga *Sargassum miyabei*.

From the mycelium of fungi we have isolated four new meroterpenoids (**1–4**), four new spiroketals (**5–8**) together with known austalide J, peneciraistin C and daldinin D. Their structures were determined by 2D NMR, MS and CD spectroscopy.

Cytotoxic activity of all obtained compounds was studied with respect to several tumor cell lines using MTS-reagent. The effect of some compounds on the oncogenic transcriptional factor AP-1 was studied as well using transfected mouse epithelial JB6 Cl41 cells.



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NOVELTY IN CHEMISTRY OF PLANT SESQUITERPENE LACTONES

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Search of sesquiterpene lactones in plants, their using at chemical modification and for molecules′ transformation as renewed material are attracted big attention of researchers.

At JSC "International research and production holding "Phytochemistry" in search of new sesquiterpene lactones was investigated a number of endemic species. As perspective sources of sesquiterpene lactones by results of the chemical screening of plant samples were determined some agents of *Artemisia*, *Cousinia*, *Jurinea*, *Centaurea* and *Tanacetopsis* genera of *Asteraceae* family.

A new sesquiterpene lactone 3-oxo-10β-hydroxy-5α,7α,6β(*H*)-guai-1(2),11(13)-dien-12,6-olide was isolated from *Tanacetopsis pjataevae* (Kovalevsk.) Karmyscheva. For the first time from *Centaurea iberica* Trevir. ex Spreng was isolated and identified sesquiterpene lactone cnicin, from *Picris rigida* Ledeb. – jacquinelin, from *Artemisia porrecta* Krasch. ex Poljakov and *Artemisia karatavica* Krasch. et Abol ex Poljak – herbolide A. Structure of isolated compounds was determined on the basis of the physical and chemical constants, data of element analysis, IR-, UV-, mass-, NMR ^{1}H, ^{13}C spectra, two-dimensional spectroscopy of NMR ^{1}H–^{1}H, ^{13}C–^{1}H (COSY, COLOC) and X-ray analysis.

The quantum-chemical calculations of argolide and arglabin molecules for their directed chemical modification were made by method HF/6-31G//PM6.

Twelve new compounds were synthesized on a basis of sesquiterpene lactones arglabin, tourneforin, argolide, ludartin. The optimum conditions were defined for cross-combination reaction of sesquiterpene lactones argolide and tourneforin with aryl halides to obtain new 7 derivatives. Correlation of arglabin and ludartin with tetrahydroborate sodium in methanol leads to new methoxyderivatives. As a result of reaction of ludartin with acetonitrile in the presence of sulfuric acid were obtained 3 derivatives, one of them was a new compound, having 3α-hydroxy,4β-acetoxy-5,7α,6β(*H*)-guai-1(10),11(13)-dien-12,6-olide structure.

The isolated sesquiterpene lactones and their modified derivatives were studied on antimicrobic, cytotoxic, antivirus, phagocytic, antibacteriophage and analgetic activities.

MECHANOCHEMICAL AND MICROWAVE EXTRACTION – ADVANCED PROCEDURES OF ALKALOIDS ISOLATION

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Natural products from medicinal plants are known to be the basis for many medicinal remedies. Routine technology of their isolation is extraction. This method is time-consuming, laborious, solvents-wasting and therefore is environmentally unsafe. Other techniques such as ultrasonic, mechanochemical and microwave-assisted extraction processes have also become of interest as alternatives for the conventional methods.

Our research has been focused on the application of green extraction techniques for the isolation of alkaloids from plant material. We applied an effective and environmentally safe mode of alkaloids isolation from medicinal plants using a mechanochemical approach. This approach was realized through the mechanical treatment of plant raw material and solid absorbents in a special ball mill, where the natural products effectively interact with the solid substances. In our experiments we used RETSCH planetary Ball Mill PM 100 with zirconium oxide balls and grinding jars. This mill is equipped with graphical menu guidance and suitable for scientific research, where the quality control process places the highest demands on purity, speed, fineness and reproducibility. The influence of sorbent addition (their nature and quantity) on the yield of alkaloids from *Aconitum septentrionale* roots and *Sophora flavescens* roots was studied. The influence on alkaloid yield of polar properties of solvent used for desorption was studied as well. The natural alkaloids were obtained with higher yield as compared with usual extraction and in some cases with higher selectivity.

We have successfully applied microwave-assisted extraction to isolation of quinolizidine alkaloids from *Sofora flavescens* roots using the Single-Mode Microwave reactor Discover S-Class, equipped with temperature, pressure and power control system and CEM Multi-Mode Microwave Reactor “MARS Xpress™ System”. We have studied the influence of power level, temperature and time on the yield of alkaloids. The extractions were carried out for 10–20 minutes using ethanol as a solvent with higher yield. The advantages of microwave-assisted extraction are: high efficiency, short time, low energy consumption and low environmental pollution.

STRUCTURE OF CYCLOASCIDOSIDE E FROM *Astragalus mucidus*

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The novel cycloartane glycoside, 3-*O*-β-*D*-xylopyranoside, 6,25-di-*O*-β-*D*-glucopyranoside-24*R*-cycloartane-3β,6α,16β,24,25-pentaol named as cycloascidoside E (**1**) was isolated from above the ground part of *Astragalus mucidus* Bunge. The structure of the glycoside was established by ^{1}H and ^{13}C NMR spectroscopy and chemical methods.

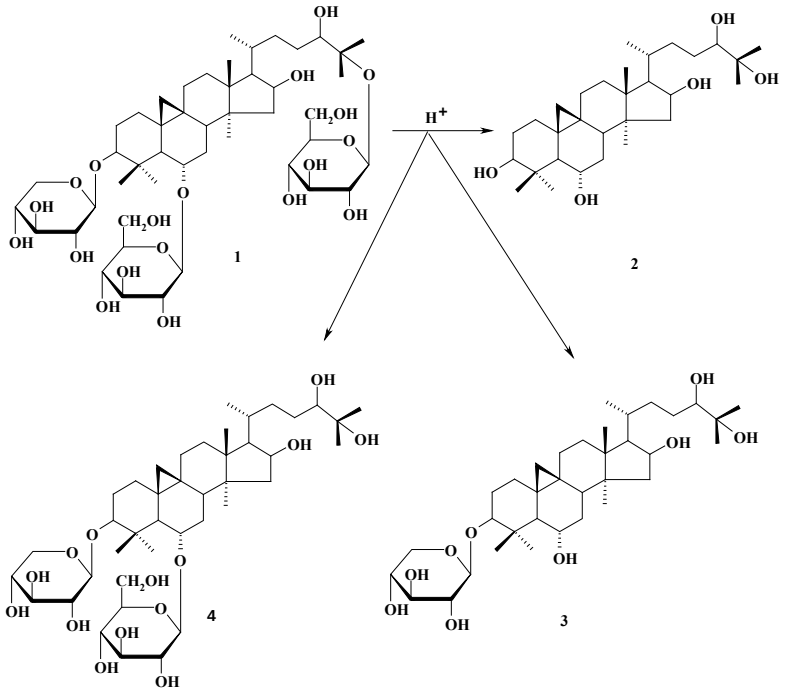
Glycoside **1** was subjected to partial hydrolysis. Beside cycloasgenin C **2**, from hydrolysate progenines **3** and **4** were isolated.

By physical and chemical constants, spectral data and by TLC comparison with known samples monoside **3** was identified with 3-*O*-β-*D*-xylopyranoside of cycloasgenine C. Bioside **4** was identified with cycloascidoside A. Aglycon moiety of the glycoside **1** was identified with cycloasgenine C.

By paper chromatography of the carbohydrate part after acidic hydrolysis *D*-glucopyranoside and *D*-xylopyranoside were found.

The anomeric protons of the sugar moieties of novel glycoside **1** in the ^{1}H NMR spectra at δ 4.71 (H-1 of β-*D*-xylopyranose), δ 4.81 (H-1 of β-*D*-glycopyranose) and δ 5.08 (H-1 of β-*D*-glycopyranose) (d, $^{3}J = 7.6$, $^{3}J = 7.5$ and $^{3}J = 7.8$ Hz appropriately).

Thus, the structure of glycoside **1** isolated from above the ground part of *Astragalus mucidus* Bunge was established as 3-*O*-β-*D*-xylopyranoside, 6,25-di-*O*-β-*D*-glucopyranoside of cycloasgenine C.



METHOD FOR INHIBITION OF ENZYMES OF THE GERMINAL PRODUCT FOR USAGE IN STRUCTURE OF FAT-FLOUR COMPOSITIONS

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One of main causes of spoilage of germinal product of wheat during the storage is activity of lipase and lipoxygenase enzymes limited the possibility of its usage in fat-flour composite mixtures.

The dynamics of lipid substances oxidation in fat-flour compositions of emulsion nature containing up to 20% of the germinal product to raw materials total on a compounding is investigated. A fat-flour composition prepared by mixing of prescription margarine components «My dream» for a baking (RC 64-00392738-02-2004) with thin dispersed germinal product (TDGP), subjected only for crushing (experiment 1) and heat treatment with the subsequent crushing (experiment 2). Heat treatment was spent at temperature 100… 105°C during 20… 30 min. Further a product samples were crushed to coarseness of dietary flour (a descent from a sieve No. 27 not more than 2%, sieve pass No. 38 – not less than 60%) and used in quality prescribed component at preparation of fat-flour composite mixture. The composition without additives was used as the control.

In research the germinal product with humidity of 8.4% and the maintenance of lipids 9.8% containing in its composition to 70% of polyunsaturated fat acids is used.

In the sample with TDGP without heat treatment after a period of storage the acid number has increased on the average by 10.5 mg the KOH/g, in the control and the sample with TDGP after heat treatment of the given indicator have raised, on 1.1 and 1.5 mg the KOH/g accordingly in comparison with the initial data. The increase of peroxide numbers of products, accordingly, in 7.0 and 1.6 times in samples with TDGP without and after heat treatment is established at control value in 1.5 times, as processes of hydrolysis and fat oxidation are interconnected. Thus, it is necessary to note absence of correlation dependence between accumulation of acids and increase in concentration of ions H^+.

The above-stated confirms the assumption of expediency of thermal processing of a germinal product in a mode offered by us. It will allow not only to lower enzymatic action of lipase and lipoxygenase, but also to raise degree of its microbiological cleanliness for the purpose of maintenance of food harmlessness both the product, and the products prepared with its use (as even for extreme thermophiles, found out among prokaryote and developing at temperatures above 70°C, the maximum temperature of growth lies in limits from 80 to 90°C), to enrich with their food and minor biologically active substances, on 100% to use botanical oil content of germs**.**

CHEMISTRY AND TECHNOLOGY FOR PRODUCTION OF THE HIGHER NUTRITIONAL VALUE PRODUCTS FROM LOCAL PLANT RAW MATERIALS

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In the conditions of market economy the requirements of the population to the quality and the range of fat-and-oil products arisen: vegetable oils, margarine and mayonnaise with the raised quality indicators and physical and chemical characteristics.

In this regard the performance of research works and practical development in the direction of improvement of quality and expansion of the range of fat-and-oil products (vegetable oil, margarine, mayonnaise) are actual and important in the long term developments of oil and fat branch of Uzbekistan. It allows arrange the production of fat-and-oil products conforming to modern requirements of the world market and market economy.

It should be noted, that the most defining factors of an assessment and application of food additives and flavoring substances in fat-and-oil products are features of their chemical structure and an arrangement of chemical compounds in a molecule. These characteristics of additives and substances allowed classify them on the separate types promoting change of quality, power ability and a nutrition value of cotton oil, margarine production and mayonnaise. Taking into account improvement of quality, expansion of the range, formations of physical and chemical indicators and consumer advantages of fat-and-oil products are developed the scientific principles of selection of food additives and flavoring substances, their quantitative contents and a ratio in a component structure of margarine production and mayonnaise is established. The most acceptable dosages of additives and substances are established within 0.05...9.0%. New component compositions of the refined deodorized cotton oil, margarine production and mayonnaise which allowed to expand the range of fat-and-oil products are offered and to increase its quality according to requirements of modern market economy. Necessary power and nutrition value of made production is provided. Regularities of dependence of quality and nutrition value of margarine production from the contents and ratio of making fatty components, food additives and flavoring substances are studied. It is established, that the defining factors are the maintenance of firm and liquid fractions of fats, their temperature of melting and hardness, and also the low contents in used firm fatty products of trans-isomers and saturated fatty acids in triglycerides. On the basis of dilatometric characteristics of margarine production studying, rationing of the maintenance of firm and liquid fatty bases ensuring resistant hardness of margarine and their long safety is reached at various temperature modes. Dependence of coefficients of refraction, temperature of melting and hardness of margarine production is defined. It is established that temperature increase of melting and increase in hardness of margarine lead to decrease in an indicator of their refraction. Industrial production of margarine of the new range with high organoleptic rates and the physical and chemical characteristics regulated by standard and technological documentation existing in world practice is arranged. The range of mayonnaise with use of effective food additives and flavoring substances is expanded, quantitative value and a ratio of making components of production, providing increase of a nutrition value of end products is established. Balancing of component and fatty acids structure of mayonnaise with the raised quality indicators and physical and chemical characteristics is reached. Necessary indicators of hygienic requirements of made fat-and-oil products are provided, high food safety of the refined deodorized cotton oil, margarine production and mayonnaise according to requirements of market economy is reached. Using methods of optimization of component composition, power ability and a nutrition value of fat-and-oil products in industrial practice the serial production of the flavored cotton oil, margarine production and mayonnaise of the new range is carried out. Necessary standard and technological documentation is approve, certificates of quality and hygienic compliances are received. In work practice the economic effect over 2 billion sums annually reached. Results of scientific and theoretical researches allowed expand and add theoretical and practical ideas of improvement of quality and expansion of the range of fat-and-oil products using food additives and flavoring substances of new generation. Scientific bases of ensuring quality and nutrition value of fat-and-oil products are formulated.

Agrobacterium MEDIATED COTTON TISSUE TRANSFORMATION WITH SynB RNAi VECTOR

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Phytochromes are gene family which regulate light perception and influence expression of other genes. They are considered as photoreceptors of red and far-red light, playing an important role in plant life.

The goal of the work was to obtain transgenic plants with somatic embryogenesis functions by knocking out of Phytochrome B (PHYB) gene using RNAi technology, and check its expression in cotton. Synthetic gene cassettes of PHYB were created and transformed into *Arabidopsis thaliana.* The main objects of the investigation were Coker-312 (*Gossypium hirsutum* L.) cotton genotype, Agrobacterium strain LBA 4404 (*Agrobacterium tumefaciens*) and Synthetic B (SynB) RNAi vector.

We have isolated genomic DNA from cotton leaves and run PCR reaction with the 35S-F (forward), 35S-R (reverse) primer pairs for confirming the SynB RNAi vector transformation into cotton genome.

To observe the phenotypic changes in the generation of SynB_T0, the seeds were planted as a T1 generation in a greenhouse together with control plants. The preliminary results show that the generation of Synthetic B_T1 plant have more developed bush, root system and mature earlier than controls.

At present, the next generations of SynB plants are in the process of development.

PURIFICATION OF HIGHLY POLAR ALKALOIDS AND THEIR BIOACTIVITY

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Alkaloids from plant comprise 15.6% of the known natural compounds and constitute almost 50% of the plant-derived natural compounds of pharmaceutical and biological significance. Alkaloids purification will finally foster the understanding of their bioactivity and improve the new drug discovery. However, the separation of alkaloids is not easy. Firstly, alkaloids present at low levels (about 1–2%) and co-exist with non-alkaloids in plants. Secondly, asymmetric peak of alkaloid usually limits alkaloid separation, since it results in broader peak with low response and poor resolution to adjacent peaks. Thirdly, there are only a few of available multi-dimensional methods for alkaloid purification. Finally, it is lack of the method for highly polar alkaloid purification.

A non-aqueous solid phase extraction method was developed for alkaloid enrichment. High recovery and selectivity of this method were obtained. Alkaloids extracted by high concentration organic solvent can be enriched by this method directly. This method can be used as the pre-treatment method for alkaloid analysis and purification.

To improve the peak shape of alkaloid and the retention of highly polar alkaloid, our group developed a serial of novel separation materials, such as C18HCE, C8PN, C8SAX, Click TE-Cys and SCX. Using these materials, three kind of two-dimensional liquid chromatography systems were established, such as RP-HILIC, RP-RP and RP-SCX. All these systems can provide high selectivity and symmetric peak shape for alkaloids.

S. tangutica Maxim is one kind of famous herb in China. The non-aqueous SPE method was used for alkaloids enrichment from this herb. Then, the alkaloids were purified by the multi-dimensional systems, C18HCE/C8PN and C18HCE/SCX. As a result, more than 100 alkaloids were obtained from these fractions. Recently, 15 alkaloids were identified by NMR, UV, IR, HRMS, CD and optical rotation. Among these alkaloids, 9 alkaloids were novel and 2 alkaloids were acquired from this herb for the first time. Bioactivities for these 15 alkaloids were evaluated with GPCR models. 9 alkaloids have the antagonist activity on M1 receptor. 1 alkaloid has the agonist activity on the μ-opioid receptor. In addition, bioactivities for 4 alkaloids were evaluated on human COMT and all of them have antagonist activities.

ANTIPARASITIC ACTIVITY OF EXTRACTS FROM SOME MEDICINAL PLANTS OF UZBEKISTAN

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Resistance of parasites to conventional synthetic antiparasitic preparations is increasing, furthermore these preparations possess a number of side effects. It would be very beneficial to use in therapy of parasitic diseases the preparations with not only etiotropic properties, but influencing on some pathogenetic aspects of parasitic diseases. So, search of remedies, efficient on parasites clinical forms, that are resistant to the conventional preparations, without negative influence on intestinal microflora and normalizing changes, induced by parasites, is of great importance. As a rule, combination of various types of biologic activity and minimal side effects is attributed to preparations of plant origin.

We studied the summary extractive preparations, isolated from a number of endemic medicinal plants. We presented the results of antiparasitic activity investigation of extracts from *Ferula assa-foetida*, *Ajuga turkestanica* and *Astragalus orbiculatus* against parasites wide-spread in Uzbekistan: *Hymenolepis nana*, *Enterobius vermicularis*, *Giardia lamblia*. White outbred mice with 18–20 g mass were used in the experiments. Antihelmintic activity was studied on the experimental model of hymenolepiasis (every animal was infested with 200 invasive eggs of *Hymenolepis nana*) and enterobiasis (infestation of every animal with 100 invasive eggs of *Aspiculuris tetraptera* (aspiculuriasis of mice is an adequate model of enterobiasis). Experimental model of giardiasis was also used. Animals were infected *per os* with 0.3–0.5 mL of suspension, containing cysts and trophozoites of *Giardia muris* (5–12 Protozoa in a field of vision). Reference preparation was "Antihelminth" (*Tanacetum Vulgare* L., *Cassia Acutifolia* Del., *Inula Helenium* L.), produced by LLC «Biomardon-Pharma», Uzbekistan.

Determination of intense-efficiency (IE) showed, that extracts of *Ferula assa-foetida* and *Astragalus orbiculatus* possess by the expressed anticestode effect (98 and 84%, respectively) and less expressed antinematode one (61 and 74%, respectively). Extract from *Ajuga turkestanica* weally affected on the viability of Cestodes and Nematodes: IE were 51.8% and 46.4% respectively. The extracts demonstrated the high antiprotozoan activity, IE of the extracts in 10-day administration accounted for 98.0 and 99.3%. Extract of *Astragalus orbiculatus* showed a significantly weaker antigiardial activity, IE was 37.6%. Analysis of the results showed, that antiparasitic activity of the extracts is comparable with activity of the known preparation "Antihelminth".

Thus, the extracts of *Ferula assa-foetida*, *Ajuga turkestanica* and *Astragalus orbiculatus* can be considered as a basis for the development of natural antiparasitic remedies.

COMPOSITION WITH ANTI-STRESS ACTION FROM EXTRACT OF THE TOMATO FRUITS AND PLANT PHOSPHOLIPIDS

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The stress is a prime cause of chronic exhaustion, adynamy, neuroses, cardio-vascular diseases, formation of ulcers in a gastrointestinal tract, violations of brain blood circulation, immunity decrease, allergy, obesity that leads to decrease in quality of life. It is known, that many pharmacological substances (energizer, nootrop, adaptogen) increase organism resistance to stress. The aim of this research was studying of influence of composition from extract of tomato fruits and plant phospholipids at single preventive introduction in a dose of 2.5 mg/kg (in terms of extract of tomato fruits) on development of sharp stress reaction in white mice (males, weight 18–20 g). Stress was caused by a psycho-emotional pressure estimated after 18-hour suspension of animals for a cervical skin fold. Stress-reaction owing to excessive muscular tension stated after long (within 4 hours) compulsory swimming. Then mice were euthanized in accordance with international principles of the European Convention for the Protection of Animals. An anti-stress action investigated substance was judged by the change in mass of the thymus gland, adrenal glands, spleen, heart and liver. In liver glycogen content, nitrogen oxide, and cholesterol, as well as the catalase activity were determined. It was founded, that a single administration of the studied compositions impede reduction of spleen and adrenal mass increase observed during stress, to a lesser extent thymus weight affecting the heart and liver. This composition manifested glycogen-saving effect in a liver, prevent the development of anaerobiosis. Under the influence of studied composition on the liver activity of enzyme of antioxidant protection of a cell of a catalase also increased.

The content of nitric oxide increasing and the amount of total cholesterol decreased. In experiment on compulsory swimming the same tendencies took place: in a similar way introduction of studied composition interfered with reduction of weight of a spleen and increase in weight of the adrenal glands, observed in control, raised the maintenance of a glycogen (both in a liver, and in a muscle) and activity of a catalase. It should be noted that in the group receiving composition from extract of fruits of a tomato and plant phospholipids all mice sustained 4-hour compulsory swimming whereas in control group of such animals there were only 40%.

The obtained data allow to draw a conclusion on ability of composition from extract of fruits of a tomato and plant phospholipids to render a stress-protective action at the animals being in adverse physical conditions.

EXPERIMENTAL EVALUATION OF THE EFFICIENCY OF DISTURBED MYOCARDIAL METABOLISM PHARMCORRECTION BY CYCLOARTANS

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The basis of most cardiovascular diseases is the pathological changes of myocardial metabolism, leading to the development of its electrophysiological and functional dysfunctions. Therefore, the necessary components of pharmacotherapy should be agents capable of stabilizing the metabolic processes that optimize the formation and consumption of energy, as well as normalizing the balance between the intensity of free radical oxidation and antioxidant protection. In this respect, Institute of Chemistry of Plant Substances carried out an extensive research on the exploration and development of cardioprotective means based on different classes of compounds isolated from domestic raw materials. As part of this work the comparative studies of 20 cycloarthane glycosides isolated from the local species of *Astragalus* carried out. Experiments were conducted on mice, rats and rabbits, and compounds were administered orally at a dose 10 mg/kg.

The results of screening studies have shown high effective compounds among the studied methylsteroids. Cycloorbycoside G isolated from *Astragalus orbiculatus* and cyclosiversiosides A and F isolated from *Astragalus pterocephalus,* displayed the most pronounced corrective activity in these experiments. Administration of these compounds to intact animals resulted in the increasing of glycogen and adenine nucleotides in cardiac muscle, greater than for inosine (riboxin – LecT, manufacturer OJSC "Tumen Chemical-Pharmaceutical Factory"). Positive action of cycloartane glycosides on the content of energetic metabolites in the heart muscle of rats under different experimental myocardium pathology (experimental myocarditis, immobilization stress, atherosclerosis), which were accompanied by energy deficiency, suppression of aerobiosis, activation of lipid peroxidation, antioxidant system depression not only persisted, but also manifested itself in an even more pronounced degree. Therapeutic-prophylactic and therapeutic administration of the tested cycloartane glycosides in contrast to the etalon drugs – riboxin and mildronate (JSC «Grindeks», Latvia) approximately equally improved the myocardium energy processes state, blocked processes of free radical oxidation, stimulated endogenous antioxidant system, had a regulatory impact on the NO-ergic system, normalize lipid metabolism in the heart muscle. It should be noted, that cycloorbicoside G and cyclosiversiosides A and F, generally exerted a similar effect on the state of the metabolic processes in cardiomyocytes, as riboxin and mildronate, were comparable in their activity.

Thus, cycloartane glycosides – cycloorbicoside G and cyclosiversiosides A and F exerted a beneficial effect on myocardial energy metabolism, especially under pathological condition. The presence of expressed antioxidant activity, inhibiting the processes of lipid peroxidation and stabilizing the NO-ergic system in cycloartane glycosides make these compounds as a promising class of cardioprotective agents for the normalization of pathological changes in the cardiomyocytes metabolism.

EXPERIMENTAL AND CLINICAL EVALUATION OF DRUGS AND SUPPLEMENTS DEVELOPED ON THE BASIS OF PHYTOECDYSTEROIDS AS REMEDIES NORMALIZING THE IMPAIRED METABOLISM IN ORGANISM

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Phytoecdysteroids are a relatively large class of natural substances, attracting increasing attention due to the fact of the development on their basis of efficient and nontoxic drugs and dietary supplements with metabolic-tonic type of action. So, drugs ecdysten, ajustan and supplements ecdysten plus, exumide and substance for manufacturing of skins care products – jistenine developed in Institute on the basis phytoecdysteroids ecdysterone, turkesterone, cyasterone isolated from *Rhaponticum carthamoides, Silene brahuica, Ajuga turkestanica*, find a wide application in clinical and sports medicine, as well as in cosmetics. Their therapeutic and preventive and curative (for dietary supplements) action is most clearly manifested in many states, associated with weakening of the metabolic (primarily protein synthesis) processes in organs and tissues accompanied by a decrease in physical and mental performance, neuroses, fatigue, deterioration of recovery after submaxiamal and maximal burdens, degenerative changes in cover tissues. Ecdysteroid-containing preparations, especially Ecdysten, are very effective in the practice of medical and biological correction of sport activities in those cases, where is necessary to improve speed and strength of athletes. In intensity of stimulating action they are superior to pharmacological non-doping herbal drugs, that are widely used in the sports and medical practice as actoprotective remedies: Ginseng Extract, Saparal, Tribestan. Ecdysteroid-containing drugs and dietary supplements facilitate the learning process, have a stress-protective effect, stimulate erythropoiesis and immunogenesis, activate regenerative processes (especially when they are integrated with the application of flavonoids and polyprenols, substances with strong antioxidant effect). An important aspect of the biological action of ecdysteroid-containing drugs is increasing of organism resistance to adverse physical factors (high and low temperatures, elevated background radiation), chemical (antinarcotic drug action in respect to the ether, chloral hydrate, hexenal, alcohol, antitoxic – to some anticancer drugs) and biological (increased survival in self-poisoning) nature.

Positive physiological changes, occurring in the functional state of human organism under the influence of phytoecdysteroids reflect the ability of these compounds to increase adaptability to extreme environmental impacts by reducing shifts in the catabolic metabolism, stimulation of biochemical reactions directed to maintenance of homeostasis of energy production, optimization of protein, lipid and carbohydrate-electrolyte metabolism.

Thus, the practical use of preparations developed by us on the basis of ecdysteroids created the new possibilities of effective pharmacological correction of various metabolic disorders in human organism.

POLYPRENOLS OF PLANTS FROM THE CENTRAL ASIAN REGION AS THE BASIS FOR DEVELOPMENT OF HIGH EFFECTIVE WOUND HEALING DRUGS

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We studied the effects of polyprenols extracted from local plants belonging to the *Malvaceae* family: *Alcea nudiflora*, cotton line L-249, and others on the healing process of the destructive changes in coating tissues. Mice (18–20 g), rats (180–200 g) and rabbits (2.5–3 kg) were used in experiments. In studying of wound healing action of polyprenols on animals, we shaved wool on the skin area, where we planned to apply polyprenols, and the remainder of the hair was removed by 10% of sodium sulfide (wetting within 2–3 min. followed by washing with warm tap water). All traumatic procedures on animals were performed under aseptic conditions or under light ether anesthesia, or after administration of Nembutal at the dose 35 mg/kg. Planar skin wounds on rats and mice were reproduced on their back by a special circular stamp of a certain diameter. Trophic ulcers in rabbits were induced by ligation of the sciatic nerve. Thermal burns were caused by pinning high temperature method. Experiments have shown, that the repeated application of polyprenols on wound surface resulted in decrease of intensity of inflammatory cell infiltration, accelerated granulation tissue formation and more rapid regeneration of epithelial, increased collagen biosynthesis and fibrillogenesis. We also found, that they exert a great pharmacotherapeutic effects in animals with destructive changes in the gastric mucosa, caused by stress exposure, as well as by a variety of ulcerogenic agents: reserpine, atofanum, butadionum, acetic acid. Gastroprotective activity of polyprenols (when administered *per os*) was manifested in decrease of ulcers number in the stomach secretion part and decrease the total number of animals with ulcerative lesions. In the mechanism of healing wounds and ulcers of the stomach under the influence of polyprenols, a main role belongs to their ability to activation the plastic processes in skin and mucous membranes, improving energy status of cell structures, inhibition lipid peroxidation and anti-exudative action. Combined use of polyprenols with vitamin E or phytoecdysteroids (ecdysterone, turkesterone) during destructive changes in coating tissues resulted in a greater therapeutic effect. It should be noted, that administration of polyprenols to animals resulted in increasing of total non-specific resistance of the organism and its adaptive capacity, stimulation of the immune processes. Thus, polyprenols isolated from the local flora, represents independent interest as individual preparations, as well as in combination with other stimulants of regenerative processes as promising remedies, contributing to the restoration of the integrity of the skin and mucous membranes.

SCREENING OF CYTOTOXIC ACTIVITY OF NATURAL COMPOUNDS FROM LOCAL PLANTS OF UZBEKISTAN

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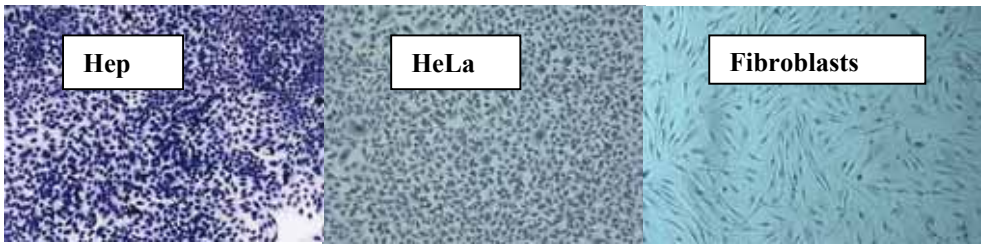
Effect of natural compounds (extracts, individual compounds and their chemical derivatives) on cervical cancer cells (HeLa), larynx cancer cells (Hep) and primary fibroblast culture have been studied.



Pic. 1. Verifying cultures of cancer cells – Hep, HeLa and primary fibroblast culture microphoto, oc. ×10, ob. ×10, staining eosin-gemotoxilin

It was established, that convolvine and its chemical derivatives have cytotoxic activity. The most selective cytotoxic ability has been revealed by alkaloids convolinine, *N*-benzyl convolvine, fillalbin and *N*-chloroacetyl convolvine. As a positive control for cytotoxicity anticancer drugs «Cisplatin Teva» and «Vinblastine-Richter» were used.

TABLE 1. **50% Inhibition of Cell Growth Under the Influence of Substances**

Substances	IC_{50}, μg/mL		
	Fibroblasts	Hep	HeLa
Extract of *V. rosea*	16.9	12	7.5
Extract of *C. krauseanus*	25	55	100
Extract of *B. sempervirens*	15	50	40
Convolvine	5	24.6	27
N-Benzyl convolvine	12	4.7	12.4
Convolinine	150	23.6	125
Convolidine	25	55	24.5
N-Chloroacetyl convolvine	4.2	7.3	6.9
Fillalbin	125	69	14.3
15-Acetoxiazametin atizine	3.5	9.3	10.9
1-*O*-Benzoil napelline	2.4	24.6	16.7
Talatizamine	49.6	25	42
Control – Cisplatine	0.4	9.3	10
Control – Vinblastine–Richter	24	10	1

It was established, that convolinine and *N*-benzyl convolvine have high selective cytotoxicity on Hep cells, also they were less toxic for the fibroblast cells. Fillalbin have high selective cytotoxicity on HeLa cells, also it was less toxic for the fibroblast cells. In addition, another derivative of convolvine – *N*-chloroacetyl convolvinepossessed by high cytotoxicity against both types of cancer cells. These compounds are perspective for further study as anticancer drugs.

TO THE EVALUATION OF PHARMACOLOGICAL EFFICACY OF SOME AGGREGATE PREPARATIONS OF THE TRITERPENE GLYCOSIDES

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Triterpenic glycosides are the basis of saponines, which are widespread bioregulators of the plant origin. In a number of experimental investigations performed on the various laboratory animals, we showed, that the sum of triterpenic glycosides isolated from the aerial part of *Climacoptera transoxana* and roots *of Medicago sativa* are of some interest as intensifying and actoprotecting agents (increasing working activity in the complicated conditions). Their activity is similar to the known medicine saparal (sum of triterpenic glycosides from *Aralia manjurica*). In the triterpenic glycozides from the plant *Silphium perfoliatum* high hypocholesterinemic activity was determined, in the triterpenic glycosides isolated from *Acantophyllum gypsophiloides* (*Allochrusa gypsophiloides*) ability to increase immunogenicity of sorbate vaccines exceeding such import preparations, was noted. The aggregated agent of the triterpenic glycosides from *Allochrusa gypsophiloides* (trade mark Allochrozide) was applied in the veterinary practice as adjuvant mean in production of antiaphthous inactivated vaccine. The cluster of triterpenic glycosides from *Zygophyllum oxianum* yielded marked hypoglycemic effect. Its sugar reducing effect was manifested both on the normal animals, and on the animals with different hyperglycemic states, induced by injections of glucose, adrenalin, alloxane. In the alloxane diabetes the aggregate of triterpenic glycosides from *Z. oxianum* showed associated hypoglycemic and hypocholesterinemic effects mostly expressed in the animals with diabetes of mild and moderate severity degree. However, its effect preserved in the rats with severe form of diabetes (blood sugar to 400 mg%). It is interesting to note the normalizing effect of the studied triterpenic glycosides on the impaired lipid metabolism in the rabbits with experimental atherosclerosis. In this case reduction as cholesterol, as triglycerides, β-lipoproteines, diene and triene conjugates, malonic dialdehyde in the blood serum revealed. There was noted less damage of aorta by cholesteric plaques.

Our researches performed the study of pharmacological properties of triterpenic glycosides, isolated from different plants, shown their further prospecting as potential therapeutic agents.

MOLECULAR MECHANISM OF MUSCARINIC RECEPTORS INHIBITION BY IMPERIALINE AND ITS HALOID DERIVATIVES

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The family of muscarinic cholinoreceptors (m-AChR) is composed by five subtypes (M_1–M_5), which may be divided on two main classes. M_1, M_3, and M_5 subtypes reveal selectivity to G-proteins of $G_{q/11}$ type, and M_2 and M_4-subtypes relating to G-proteins of $G_{i/o}$ type.

Difficulty in elaboration of selective M-cholinotropic compounds is related to the structural relativity of ligands connecting centers of all five members of the family. Publications on M_2 and M_3 receptors structures give the base for continuation of works, directed to rational molecular design of selective M-cholinotropic compounds.

Orthosteric binding site composed by 12 aminoacids – ASP103, TYR104, SER107, ASN108, THR 190, ALA191, RHE195, TRP400, TYR403, ASN494m CYS429, and TYR430, which is identical in all 5 mAChRs sybtypes. ASN404 and ASP103 have tied with ligands by hydrogen bounds. The layers of tyrosine residues forms aromatic top, that limits the dissociation of bounded ligands.

Imperialine and it derivatives are perspective selective inhibitors of M_2-subtype of muscarinic receptors. We have carried out molecular docking of imperialine haloid derivatives with the purpose of elucidation of molecular mechanisms of their action on M_2- and M_3-muscarinic receptors.

On the base of performed calculation it may be concluded, that all mentioned ligands are related to allosteric modulators of m-AChR. In spite of similarity of structures bounding the allosteric centers, radical differences exist. One of these differences appears in second extracellular loop (ECL2), which is a place of allosteric modulators connection. Differences in ECL2 provided by the pocket presence in M_3-subtype and absent in M_2-subtype. Other differences connected to orientation of aromatic residues, related to allosteric sites participated in selectivity of imperialine and it derivatives.

In view of growing interest to elaboration of allosteric ligands for receptors, connected to G-proteins (GPCRs), the obtained finding may be used in rational elaboration of drugs on imperialine base.

CYTOTOXIC ACTIVITY OF EXTRACTS FROM *Cuscuta*

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In the last decade a great attention of the researchers working in the field of chemotherapy, has been paid to plant extracts and compounds isolated from plants, among them plant-parasites, such as white mistletoe (*Viscum album*), and *Cuscuta capture*.

The aim of this work is to study cytotoxic activity of different (aqueous, alcoholic, aqueous-alcoholic) extracts and glycoproteids isolated from *Cuscuta europaea*, growing in the Central Asia, on grassland plants and the shoots and shrubs in interrupting lines of cell cultures.

Plants were collected in summer and 3-day, 7-day and 14-days aqueous and 20% alcoholic, 40% alcoholic extracts were made. From the seeds of cuscuta glycoprotein fracrion, acquiring hemaglutinating activity was extracted.

The quantities of proteins (by Lowry) and total sugars (by Antronov) in obtained extractions were determined.

Cytotoxic activity of obtained compounds in different lines of cell cultures was studied.

In order to determine cytotoxic activity cells were spread on 96 alveolar plate by 40 000 cells/mL in 100 μL RPMI 1640 culture with 10% fetal calf serum and cultivated in CO_2 incubator (37°C). The next day extracts at doses 1, 5, 10 μL per 100 μL of culture were introduced. The cells were cultivated for 24 h. Further MTT (3-(4,5-dimethyldiazol-2-yl)-2,5 diphenyl tetrazolium bromide) was injected. After incubation for an hour cultures were cautiously dumped, and DMSO was added and incubated for 20 minutes. Thereupon the optical density of the solution was measured at a wavelength 620 nm.

For the establishment of suppression of cell growth, the number of live cells was counted. For that purpose the cells were taken, painted with trypan blue, and the calculation of cells was made under microscope.

With the obtained data, it was shown, that extracts from *Cuscuta europaea* reveal different cytotoxic activity on different cell types. These data correlate with those, obtained with the calculation of cells painted by trypan blue.

STUDYING OF BIOLOGICAL ACTIVITY OF DITERPENOID ALKALOIDS FROM *Aconitum* SPECIES AND ITS DERIVATIVES

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Diterpenoid alkaloids were isolated from the plant *Aconitum Karacolicum* (*Ranunculaceae*). Cytotoxic activity of one of the diterpenoid alkaloids synthetical derivatives have been studied on HeLa and X Ag 8.653 cells. On HeLa cells line this substance in doses from 1 to 10 μg/100 μL in a dose-dependent manner suppressed growth of cells on the average on 81% in comparison with control (cells without substances). On X Ag 8.653 cells line of the given substance suppressed growth of cells in the same concentration on the average on 60% in comparison with control. The received results demonstrated the high cytotoxicity of the given substance. Antioxidant activity of diterpenoid alkaloids synthetical derivative on mitochondrions of rat liver and on HeLa and X Ag 8.653 cells also has been studied. In doses of 1 and 10 μg/100 μL the substance reduced malondialdehyde concentration for 35 and 68% in comparison with control. On HeLa cells the given substance in doses of 1 and 10 μg/100 μL reduced formation of malondialdehyde by 67.2 and 81.3%, on X Ag 8.653 cells – on 50.4 and 29% accordingly. The received results had shown antioxidant properties of this substance. The results indicated that further investigations needs due to the significance of the biological properties of these diterpenoid alkaloids and its derivatives.

UZBEKISTAN TERMITES CHEMORECEPTION

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Termites are one of the dangerous pest′s insect. In Uzbekistan termites bring great impact to buildings, historical monuments. A huge harm *Anacanthotermes turcastanicus* Jacobs, 1904, and big undercaspian *A. ahngerianus* Jacobs, 1904 applied.

In Institute of Bioorganic Chemistry, Uzbek Academy of Sciences the researches of termite′s chemoreception are carried out, special for managing of population′s quantity.

The attractants 2-phenoxyethanol; 2-naphtalenemethanol; 1-octen-3-ol; β-oxynaphtaldehyde; sodium salt of 1-naphtol-5-sulfurus acid; threecrezylphophat had been synthesized. Such substances increase attractiveness of allure traps.

The termites prefer to eat the sunflower, maize and alhagi. We have been extracted natural carbohydrates. Biological testing has showed the positive results for attractiveness of such carbohydrates.

We have been synthesized the substances affecting on living process of termites. Sodium salt of *n*-hydroxynaphtalamide destroys the intestine microorganisms of termites, which help to metabolize the cellulose and activated digestive activity.

Lacton of *D*-glucon acid blocks termites' immune system and let to fungal infection development.

We have been received mono-butyl and mono-ethyl ethers of ethylenglycol and diethylenglycol, which are the analogs of trail′s pheromone for a few species of termites. According to the biological testing, mono-ethers of glycols haven′t activity as analogs of trail pheromone for Uzbekistan termites.

We have synthesized substances with juvenile and antijuvenile activity, on a base of natural alkaloids (ephedrine and pseudoephedrine). We have conducting laboratory and field testing of the synthesized substances and received positive results.

We have studied the plants which are attractive to termites especial for Uzbekistan. Hexan, alcohol, and water fractions have been extracted from flesh of stems of sunflower, alhagi and maize.

Also benzoic and naphthalene structures and alcohol and ether functional groups, phosphorousorganic substances have been obtained. All these objects have been chosen for using in allure traps.

SOME MOLECULAR MECHANISMS OF DEVELOPMENT OF ISCHEMIC STROKE

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Recent studies discuss biochemical mechanisms of development of stroke. Endothelial dysfunction conditioned by nitric oxide (NO) and acetylcholine synthesis play the main role in the pathogenesis of cerebrovascular diseases and mechanisms of neurotransmitters′ disturbances.

To study the role of NO and cholinergic system in different subtypes and severity degree of ischemic stroke (IS).

The study included 100 patients with IS (mean age – 62.63 ± 4.68 years old) at acute and acutest stages. Depending on stroke subtype, all patients were randomized into three groups: 42 patients with atherothrombotic stroke (ATS) (which occurred because of atherosclerosis), 41 patients with lacunar stroke (LS) (because of hypertension), and 17 patients with cardioembolic stroke (CES) (because of heart diseases and cardiac dysfunctions). The stroke severity and functional status were measured as well. By spectrophotometric method in blood serum were investigated the levels of NO_2^-, NO_3^- and acetylcholinesterase. Control group consisted of 20 patients without stroke and severe diseases at the same age. The digital material was proceeded using methods of variation statistics.

The level of NO significantly decreased on 37.3%, in comparison with control. The most significant decrease of NO level was noted in CES (on 40.4%; 13.20 ± 1.02 mkmol/L) than in LS (on 36.8%; 14.00 ± 0.35 mkmol/L) and ATS (on 34.7%; 14.46 ± 0.39 mkmol/L). At the same time, serum level of acetylcholinesterase decreased on 24% (76.73 ± 1.61 mmol/(h·L)), in comparison with control (100.1 ± 1.76 mmol/(h·L)) that is evidence of deficit of cholinergic system in stroke. The most significant decrease of acetylcholinesterase level was revealed in CES (on 31.5%) than in LS and ATS (on 20.3% and 18%, respectively). Thus, we could find significant endothelial dysfunction and cholinergic deficit in CES and LS. In this case, the roughest changes in NO and cholinergic system, testifying to decrease of synthesis and elevated inactivation of NO and acetylcholine, were registered in poor outcome of each stroke subtype, especially on the background of heart diseases, diabetes mellitus, hypertension, and hypercholesterolemia. Correlation analysis showed that NO level was straightly proportionally dependent on acetylcholinesterase level. This may indicate decreased stimulation of endothelial relaxation factor (NO) in stroke. We could find straight correlative interrelation of deficits of these substances in stroke subtypes, which was stronger in CES ($r = 0.79$) and LS ($r = 0.72$) and weaker in ATS ($r = 0.68$).

Endothelial dysfunction, characterized by endothelial NO reduction, and cholinergic neuromediation deficit, conditioned by decrease in cholinesterase level in blood serum of patients at acutest and acute stages of IS, are considered to play the important role in the development of IS, especially on the background of arterial hypertension and cardiac pathology. Based on biochemical studies, we could demonstrate a scheme of proposed pathobiochemical ischemic cascade with inclusion of cholinergic neurotransmission and endothelial dysfunction in acute ischemic stroke.

BIOLOGICAL PROPERTIES OF THE NEW COMPOUNDS SYNTHESIZED FROM TROPOLONE ALKALOIDS

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In laboratory for developing of anticancer drugs of RSCO HM RUz the biological properties of more than 70 novel compounds derived from tropolone alkaloid colchicine and colchamine synthesized by introducing of various substituents into tropolone alkaloids geptadien rings are studied.

Some substances have high antitumor activity and some also radiosensibilizing, several substances after treatment reduces immunity and hematopoiesis. Also, a number of substances have shown a higher polyploidy activity, higher than that of colchicine, there are substances that greatly improve the productivity of the silkworm.

On the basis of toxicity studies, which reduced to 10–400 times in comparison with colchicine, and antitumor activity – howling as in vitro in the NCI, as *in vivo* on 3 solid tumors of new derivatives selected 15 new drugs, which are at different stages of study.

Decocine, colhiprite and decovine passed the stage of preclinical studies examined on 7–10 types of animal tumors of needed pharmaco-toxicological research and permission to conduct clinical trials get for them. K-48, K-42, K-19 are currently on the preclinical stage.

These 6 compounds in 14–360 times are less toxic than colchicine, their anti-tumor effect is higher than that of colchicine and colhamine 20–70%, and in some cases known cytostatic agents, including tubulin interactive (taxol, etoposide) used as control.

In the study of the mechanism of action of compounds introduced, it became clear that all of them have multifunctional action: combine mitotic activity, alkylating action, active inhibition of topoisomerase I and II, and the ability to overcome multidrug resistance (MDR) can stimulate the spleen colony-forming units (CFUs), some to drain rate (K-48 to 40–60 units), this leads to further stimulate hematopoiesis and immunostimulators. All parameters are present in varying degrees for each substance. Decocine, decovine and K-19 – active radiosensitizers, their effect is greater than that effect of 5-FU as agents affecting DNA synthesis and mitosis in M/G2 block phase up to 70%.

Currently decocine is introducing into health care practice for the treatment of 3 tumor localization (skin cancer, colorectal cancer and cervical cancer) as an anticancer drug to the radiosensitizing effect. The permission to conduct clinical trials of Colhiprite injection form for treatment of bladder cancer, and Decovine, for the treatment of lung cancer and other tumor localization, not only as an anticancer drug, but also the mean reinforcing effects of radiation.

Extending study of the activity of new drugs 9-th of drugs is conducted. It have shown high antitumor activity on 3 strains of tumors exceeding 90% for a number of tumors.

VARIETY OF ANTIMICROBIAL PEPTIDES IN SEEDS OF THE GARDEN FENNEL FLOWER *Nigella sativa*

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Study of natural compounds with antimicrobial activity has both a theoretical value for the study of the molecular components and mechanisms of resistance of plants to pathogens, and of great practical importance for agriculture and medicine.

For protection against pathogenic microorganisms the plants produce a range of different proteins that possess by direct antimicrobial activity (AMP)-polypeptides, inhibiting growth, differentiation, reproduction and/or dissemination of microorganisms (fungi, bacteria and viruses) that fall to the surface or inside plant tissue.

The purpose of this work was isolation of a number of individual antimicrobial peptides from the seeds of the garden fennel flower and characterization of them. *Nigella sativa* L. is an annual herbaceous plants of the family *Ranunculaceae* with medicinal properties and is used in the food industry.

Different types of chromatography methods were identified 6 new individual antimicrobial peptides, among them: a novel protein with a molecular weight of 9602 Da, called Ns-LTP1, belonging to the subfamily 9 kDa LTP. Selected protein effectively suppressed the germination of conidia of the fungus *Fusarium oxysporum* lesion and *Phytophthora infestans* in oomiceta zoosporangia IC_{50} equal 60 and 115 μg/mL, respectively; two peptides Ns-D1 and Ns-D2 with molecular masses of 5485 Da and 5498Da, belonging to class defensins, and possess a high degree of homology with the defensins family of *Brassicaceae*. Defensin Ns-D2 showed the highest antifungal activity against a number of farming pathogens and antimicrobial activity against a number of micro-organisms pathogenic to human body.

Two peptides Ns-W1 and Ns-W2 with molecular masses of 5143 Da and 5070 Da, homologous γ-purotionins cereal shown the high antifungal and antibacterial activities against several pathogens.

Ns-G1 peptide with molecular weight 5696 Da contains the 8 cysteine residues. Based on the definition of partial *N*-terminal amino acid sequence of the peptide has no homology with known peptides.

Selected antimicrobial peptides, having a wide spectrum of biological activity can serve as a vector for creating genetic designs for genetic engineering modification of cotton and other crops and plants with increased generation of abiotic compounds and be used as antimicrobial agents against strains of microorganisms and fungi, have resistance traditionally used the antibiotics and antimicotics.

PHARMACOKINETICS OF *N*-NITROSOAMINES IN NORMAL STATE AND PATHOLOGY

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Biotransformation of 12 nitroso- derivatives of various heterocyclic amines in organism has been researched both intact and tumourous animals. Research has shown that biotransformation of nitrosoamines runs with formation of hydroxyderivatives which have little or absent electrophilic reactivity to cellular nucleophilic centres. Normal cells become released from introducted nitrosoamine or/and its metabolites faster in contrast to timorous cells, in which depositing of preparation has been observed. Notable differences are observed in qualitative and quantitative spectrum of metabolites, in urine of intact animals mainly lactam, aminocarboxylic and dicarboxylic acids are detected, as opposed to timorous animal′s urine where hydroxyderivatives and lactons are dominant.

Detected among the metabolic products *N*-nitrosopiperidine and *N*-nitrosohexamethylenemine, glutaric, adipic, aminocapronic acids authenticate metabolic disruption of cyclic *N*-nitrosoamines ring. According to the research of biotransformation of chloralkylamine derivative heterocycles of metabolites, metabolic disruption of the ring was not detected.

Apparently, during metabolic disruption of cyclic *N*-nitrosoamines ring the specific part takes electronegative characteristics of N-nitrosogroup.

TABLE. **Anticancer Activity of 12 Nitroso-Derivatives of Various Heterocyclic Amines**

№ n/n	Compound	LD_{50}, mg/kg	Dose, mg/kg	Growth inhibition of tumors, %			
				АРЭ	S-180	La	К.Г
1		100	60	75	81	10	20
2		110	60	28	22	–	–
3		17	5	28	28	13	–
4		120	40	22	27	–	–
5		80	40	20	16	–	–
6		420	150	51	37	–	–
7		400	150	76	75	20	–
9		560	300	68	52	18	18
10		385	100	64	85	16	76
11		150	50	52	60	12	–
12		140	60	92	88	30	44

HYPOTENSIVE AND ANTIOXIDANT ACTIVITIES OF *Crataegus azarolus* L. LEAVES EXTRACTS

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Crataegus azarolus L. (*Rosaceae*), commonly known as "Zaarour" in Algeria, is widely used as natural remedy for hypertension in folk medicine. In the present study, the hypotensive effect of methanolic extract (ME) administrated intravenously, was evaluated in anaesthetized rats using the invasive method of blood pressure recording. Moreover, the antioxidant potential of methanolic extract (ME) and its fractionated extracts (Chloroform (ChE), ethyl acetate (EAE) and water (AE)) have been investigated, using four different established testing systems, namely scavenging activity on 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical, ferrous ion-chelating assay, reducing power assay and β-carotene bleaching method. The quantification of total polyphenols and flavonoids was determined using Folin–Chiocalteu reagent and $AlCl_3$, respectively.

The results showed that the amount of total polyphenols ranged from 38.25 mg GAE/g of dry extract to 396.04 mg GAE/g of dry extract, whereas total flavonoids varied from 2.23 mg QE/g of dry extract to 32.73 mg QE/g of dry extract. Similarly, EAE exhibited the highest DPPH radical scavenging activity, with IC_{50} value of 0.0062 mg/mL and the highest relative antioxidant activity in inhibiting linoleic acid/β-carotene coupled oxidation (89.21%). Ferrous ion chelating capacity assay showed that WE and ME are the most active with IC_{50} values of 0.572 mg/mL and 0.352 mg/mL respectively. All extracts exhibited a good reducing power but EAE possessed significantly the strongest effect at 0.1 mg/mL.

The methanolic extract of *Crataegus azarolus* caused hypotensive effect in anaesthetized rats. The intravenous administration of extract at a dose range of 0.04 to 12 mg/kg body weight, produced a 28% fall in the systolic and diastolic blood pressure, in a dose-dependent manner. Therefore this investigation is useful for clarifying of pharmacological activity of *Crataegus azarolus* and present new benefit of this plant in hypertension therapy.

BIOLOGICAL ACTIVITIES OF FERMENTATIVE EXTRACTS FROM ENDOPHYTIC FUNGI ISOLATED FROM *Retama raetam* (FORSSK.)

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The aim of the present study was to evaluate the antimicrobial and antioxidant activites of endophytic fungi isolated from branches of *Retama raetam* (Forssk.) collected during the winter of 2010 from Bordj Bou Arreridj (Algeria) region. After isolation, a preliminary screening of the antagonistic activity by dual cultures led to the selection of six isolates potentially active, the antimicrobial activity of extracts of these latter was tested by the disk diffusion method and showed inhibitory activity on at least one or more pathogenic microorganisms, with inhibition zones ranging from 0 to 25 mm for the ethyl acetate extracts and from 0 to 19 mm for the chloroform extracts. The antioxidant activity of ethyl acetate extracts was evaluated by β-carotene/linoleic acid method, and results showed inhibition percentages up to 83% of inhibition obtained with the extract of *Penicillium* sp. The results of the present work show that these endophytic fungi could be a promising source of bioactive compounds, and warrant further study.

DRUGS AND DRUG DELIVERY SYSTEMS ON THE BASE OF PLANT PHOSPHOLIPIDS

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The development of a new generation of pharmaceuticals-nanopharmaceuticals – provides both the usage of novel nanomaterials (not existed before) and the application of new technologies allowing to produce the new pharmaceutical forms from the known substances. It is known that the new nanopharmaceuticals modify the kinetics, body distribution and release of associated drugs. These new formulations are distinguished by high efficiency, bioavailability and absence or decrease of side-effects.

Now it is proved that phosphatidylcholine may act as both a substantive drug and a carrier for drug delivery. An example of the usage of phospholipid nanoparticles as a drug is Phosphogliv – the first Russian nanopharmaceutical elaborated in our Institute by the researchers′ group. Phosphogliv has no analogs in the world. The production of both the capsule and injection forms is based on the unique, nonstandard technology. For the capsules it is technology that enables obtaining of a dry granulated substance from lipophilic materials. The injection form of phosphogliv is freeze-dried powder, which when dissolved in water gives a stable nanoemulsion with particle size 35–40 nm. Phosphogliv has the known mechanism of action. It can reconstruct the damaged cell membranes and their functional activity. It acts as a "membrane glue". Another component of the preparation is the salt of glycyrrhizic acid possessing antiviral and immunomodulating properties. It induces the synthesis of γ-interferon in the body. Phosphogliv has no side-effects. It demonstrated high efficiency in the treatment of viral hepatitis, in particular – hepatitis C.

Besides, phosphatidylcholine is known as a antiatherosclerotic remedy due to its property to activate the reverse cholesterol transport. This activity is suggested to be more pronounced for phosphatidylcholine nanoformulations, that has to allow their usage as an effective nanopharmaceuticals for delay of atherosclerosis progression.

In the last 20 years the most significant success was achieved in elaboration of phospholipid transport systems, phospholipid nanoparticles (micelles, liposomes) that have a number of preferences as compared with the others, for example – with polymer nanoparticles. They are non toxic, biodegradable, do not induce allergic reactions. Phospholipid nanoparticles have high affinity to cell membranes, that allows the delivery of drug into the cell.

In the laboratory of nanopharmaceuticals in our Institute we have elaborated a transport system based on phospholipid nanoparticles that are extremely small in size. The diameter of the particles in our delivery nanosystem is 15–25 nm. The incorporation of a drug, particularly poorly soluble, into phospholipid nanoparticles sufficiently influences its bioavailability, distribution across the tissues, binding to blood components. The usage of phospholipid nanoparticles as the drug delivery system provides the essential decrease of its therapeutic dosage.

Thus, the usage of new technology approaches opens the prospects in the elaboration of new drugs (or new drug formulations) and systems of their transport in organism.

CHEMICAL DIVERSITY AND BIOLOGICAL ACTIVITY OF *Juglans* OILS FROM TURKEY

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The *Juglandaceae*, also known as the *Walnut* Family, is a family of trees, or sometimes shrubs, in the order *Fagales*. Various members of this family are native to the Americas, Eurasia, and Southeast Asia. Walnut tree (*Juglans regia* L.) is native or naturalized in many places in Turkey, especially in E. Anatolia [1]. It is cultivated almost throughout Turkey for its edible fruits (walnuts, in Turkish ′Ceviz′) and timber. Walnut fruits are rich in polyunsaturated fatty oils that have been suggested to reduce the risk of heart diseases [2]. Commission E considers aqueous leaf extracts in the treatment of scrofulous diseases, herpes, eczema and wounds. In Germany, walnut leaf is listed in the Drug Codex approved in the Commission E monographs and a decoction form for external use is official in the Standard License monographs. In France, walnut leaf is used topically to treat sunburn, dandruff and itch-relieving treatment in skin disorders. In India, walnut leaf decoction is used externally as a wash for malignant sores and pustules [3]. Gas chromatographic-mass spectrometric analysis coupled with GC-FID and Preparative GC techniques were employed for volatiles profiling in leaves of *Juglans regia*. Sesquiterpenes dominated the volatile blend of all samples. Extracts or essential oils may be alternative sources of mosquito control agents since they are rich in phytochemicals that potentially suitable for use in biopesticides. Since most mosquito species spend much of their life cycle in the larval stage, mosquito larvae control is important. In this perspective, *Juglans regia* leaf essential oil was investigated against one day old yellow fever mosquito, *Aedes aegypti* L. Detailed results will be discussed in the presentation.

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BIOLOGICAL ACTIVITY GUIDED FRACTIONATION IN COMBINATION WITH PREPARATIVE GC-FID AND GC/MS TECHNIQUES

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Biological activity of volatile constituents isolated from essential oils is important. For this purpose, carrying out compound separation procedure along with activity control allows to determine and isolate correct active constituents. However, thermal degradation or conversion situations encountered when handling with heat-sensitive compounds during isolation steps reveal the need to perform separation work very carefully and sensitively.

In this study, activity guided research – backed isolation work applied in the case study of ceased activity during the isolation of the compound (responsible for the activity) transformed due to thermal effects will be discussed. One-step fractionation of the oil and separation of target constituents were performed using preparative capillary gas chromatography connected to a preparative fraction collector system. This combination allowed separation and recovery of sufficient quantities of target compounds with high purity from complex oil matrix. Separation conditions (column temperature, cooling temperature, flow rate, injection volume, and cut time) were optimized to achieve the best isolation and successful collection. The target thermolabile compounds were separated from the oil using a preparative capillary column in rapid one-step manner with > 95.0% purity.

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STUDY ON XANTHINE OXIDASE INHIBITORY ACTVITY IN UIGHUR MEDICINE *Capparis spinosa* L. BY SPECTROPHOTOMETRY

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In this study, a comparative study of traditional Uighur medicine *Capparis spinosa* .L different parts of different solvent extracts *in vitro* xanthine oxidase inhibitory activity of the active site, looking for *Capparis spinosa* L. role of inhibition of xanthine oxidase (XOD). Xanthine oxidase inhibitory activity was assayed spectrophotometrically under aerobic conditions determine the *Capparis spinosa* L. different parts of different solvent extracts (cyclohexane extract, dichloromethane extract, methanol extract) inhibition of xanthine oxidase activity.The different solvent extracts of *Capparis spinosa* L. (fruits, leafs and flowers) displayed xanthine oxidase inhibitory activity. In 100 mg/mL concentration, the medicine in three parts (leaves, fruits, flowers) in three different solvent extracts to varying degrees, for XOD inhibition effect, concentration of 100 ug/mL, leaf cyclohexane extract, leaf dichloromethane extract, leaf methanol extract, fruit cyclohexane extract, fruit dichloromethane extract, fruit methanol extract, flower methanol extract inhibits the rate of more than 50%; concentration of 50 ug/mL, three different extracts showed inhibition and which three extracts exhibited higher than 50% inhibition rate; at the concentration of 25 ug/mL, one extract xanthine oxidase inhibitory activity higher than 50%; while eight extracts presented activity at 10 ug/mL, with none having greater than 50% inhibition. The most three active extracts were the leaf methanol extract, fruit dichloromethane extract, fruit methanol extract with IC_{50} value of (15.82 ug/mL, 35.17 ug/mL, 39.3 ug/mL, respectively). The IC_{50} value of allopurinol used, as the standard was 6.33 ug/mL. These results suggest that the use of *Capparis spinosa* L. for the treatment of gout could be attributed to its xanthine oxidase inhibitory activity.

TABLE 1. ***In vitro* Xanthine Oxidase Inhibitory Activity of the Extractions of *Capparis spinosa* L. (x ± s)**

Plant species	Extract	Yield, %	Inhibition at different concentrations (%, x ± s), ug/mL				IC_{50}, ug/mL
			10	25	50	100	
Root	Cyclohexane	0.55		–	–	–	–
	Dichloromethane	0.51	0.65 ± 0.29	2.12 ± 0.36	3.51 ± 0.16	6.86 ± 0.16	–
	Methanol	3.73	3.24 ± 1.77	12.05 ± 1.11	16.61 ± 0.36	20.78 ± 0.22	–
Stem	Cyclohexane	0.3	–	–	–	–	–
	Dichloromethane	0.25	–	–	–	–	–
	Methanol	4.31	–	–	–	–	–
Leaf	Cyclohexane	1.55	4.50 ± 0.46	18.78 ± 0.23	38.49 ± 0.66	67.52 ± 0.63	64.29
	Dichloromethane	8.25	13.32 ± 0.58	23.72 ± 0.33	33.83 ± 0.18	77.67 ± 0.33	54.26
	Methanol	6.17	20.86 ± 0.16	24.76 ± 1.30	66.78 ± 0.29	81.45 ± 0.79	35.17
Flower	Cyclohexane	2.49	–	–	–	–	–
	Dichloromethane	3.01	–	–	–	–	–
	Methanol	37.3	–	14.17 ± 0.72	39.83 ± 0.18	50.79 ± 0.21	68.59
Fruit	Cyclohexane	4.88	7.38 ± 0.96	21 ± 0.80	37.88 ± 0.15	64.81 ± 0.17	66.95
	Dichloromethane	1.41	16.67 ± 0.43	28.95 ± 0.95	57.26 ± 0.64	79.66 ± 0.33	39.3
	Methanol	9.41	40.79 ± 1.12	54.43 ± 0.19	80.60 ± 0.44	85.38 ± 0.62	15.82
Allopurinol		–	63.26 ± 0.83	73.67 ± 0.49	83.74 ± 0.25	92.89 ± 0.09	6.33

BIOLOGICAL ACTIVITIES AND ESSENTIAL OIL COMPOSITION OF *Chrysanthemum coronarium* L. FROM CYPRUS

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Previous reports on the essential oils of *C. coronarium* showed variation from plant material originating from different geographical locations. Camphor, α-pinene, β-pinene, lyratyl acetate, *trans*-chrysanthenyl acetate, *trans*-chrysanthenyl isovalarate, *cis*-chrysanthenyl acetate, camphene, bornyl acetate, myrcene, α-bisabolol, β-farnesene and palmitic acid were previously reported as main components of *C. coronarium* oils [1–6]. In the present investigation, we report on essential oil composition of *C. coranarium* from three different geographical locations in Cyprus as well as their biological activities (PRAP, DPPH, Phytotoxicity and Insecticidal). The plant materials were collected during the flowering period (Feb.–Mar./2012) from Lefkose (Nicosia), Salamis, and Degirmenlik. In the investigated essential oils from three different locations 34–31 components were identified representing 86.2 ± 0.7% – 93.8 ± 0.0% (n = 3) of the oils. All of the investigated oils presented similar main components with varying amounts. Camphor 25.2 ± 0.1% – 9.1 ± 0.3%, santolinatriene 21.7 ± 0.1% – 3.6 ± 0.1%, yomogi alcohol 12.6 ± 0.1% – 3.6 ± 0.1%, *cis*-chrysanthenyl acetate 10.7 ± 0.1% – 6.8 ± 0.1% and bornyl acetate 11.0 ± 0.5% – 5.7 ± 0.0% were identified as the main components of the oils. Highest DPPH scavenging and PRAP activity was observed for the oil of Lefkose sample (49.59 ± 0.19 (n = *5*) and 812.77 ± 4.34 (n = *5*)) at 10 mg/mL concentration. However when compared with positive controls at the same concentration this oil showed low DPPH scavenging activity but considerably high PRAP activity. Highest *L. minor* phytotoxic activity was observed for the oil obtained from Salamis when number of fronds were taken account in growth inhibition calculation (100.0%). Highest insecticidal activity was observed for Lefkoюe sample which afforded 97.82 ± 1.79% mortality against *Sitophilus granarius* in fumigant toxicity assay at 10% (v/v) concentration. Salamis and Degirmenlik oils also presented high activity ranging between 87.94 ± 0.32% – 87.82 ± 0.09% at the same concentration.

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PLANT POLYSACCHARIDES FOR MODIFY OF ANTHELMINTIC DRUGS

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Plant polysaccharides, having a broad set of practically useful physical, chemical and technological properties, as well as its own biological activity, are promising to modify the properties of known physiologically active substances. In recent years, based on polysaccharides have developed so called Drug Delivery Systems (DDS).

This paper deals with the development of DDS based on the known anthelmintic drugs (Medamin, Albendazole, Fenbendazole, Fenasal, Azinox) with the involvement of following polysaccharides – Pectin, Arabinogalactan, Hydroxyethyl starch (HES) etc. The resulting new anthelmintic drugs had not only increased activity against *intestinal Nematodes***.**, but also showed a new range of action against *larval Echinococcus.* For this technology was used the way of mechanochemical modification of poor soluble substances with water-soluble polymers. It is known that substances of a.m.drugs are poor soluble or not soluble in water and physiologically active solutions (for example, gastric juice).

Taking into the consideration that the activity of drugs is largely determined by their solubility and bioavailability, we have been tasked to increase the water solubility of these drugs in highly stressed joint machining of substances and various types of polymers (polysaccharides, synthetic and plant polymers). In this case, products were obtained, which are called as supramolecular complexes. These complexes have not only considerably increased water solubility and dispersion (formation of nano-sized particles) but higher anthelmintic activity as compared with known preparations. In addition, newly obtained complex ("Medapec" by name) has a new type of activity – it can be used against *Echinococcosis granulosis* when tested *in vivo*. Such properties of this complex suggest the formation of nano-sized anthelmintic DDS.

This technology of mechanochemical modification of anthelmintic drugs is universal and acceptable to search of effective drugs in a number of other organic compounds with poor water solubility (for example, cancer drugs etc.).

TURKISH ROSE PRODUCTS: CHEMISTRY AND PROPERTIES

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R. damascena is widely accepted to have originated from the hybridization of *R. gallica* L. and *R. Phoenicia* Boiss., both of which grow wild in Anatolia. *Rosa* species have been recorded in the Flora of Turkey.

Rose oil is produced in Turkey and Bulgaria by hydrodistillation of the fresh flowers of *Rosadamascena* Miller (Damask rose). Oil is generally obtained in 0.02% yield and the aqueous distillate which in left out of distillation is used and sold as rose water.

Rose concrete is obtained by extracting fresh roses with *n*-hexane. Removal of hexane leaves highly fragrant solid extract. When rose concrete is extracted with ethanol and cold-filtered upon evaporation of ethanol under vacuum, the dark liquid obtained is rose absolute.

Results of analysis of Turkish rose oil for a period of 22 years will be given and the main odorous components characterising the Turkish rose oil will be indicated.

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BIOLOGICAL ACTIVITIES AND PARTHENOLIDE CONTENTS OF *Tanacetum* SPECIES GROWING IN TURKEY

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The genus *Tanacetum* L. (Emend. Briq.) (*Asteraceae*) consists of approximately 160 species worldwide and is represented by 45 species in the flora of Turkey. *Tanacetum parthenium* (L.) Schultz Bip., a well-known medicinal species, has anti-inflammatory, anti-ulcerogenic and anti-migraine activities due to its parthenolide content. As part of our ongoing investigation of *Tanacetum* species growing in Turkey, we have explored parthenolide content, anti-cholinesterase and anti-oxidant activities of the extracts of several *Tanacetum* species.

The extracts obtained from the different parts of various *Tanacetum* species were tested for their inhibitory activity against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), the key enzymes in pathogenesis of Alzheimer′s disease, using microplate assay. Antioxidant activity of the extracts was tested using DPPH radical scavenging activity and ferrous ion-chelating capacity assays. Most of the extracts displayed a remarkable AChE inhibition where the leaf of *T. argenteum* subsp. *flabellifolium* had the highest inhibition (96.68 ± 0.35%). The extracts had moderate inhibition towards BChE, in which the stem of *T. argyrophyllum* var. *argyrophyllum* showed the best inhibition (63.81 ± 3.64%). In contrast to the low level of DPPH scavenging activity observed with the extracts of *Tanacetum* species, most of them showed significant ferric ion-chelating capacity. Total flavonoid content of the extracts was determined spectrophotometrically. Parthenolide, a sesquiterpene lactone, was quantified in these taxa by LC-MS and the leaf of *T. argenteum* subsp. *argenteum* possessed the highest parthenolide amount (2.261 ± 0.002%).

EVARADIX, A PLANT DRUG TO CORRECT ERECTILE DYSFUNCTION: EVIDENCE OF SPECIFIC ACTIVITY

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Erectile dysfunction is a serious disease, as a rule associated with psychological and hormonal problems. In the experimental conditions, erectile dysfunction is modeled in rodents (rats, mice). There are two approaches to study erectile dysfunction: firstly, implant special devices into penis cavernous bodies to register local blood flow in them and extrapolate the data on the sexual behavior; secondly, to study all form of male sexual behavior activated by receptive female after its special preparing (gonadectomised female treated with estradiol 50 μg/rat 48 h before and progesterone 0.5 mg/rat 4 h before testing). A number of mounting the female, intromissions (vaginal penetration) and ejaculations as well as the frequency and latency of them are registered during 20 min test interval. In order to correct erectile dysfunction, a lot of drugs are used: yohimbine (alkaloid from *Corynanthus yohimbe* tree; antagonist of alpha-2-adrenoreceptors); stimulants of the spinal cord functions (Strichninum, Securininum); anticholinesterase inhibitors (Physostigmine, Pyridostigmine, Aminostigmine, Proserinum); phosphodiestherase V inhibitors (Sildenafil – Viagra, Mirodenafil, and analogs); dopamine agonists (Apomorphine, Amphetamine, Cocaine); prostaglandine derivatives (Alprostadil – Caverject, Mews, and analogs); plant adaptogens (drugs from Radix Ginseng, Ginsana, Bioginsengum, Extractum Eleutherococci fluidum, Fructus Schizandrae, Extractum Phodiolae fluidum, Tinctura Echinopanacis, Tinctura Araliae, Tinctura Sterculiae, Extractum Leuzeae fluidum, Ectistenum, Saparalum etc); metabolic protectors (Metaprot, Hypoxen, etc). The purpose of the present work was to study specific activity of food supplement Evaradix positioned as a tool to correct erectile dysfunction. Food supplement Evaradix was registered in Russia by RIA Panda Company as an additional source of vitamins B_6, B_{12} and folium acid, source of quercetine, indol-3-carbinol and panaxosides contained *L*-arginine, yohimbine and cumarines. The main active component of food supplement Evaradix is biomass of *Epimedium macrosepalum* and *Cnidium monnieri* plant cells which are produced by biotechlological method of plant cell cultures in bioreactors. Food supplement Evaradix are recommended for sexual and mental health support for males with erectile dysfunction and other sexual problems. Evaradix (6 mL/kg) and Mirodenafil (5 mg/kg), a drug of comparison, were administered to rats within 13 days with food. The sexual behavior was registered before administration of drugs, on 7^{th} and 13^{th} days of administration and on $7–10^{th}$ day after withdrawal of them. Both Evaradix and Mirodenafil enhanced the frequency of ejaculations, shorted the latencies of mountings, intromissions and ejaculations as well as interejaculations interval. There was the difference in actions of drugs: Evaradix acted as a rule on 7^{th} day of administration (earlier), but Mirodenafil did on 13^{th} day of administration. Besides, there was a period of postaction (7–10 days) after a course of Evaradix, whereas it was not registered after administration of Mirodenafil. Both drugs (Evaradix and Mirodenafil) increased dopamine, noradrenaline and serotonin concentrations in hypothalamus, hippocampus and amygdala and recovered the reduced indices of neurotransmitters levels in gonadectomised rats, did not effect on the blood contents of testosterone, luteinizing and follicule stimulating hormones both in intact and gonadectomised rats (Evaradix slightly increased testosterone level in intact rats). Therefore, the mechanism of Evaradix action involves the direct stimulation of sexual behavior, increase of dopamine in emotiogenic structures of the brain, normalization of testosterone concentrations in gonadectomised animals as well as switching on the positive feedback of neural and hormonal connections. So, Evaradix can be used as a tool to correct the erectile dysfunction in men.

NEUTRAL LIPIDS OF FRUITS PEEL OF *Lycopersicon esculentum*

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Recent research revealed the high antioxidant properties of lycopene that is the bright red pigment of carotenoid group of plants. A rich source of lycopene is the fruits of *Lycopersicon esculentum* (tomato edible, *Solanaceae* family). While the chemical composition of fruit pulp has been studied, there is no data on the lipid composition of tomato peel.

We investigated the neutral lipids (NL) of ripe tomato fruit peel cultivated in the soil (I) and greenhouse (II) in the Tashkent region′s conditions.

Peel was separated from the fruit by hand and air-dried to 6.5% of residual moisture and then sifted with the mesh size of 0.5 mm. Lipids were extracted from peel by petrol (bp 75–80°C). Yield of lipids was 1.25% (I) and 1.22% (II).

According to photoelectric colorimetry results, the content of carotenoids in the peel extract I was 3.7%, and in the peel II – 3.2%. To determine the NL composition, extracts were separated by means of CC on silica gel using petrol with 0–50% diethyl ether. The obtained fractions were re-chromatographed by means of TLC with silica gel in the typical solvents systems. Lipids were identified by comparison with model compounds, specific reagents and by chemical reactions.

In the neutral lipids (NL) of tomato peel I and II we identified the following classes: hydrocarbons, β-carotene, lycopene, esters of fatty acids with aliphatic and cyclic alcohols, triacylglycerols, free fatty acids, fatty alkanols, triterpenols, sterols, xanthophylls and unidentified components.

The extracts I and II were hydrolyzed with 10% alcoholic solution of alkali, the unsaponifiable substances were isolated with yields 0.3 and 0.4% of peel weight. According to photoelectric colorimetry results, the unsaponifiables I and II contained 9.0% (I) and 9.3% (II) of carotenoids enriched in lycopene (77–76%).

Composition of fatty acids isolated from extracts of peel I and II was determined by GLC-method, using the Agilent Technologies 6890N chromatograph with a flame ionization detector and capillary column HP-5 (Table).

TABLE. **Compositions of Fatty Acids of Tomato Peel Extracts I and II**

Extract	Fatty acid, % from mass								
	10:0–14:0	16:0	16:1	18:0	18:1, 18:3	18:2 ω-6	20:0-24:0	$\Sigma_{sat.}$ FA	$\Sigma_{unsat.}$ FA
I	4.3	48.7	0.7	8.1	8.9	27.5	1.8	62.9	37.1
II	8.6	46.7	2.5	9.4	10.1	20.7	2.0	66.7	33.3

Thus, content and qualitative composition of neutral lipids of tomato peel cultivated in the soil and in the greenhouse differ each from other. Fatty acids of the sample 1 (in the soil) have a higher content of ω-6 18:2 than those of sample II (in the greenhouse).

LIPIDS OF *Onosma irrigans* FRUITS

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Onosma irrigans (M. Pop. ex Paul) is perennial, endemic herbaceous plant belongs to *Boraginaceae* family. Ten species of the Onosma genus in the Flora of Uzbekistan are described. This plant is endemic one and it is extended in Tyan-Shan and Pamir-Alayi regions.

We studied lipids of the *O. irrigans* fruits, collected in the Djizak district. Free lipids (or neutral lipids NL) from the ground fruits were isolated by infusing with extractionic benzene (t_b 72–85°C) three time in the 8 of o′clock every time at the indoor temperature. From depriving fat material the connected lipids were isolated by chloroform methanolic mixture (2:1). Yield of NL was 19.4%, and the connected lipids – 0.85% from mass of the fruits.

Photoelectrocolorimetric method allowed to establish, that connected lipids contain 498.6 mg% of chlorophyllic pigments. The connected lipids were separated into NL, glycolipids (GL) and phospholipids (PL), using column chromatography on silica gel, NL were eluted by chloroform, GL – acetone and PL – methanol. Yields of them were % – 0.35; 0.26 and 0.24 accordingly. ATLC on the silicagel of NL, GL and PL of *O. irrigans* fruits showed, that NL contain triacylglycerols (as the main class), hydrocarbons, carotinoides, free fatty acids, aliphatic alcohols, tocoferols, triterpenols and sterols. GL contain as the principal component sterilglycosides, besides they contain digalactosil- and monogalactosildiacylglycerides, ether of sterilglycosides. Among of the classes of PL phosphatidilcholines are predominated, besides phosphatidilethanolamines, phospatidilinosites and phospatidic acids are presented. We used universallic systems of dissolvents, model substances and qualitative reactions. After alkaline hydrolysis of NL, GL and PL from them fatty acids were isolated, and they as methyl ethers were analyzed by GLC with the instrument Agilent Technologies 6890 N with flamingionization detector using capillary column length 30 m and unpolar phase HP – 5 at the temperature from 150 to 250°C, gas-float was helium.

Compositions of fatty acids are given in the Table.

TABLE 1. **Composition Fatty Acids at NL, GL and PL of *Onosma irrigans* Fruit**

Lipid	10:0–14:0	16:0	16:1	18:0	18:1–18:3	18:2	г 18:3	18:4	20:0–24:0	20:1–24:1	Σ_{sat}	Σ_{unsat}
NL	0.3	8.5	0.3	2.8	48.7	22.4	8.1	7.0	0.1	1.8	11.7	88.3
GL	2.9	24.7	–	5.4	36.3	19.4	3.3	5.7	1.2	1.1	34.2	65.8
PL	0.4	25.4	0.2	6.4	28.5	29.3	1.8	6.1	0.9	1.0	33.1	66.9

From data of these we can see, that polyunsaturated fatty acids, which are characteristic for the *Boraginacea* family – 18;3 (6,9,12) or 18;3-w-6, and 18;4 (6,9,12,15) are presented in the all classes of this lipids, but they little are predominated in the NL.

Lipids of *O. irrigans* fruits are studied at first.

CHEMICAL STUDY OF SEEDS OF *Gossypium hirsutum* NEW SORTS

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Selectionists of Uzbekistan continue works on the creation of the new sorts of cotton *Gossypium hirsutum* L. with improved properties of the seeds and fiber.

We studied oil content, fatty acid composition, yield and fiber length of new cotton sorts S-8292 and "Charos". Sort S-8292 was obtained from hybridic combination of L-59 × L-9 by repeated individual selection on *Verticillium dahliae* Kleb. infection background. Sort "Charos" was obtained using repeated individual selection by intra- and interspecific hybridization of hybrid combination (F1 (SBE-25, 2 (Mexico) x S-9072) × S-9072. Results are shown in the Table 1.

TABLE 1. **Indicators of Seeds and Fiber of New Sorts of Cotton *Gossypium hirsutum***

Sort	Weight of 1000 seeds, g	Oil content, %	Yield of fiber, %	Length of fiber, mm
S-8292	124.0–125.0	20.6	36.5–37.5	33.2–33.5
"Charos"	105.0–106.0	20.8	38.0–38.5	33.0–34.0

Fatty acid composition of oil, isolated from seeds is determined by GLC on the Agilent Technologies 6890N chromatograph with a flame ionization detector, capillary column HP-5 (30 m × 0.32 mm, the thickness of the stationary phase, 0.25 mm), carrier gas-helium, temperature programming from 150°C to 270°C. Compositions of fatty acids are presented in the Table 2.

TABLE 2. **Fatty Acid Composition of Seed Oil of New Sorts of Cotton**

Sort	14:0	16:0	16:1	17:0	18:0	18:1	18:2	20:0	22:0	Σ_{sat}	Σ_{unsat}
S-8292	1.2	27.4	0.7	0.1	2.2	17.5	50.6	0.2	0.1	31.2	68.8
"Charos"	1.3	29.6	0.8	0.1	2.3	18.3	47.2	0.3	0.1	33.7	66.3

Thus S-8292 sort compared to "Charos" has a lower yield and fibre length, but it has large mass of seeds with comparable oil content in their and higher (3.4%) content of biologically active omega-6 linoleic acid.

STRUCTURE OF KOPSININE

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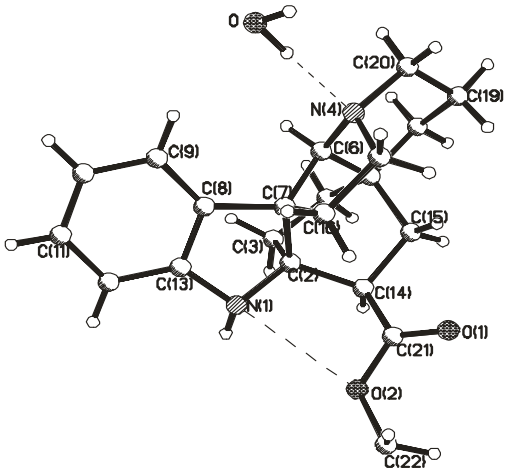
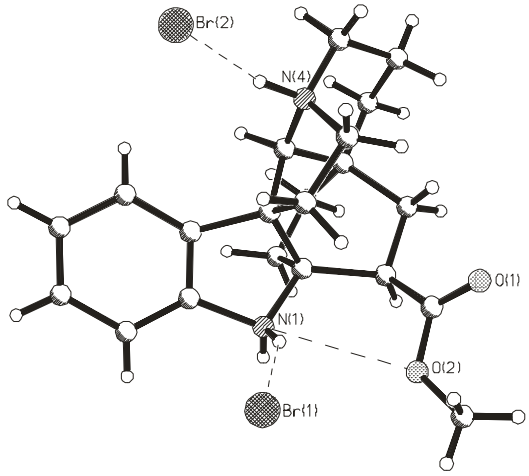
Indole alkaloid kopsinine with analeptic pharmacological properties [1] is isolated from the plant *Vinca erecta*, the structure and stereochemistry of which was thoroughly studied [2]. The absolute configuration of kopsinine (**1**) have established by the X-ray analysis, for which also hydrobromide crystals were obtained and studied (**2**).



Kopsinine (**1**)



Kopsinine dibromide (**2**)

Asymmetric centers of alkaloid (according Flack parameter (0.02 (4) 2) have the following meanings: 2*R*, 5*R*, 6*S*, 7*R*, 14*R*. Protonated N4 atom in the molecule **2** accepts the *R*-configuration.

The molecular structure of the base and salts kopsinine is identical despite of deprotonation N1 and N4 atoms of the salt, which indicates rigidity of heterocyclic skeleton. Five-membered ring in the indoline nucleus takes 2α-envelope, and the other five-membered heterocyclic ring has 4β-envelope conformation. Six-membered rings adopt the conformation of a bath - and heterocyclic–armchairs.

Crystals of **1** were found as monohydrate containing water molecules in a 1:1 ratio. In the crystal, the H atom of the water molecule is H-bonded to the atom N4. The second H atom of water bound by weak H-bond with the carbonyl group of converted alkaloid molecule.

In the crystal of **2** protonation of both N1 and N4 nitrogen atoms observed. One of Br atoms bounds to protonated N4 nitrogen, and second Br atom - to NH_2-group.

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N-DIMETHYLETHANOLAMINE AND ISATROPIC ACID ESTER

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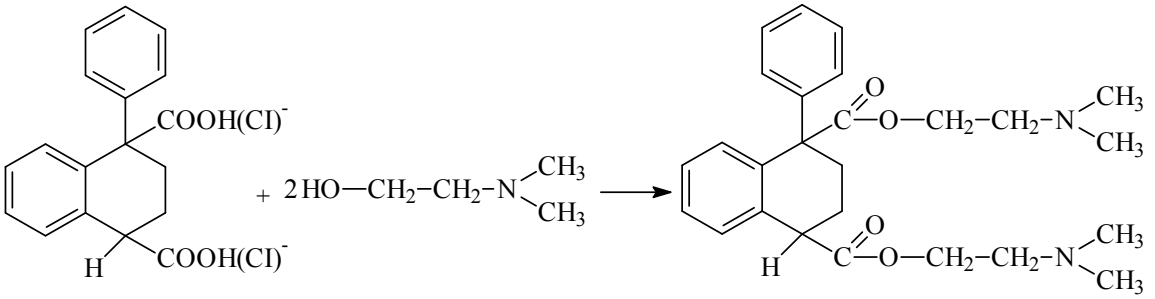
It is known that tropane alkaloids of *Solanaceae* family have a high physiological activity, and some of them are used in medicine as useful medicinals. For example, atropine, hyosyamine, scopolamine are main alkaloids of *Solanaceae* family plants, however dimeric tropane bases separated from species of this family (*Datura stramonium, D. inoxia, Physochlaina alaica* etc.) in minor amounts displayed interesting pharmacological properties. Thus, α- and β-belladonnins and α- and β-scopodonnins are isolated from these plants, and a number of derivatives of practical interest were synthesized.

Continuing this works, we synthesized compound **1** on the base of isatropic acid obtained by hydrolysis of a mixture of α- and β-belladonnins formed during pyrolysis of available alkaloids atropine and *N*-dimethylethanolamine. From the resulting dl-isatropic acid with melting point 208–209°C by reaction with thionyl chloride the dichloroanhyidride was synthesized, which further was estherified with *N*-dimethylethanolamine in the presence of triethylamine in toluene. The reaction product, m.p. 186–187°C has the structure **1** and the following spectral characteristics. IR spectrum (cm^{-1}): 1730, 1600, 1500. Mass spectrum (*m/z*): 438 (M), 367 $(M - 71)^+$, 322 $(M - 116)^+$, 252 $(M - 176)^+$, 71. Peak of ion with *m/z* 367 corresponds to the separation of $-CH_2-CH_2-N(CH_3)_2$ group from the molecular ion, peak of ion at *m/z* 322 corresponds to the loss of $CO-O-CH_2-CH_2-N(CH_3)_2$-group by M^+, peak of ion with *m/z* 252 formed by splitting of two $-O-CH_2$ $-CH_2-N(CH_3)_2$ group fragments from M^+. Peak of ion at *m/z* 71 is splinter fragment of $-CH_2-CH_2-N(CH_3)_2$ group. Reaction of compound **1** to methyl iodide gives diiodomethylate soluble in water.



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WATER SOLUBLE NITROGEN-CONTAINING COMPOUNDS OF *Crambe* GENUS

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Crambe orientalis Butk. et Majlun. and *C. kotschyana* Boiss. are the endemic perennial herbs of *Cruciferae* family are widespread in Uzbekistan. For the first time, we studied alkaloids and their low molecular metabolites of these species. The existence of alkaloids in these species was established for the first time.

The chloroform fraction of alkaloids from the alcoholic extract of the aerial parts and roots of two *Crambe* species were separated according to their solubility in various organic solvents. Using column chromatography on silica gel the sulfur-containing alkaloids goitrin and goitridin, as well as *N*-(2-benzimidazolyl)-*O*-ethylcarbamate known from the literature had been isolated.

Following these studies, an aqueous-alkaline solution left after separation of total alkaloids, in which the nitrogen-containing compounds presented, were assayed for amino acid content.

It is known that some species accumulate free amino acids that are typical for this species. Determination of free and bound amino acids is widely used in the study of individual stages of nitrogen metabolism and study of nutritional value of plants.

In connection with the abovementioned, we made the separation and quantitative determination of protein in aqueous-alkaline solution. The solution contained 8% of protein. Free and bound amino acids were determined on amino acid analyzer T339. Bound amino acids were determined after acid hydrolysis by 5,7-*N* hydrochloric acid at 110°C for 24 h under vacuum. It was established that bounded amino acids are prevailed. Amino acid composition of the protein isolated from *Crambe* contained essential amino acids–valine, threonine, isoleucine, leucine, lysine, phenylalanine, histidine, arginine. The replaceable amino acid content in the protein is balanced too.

We used HPLC method to determine the molecular weight of the isolated protein. The molecular weight was determined by constructing a calibration curve using the dependence of protein molecular weight logarithm from the retention volume. It was established that the molecular weight of the protein (peptide) is 10 kD.

INFLUENCE OF COTTON SEED GRADE OF QUALITY ON THE COMPOSITION OF SOAPSTOK

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Cotton soapstok is a great waste of rubbish which comes into being in the process of raw cotton oil recycling. Rising effect of its recycling and widening sphere of using the soapstok in agriculture is an important problem in the oil branch. Its decision is being retained because of lack of information on components of this waste.

The facts on influence of quality of cotton seed on chemical composition of soapstok are not much enough, that′s why this research is being remained actual.

We analyzed the composition of soapstok appeared during the chemical fining of of oil. Oil obtained by recycling of mixture of average grade and high grade cotton seed of selection sort "Bukhara-8" at the factory "Karshi yog′ ekstraktsiya".

Total oil (TO) and neutral oil (NO) are isolated from the soapstok by the famous methods with yields of 18.2 and 2.5% accordingly. In order to determine the composition of oils the samples were separated by TLC on silica gel using petrol (72–78°C) – diethyl ether (8:2). In TO and NO accordingly (% from weight); hydrocarbons (2.7 and 5.8); triacylglycerols (TAG, 49.5 and 30.1); free fatty acids (FFA, 27.6 and 31.2); triterpenols and sterols (9.0 and 21.9); polar components (11.2 and 11.0) were identified.

Composition of fatty acids isolated from TO, NO, TAG and FFA was determined by GLC-method, using the Agilent Technologies 6890N chromatograph with a flame ionization detector and capillary column HP-5 (Table).

Oil, Class of lipid	Fatty acids, % from mass								
	14:0 15:0 17:0	16:0	16:1	18:0	18:1	18:2	20:0, 22:0	$\Sigma_{sat.}$	$\Sigma_{unsat.}$
Total oil:									
TAG	1.6	32.5	0.9	2.9	20.6	41.2	0.3	37.3	62.7
FFA	1.5	35.4	0.7	3.0	22.7	36.3	0.4	40.3	59.7
Neutral oil:									
TAG	1.9	26.3	0.9	2.6	19.3	48.4	0.6	31.3	68.7
FFA	1.1	16.6	1.0	1.5	24.3	55.5	–	19.2	80.8

So, the investigated soapstok obtained from the oil of average grade and high grade cotton seed of "Bukhara-8" sort is characterized by low contents of TO and NO, NO of this soapstok is enriched by sterols and triterpenols (22%), while 55% free fatty acids of NO consists of ω-6 18:2 (linoleic) acid.

DESIGNING OF RECOMBINANT PLASMID DNA pYES2/CT-PreS2-S, ENCODING PRES2-S REGION OF THE HUMAN HEPATITIS B VIRUS

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The recombinant plasmid DNA containing rDNA M-HBsAg of human hepatitis B virus was designed. The recombinant plasmid DNA is created on the basis of high copy replication vector pYES2/CT, which designed for expression of recombinant proteins in *Saccharomyces cerevisiae*, containing the following elements (genes): *GAL1* promoter, polyhistidine (6xHis) *tag*, *URA3* auxotrophic marker for selection of yeast transformants and Ampicillin resistance gene for selection in *E. coli.* For cloning, in accordance with the physical map, the vector pYES2/CT, as well as the previously obtained plasmid for baculovirus expression system pBacPAK8-polh-preS2-S containing this gene were digested by *EcoRI* and *NotI*.

As a result the preS2-S fragment (by elution) and pYES2/CT vector with complementary "sticky" ends were obtained. After ligation in molar ratio of 1:10 (vector: insert) using the T4 DNA-ligase, the obtained plasmid was transformed into *E. coli* NEB-5α.

Identification of the recombinant clones was carried out using PCR and restriction analysis.

This plasmid DNA may be used for expression in yeast the recombinant M-HBsAg encoded by the preS2-S region of human hepatitis B virus.

QUANTITATIVE DETERMINATION OF FLAVONOIDS IN AERIAL PART OF *Glycyrrhiza glabra*

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The aerial part of *Glycyrrhiza glabra* contains saponins, tannins, flavonoids, essential oils, sugars, pigments and other substances. This opens up prospects for the use in medicine herb of *Glycyrrhiza glabra* as a possible raw material for the creation of anti-inflammatory, antispasmodic, anti-viral action agents.

Previously, when studying the pharmacological properties of flavonoids, isolated from the aerial parts of *Glycyrrhiza glabra*, is set that is inherent in them an anti-inflammatory action [1].

Glycyrrhiza glabra grows in floodplains Amu Darya, Syr Darya and Zarafshan in Uzbekistan, as well as on the banks of its tributaries, and it forms almost pure liquorice bushes [2]. Despite this, the dynamics of the accumulation of flavonoids in the aerial parts of the plant, depending on the location of growth is still poorly understood.

In order to create medical preparation with anti-inflammatory action on the basis of licorice flavonoids were analyzed raw materials harvested in different regions of Uzbekistan in 2011 and 2012.

Quantitative determination of flavonoids in alcoholic extract of aerial parts of *Glycyrrhiza glabra* was performed by spectrophotometer method. The absorbance of the test solution was measured on spectrophotometer at a wavelength of 292 nm. The absorbance of the reference solution of pinocembrin was measured in parallel [3].

Thus, on the basis of the obtained results showed that the content of flavonoids in the samples of raw materials harvested in 2011 in the Syrdarya region was 0.95%. Also found that in the aerial parts of *Glycyrrhiza glabra*, harvested in 2012, the flavonoid content varies from 1% to 3% depending on the place of growth.

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EXTRACTION OF FLAVONOIDS FROM ROOTS OF *Ammotamnus lehmannii*

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Nowadays at the Institute of the Chemistry of Plant Substances on the base of flavanoids from *Ammotamnus lehmannii* researches for develop of new medical preparation for treatments of disease of liver are continued.

For the reason undertaking the efficient extraction were studied parameters, influencing upon yield of flavanoids from roots of *Ammotamnus lehmanni* such as selection solvents and crushed of the raw materials.

Results of investigations have shown that the optimal solvents for extraction of raw material with a high yield of flavanoids are methanol and ethanol with concentration not less than 90%. Also it was established, for extraction of the sum flavonoids are recommends used crushed raw material with sizes of particles 2–6 mm.

For choice of the optimal methods of extractions of flavanoids from roots of *Ammotamnus lehmanni* were considered such methods as maceration, maceration with mix, extraction by Sokslet method and battery way of extraction.

As a result called on experience is revealed that when undertaking the extraction by maceration method with mix grows shorter time, necessities for extractions of raw materials, however, hydromodul of process increases in 2 times nearly. But this in turn brings for increase the consuption of solvents (ethyl alcohol).

At extractions of raw materials by battery way and by Sokslet method hydromodul and time of the process of extraction grew shorter in 3–4 times in contrast with extraction by maceration method.

The results have also shown that yield of flavanoids greatly does not change from chosen way of extraction. Considering consumption of used solvent, and time, necessities for extraction, are offered battery way and extraction by Sokslet method.

ALKYLATION OF THIOPHENE ANALOGIES OF QUINAZOLIN-4-ONES IN INTERPHASE CATALYSIS CONDITIONS

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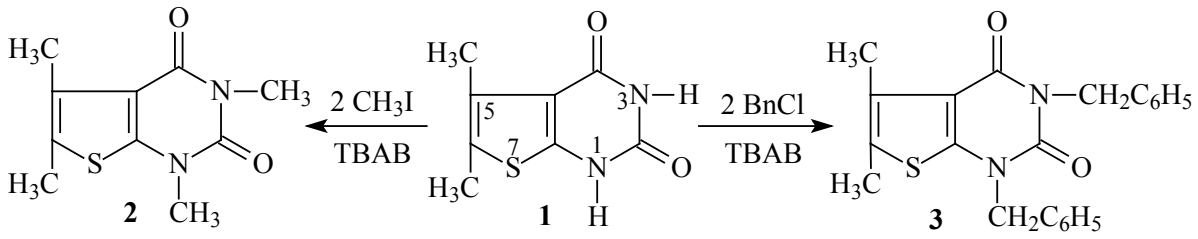
Pyrimidine moiety is part of many natural (alkaloids, nucleic acids) and synthetic (furo-, thieno-, pyridopyrimidin-4-ones) compounds. There are many biologically active substances, which recommended for application in medicine and agriculture [1–3].

Pyrimidin-4-ones, condensed with thiophene ring (thieno[2,3-*d*]pyrimidin-4-ones) are plural reactivity heterocyclic compounds. For example, 2-oxo-5,6-dimethylthieno[2,3-*d*]pyrimidin-4-one (**1**) has some reactionary centers: nitrogen atoms (N1, N3), carbonyl groups at C-2 and C-4, methyl groups at position 5, 6.

In order to determine the influence of the temperature and the nature of alkylating agents and solvents we have studied the alkylation of 2-oxo-5,6-dimethylthieno [2,3-*d*]pyrimidin-4-one (**1**) with methyl iodide and benzylchloride in absence and presence of interphase catalysts:



2 **1** **3**

Reactions were carried out in interphase catalysis (IPC) conditions in the presence of TBAB (C_6H_6/H_2O) at 55–60°C and corresponding 2-oxo-1,3-dimethyl(dibenzyl)-5,6-dimethylthieno[2,3-*d*]pyrimidin-4-ones (**2, 3**) were synthesized in yields 61–75%. It is necessary to emphasize, that at absence of the interphase catalyst the reaction products are formed in low yields.

These compounds (**2**, **3**) will be used as synthones for investigations of electrophylic ipso-substitution reactions.

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TAUTOMERY OF α-HYDROXYMETHYLIDENE-MACKINAZOLINETHIONE

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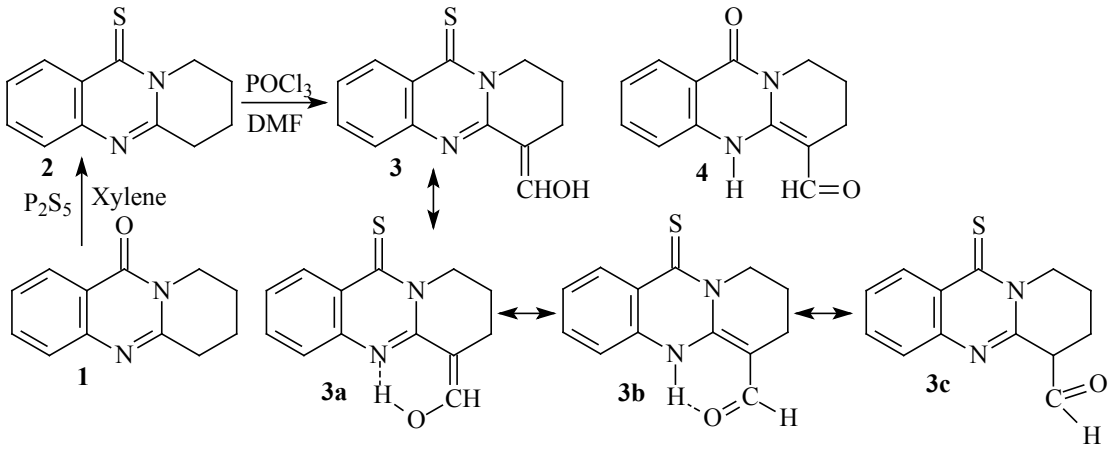
Tricyclic quinazoline alkaloids represent the certain practical interest as well as some of them have found wide application in medical practice [1, 2]. Thioanalogues of these compounds are also interest from the theoretical point of view for comparison of their reactionary ability with oxygen analogues – corresponding quinazolin-4-ones.

Previously mackinazolinone (**1**) was isolated from plant [3], and its reactions with various electrophylic reagents were investigated [2, 4].

Recently it is revealed by us, that at interaction of mackinazolinone (**1**) to phosphorus pentasulphide mackinazolinethione (**2**) is formed, which exclusively turns in α-hydroxymethylidene-mackinazolinethione (**3**) under action of Vilsmeier-Haack reagent ($POCl_3$-DMF) [5]. It has been shown, that the oxygen analogue of compound **3** is in stable enaminoaldehyde form (**4**). Formylation of compound **2** can proceed with formation of isomers – iminoenol (**3a**), enaminoaldehyde (**3b**) and iminoaldehyde (**3c**) forms which may be in the following resonance forms:



Formation of intramolecular hydrogen bonds in iminoenol isomer (**3a**) leads to increasing of its stability, that was established by IR- and ^{1}H NMR-spectroscopy. The data on tautomeric statuses in various solvents will be discussed.

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THE INFLUENCE OF ULTRASONIC WAVES ON MAIZE PROTEIN

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The protein molecules in the field of ultrasonic waves are exposed to various chemical and physical-chemical transformations, which may be controlled in the most cases. These changes relate to the structure, shape and function of the sonicated protein. The nature of these changes depends largely on the structure of side and end groups of protein and the nature of gas present in the sonicated aqueous medium.

The milled maize grain of Uzbekistan 420 sort is used as the test object. Extraction was carried out with an ultrasonic device Bandelin Sonorex RK 100 in order to increase yield and reduce the time of extraction. Extraction of protein from maize grain was carried out using an aqueous extraction at various ratios (1:2. 1:5, 1:10) at temperature 15°C. The results are shown on the Fig. 1.

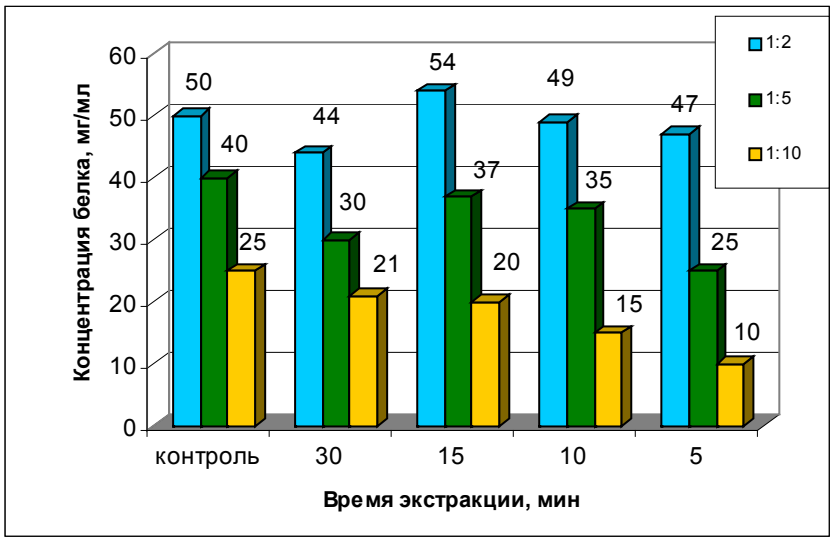

Fig. 1. Dynamics of water-soluble proteins output change and determination of the optimal hydromodulus in ultrasonic treatment

As the above data shown, the optimal ratio in ultrasonic extraction of proteins is the ratio of the grain sample to extractive solvent (water) equal to 1:2. Ultrasonic extraction have to carry out at 10–15°C. The optimal duration for the extraction of this ratio was 15 min. There is no significant temperature rise resulting in denaturation of proteins in this period.

As the results shown, under the ultrasonic wave influence the yield of bifunctional proteins is higher as compared to extraction with a magnetic stirrer [1].

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IMPROVING OF THE METHANOGENESIS PROCESS OF PLANT WASTE

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The main components of plant′s waste are polysaccharides, the number of which in different kinds of raw materials varies from 40 to 75% and lignin – non-carbohydrate component whose content is 15–38% [1]. Anaerobic methanogenesis of the vegetable waste's rich of lignocellulose – a long process with a small out of biogas (0.2 m^3 kg of dry mass withdrawal).

The aim of our study showed him smiling and accelerating the methane plant waste pharmaceutical production by their first pre-solid phase and fermentation (PSP) followed methanogenesis hydrolyzate.

Vegetable waste (10 kg) after separation from their biologically active substances with humidity awn 85–90% seeded communities of soil microorganisms-destructors. PSP performed in plastic ditches, for 3 days, at 30°C with occasional stirring. Thereafter, the substrate was filled with hot water (45–50°C) with stirring to within hours, the solid and liquid phases were separated by filtration, the solid residue was further PSP.

The liquid phase is used for methane fermentation of by anaerobic methanogenic microorganisms, which was carried out in an airtight plastic reactor volume 5 L, periodical regime, with temperature of fermentation 30–35°C, pH 6.5–7.0 (experiment I). For comparison, vegetable waste (10 kg) were subject to anaerobic methanogenesis without aerobic hydrolysis (experiment II). To reduce the acidity of the medium in both experiments using lime. Biogas production was measured using a graduated wet gas tank. The degree of decomposition of the substrate was determined by a known method [2]. The results are shown in Table 1.

TABLE. **Effectively of Methanogenesis of Plant waste with pre-solid fermentation and without it (PSP)**

Experiment	T, °C	pH	The duration of the fermentation, day	Biogas production, m^3	The degree of decomposition of the substrate, %
I	35.0	6.5	11	7.0	66.0
II	35.0	6.5	38	2.4	30.0

Thus, PSP plant waste increases the decomposition of substrate by 36%, the yield of biogas is almost 3 times reduces duration of the process of methanogenesis is more than three times compared to traditional anaerobic methanogenesis.

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FERMENTATIVE ISOLATION OF STRONGLY BOUND LIPIDS FROM COTTON SEEDS

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The seeds of oil plants lipids are free, bound and strongly bound forms. Free (FL) and bound lipids (BL) can be easily extracted from the seed kernels by organic solvents without degradation. After removal of FL and BL strongly bound lipids (SBL) is isolated by acid hydrolysis, but not in the native form, however they component composition is poorly understood. It is shown that native SBL can be identified by proteolysis solvent cake [1]. Found in the products of proteolysis neutral lipids and glycolipids, phospholipids, but not detected.

We have to isolated SBL from cotton seed varieties S-9085 for the first time, by the complex of enzymes of microscopic fungi (experiment I). For comparison, SBL are isolated by protease «Rockenzym 6500-L», (Iran) (experiment II) and acidic hydrolysis (experiment III). The FL and BL have to extracted from the ground seeds with a mixture of chloroform–methanol (1:2). Proteolysis of solvent cake conducted with 2% protease (weight of substrate) at pH 7.0 and a temperature of 45–50°C, with stirring, for 5 h.

After finish proteolysis the substrate was separated by filtration, SBL from the aqueous phase extracted with chloroform, from the cake - Folch method. Fermentation of complex of enzymes were 1% of enzymes at pH 5.0, a temperature of 45–50°C, with stirring, for 3 h. The reaction products were isolated as described above. Acid hydrolysis was carried out by a known method. The experimental results are shown in Table.

TABLE. **Yield of Strongly Bound Lipids from Cake of Cotton Seeds**

Experiment	Duration of hydrolizatoin, h	Yield of strongly bound lipids from a mass of cake, %		The sum of strongly bound lipids, %
		solid phase	liquid phase	
I	3	0.010	0.038	0.049
II	5	0.008	0.002	0.010
III	48	0.065	–	0.065

Composition of lipid determined by TLC on Silufol plates and the solvent system used for analysis of neutral lipids, phospholipids and glycolipids. To identify the lipid classes chromatograms were developed in iodine vapor, 50% H_2SO_4 with heating and reagent Vaskovsky. In fermentation experiment I major classes identified above groups of lipids, including phospholipids.

Thus, enzymes microscopic fungi allow deeper hydrolyze complex polysaccharides, proteins and lipids of solvent cake than protease and liberate more SBL and phospholipids in native form.

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ANTIARRHYTHMIC ACTIVITY OF ZERAVSHANIZINE

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Showing antiarrhythmic activity of diterpene alkaloids were defined by F. N. Dzhakhangirov and other scientists. Zeravshanizine is a diterpene alkaloid isolated from *Aconitum zeravschanicum* plant. Taking into consideration its anesthetic and analgesic activities, in our researches we studied antiarrhythmic activity, which is connected with its mechanism.

The purpose of our work is studying an antiarrhythmic activity, and its influence to conducting system of heart, also defining poisoning dose LD_{50}.

The antiarrhythmic activity of the zeravshanizine was studied by the method of the aconitine arrhythmia on narcotized rats (sodium pentobarbital, 50 mg/kg, intraperitoneal introduction), their weight were 200–240 g. It was studied comparing with antiarrhythmic preparations in the same condition. The antiarrhythmic activity of preparations and zeravshanizine were recorded on electrocardiograph. LD_{50} and ED_{50} of preparations were defined by the method of Litchfield–Wilcoxon.

The antiarrhythmic activity in intravenous injection of zeravshanizine was 30–100% in 0.25–1 mg/kg doses. Basing on the abovementioned results, the ED_{50} 0.5 mg/kg, LD_{50} 34 mg/kg and (LD_{50}/ED_{50}) 68 were calculated. The results obtained from experiments showed, that this diterpene alkaloid is better than antiarrhythmic preparations – quinidine, novocainamide, aymaline, rytmilen and mexitil in antiarrhythmic effect and breadth of therapeutic action. Also, analyses of ECG rates showed, that zeravshanizine reduced impulse transfers from AV node to the bundle of His, conduction oa ventricular internal impulse, lowered belong dose of the automatism of the heart.

Thus, zeravshanizine displayed antiarrhythmic activity higher, than I class antiarrhythmic drugs. It is desirable to continue investigation of pharmacological activity.

BILE SECRETORY AND HEPATOPROTECTIVE ACTIVITY OF *Codonopsis clematideae* PLANT

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The problem of diseases of the liver, gastrointestinal tract, kidney and urinary bladder attracted attention of researchers and remains one of the most complicated health pathologies. Hepatoprotective range of funds in the pharmaceutical market is currently inadequate and represented a fairly narrow range of active ingredients, which often differ only by trade names and manufacturers.

Modern hepatoprotective and cholagogic means not fully meet the requirements of practical medicine. They are not effective for long-term use, in connection with the potential to cause side effects and complications. In this regard, high-performance search therapeutics, providing multilateral positive effect on the functional state of the liver in view of its defeat polyetiology continues to be one of the leading problems of modern pharmacology.

The import drugs of this action type, such as Liv-52, Karsile, Silybine and Legalone have a temporary effect, i.e. after the termination of their admission the symptoms of liver disease are renewed. Another well-known drug of similar action – *Essentiale* also has side effects without improving the antitoxic function of the liver and intrahepatic cholestasis worsens.

Therefore, the search for effective drugs with low toxicity is important. One of these drugs can be developed by our local drug derived from plants *Codonopsis clematidea*, which grows everywhere in Central Asia.

The preparation consists of water-soluble alkaloids *Codopsinine* and *Codonopsinine*, as well as the flavonoid *Luteoline.* Screening studies have shown, that the total alkaloid-flavonoid complex of plants *Codonopsis clematidea* is quite effective drug, surpassing more than two times the action of commonly used in medicine *Berberine* and *Flamine*.

The drug has a normalizing effect on the disturbed metabolism, exhibits strong antioxidant, cholagogic and hepatoprotective effect.

The drug is recommended for prophylaxis and treatment of hepatitis of various etiologies, including viral treatment of acute and chronic liver disease. It can also be used at gepatoholecystites, fatty degeneration of the liver, liver disease with functional loads caused by poisoning, conditions associated with an increased influx of substances that burden the liver function.

In hepatoprotective properties the alkaloid-flavonoid complex of plant *Codonopsis clematidea* surpasses the imported drugs Liv-52, Essentiale, Legalone, Carsile and Flamine. The main indications for testing of the drug in medicine are acute and chronic liver disease (toxic, viral hepatitis), hepatocholecystitis, cholangitis, biliary dyskinesia.

POLYPRENOLS OF LEAVES OF THE *Malvaceae* FAMILY PLANTS

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Malvaceae plants are rather wide spread in Uzbekistan. In the republic 6 species grow: *Gossipium, Althaea*, *Alcea*, *Malva*, *Abutilion, Hibuscus* and some other types [1].

It is known, that different solvents or their mixture, for example alcohols, hydrocarbons and their mixtures are used for extraction of polyisoprenoids from plant raw material [2]. For making biologically active additives activations to nutrition the safe pollution-free solvents are preferable. Proceeding from that, we obtained alcoholic extracts of plants *Gossypium hirsutum* L. (Namangan-77 and 108-F sorts), *Althaea armeniaca, A. officinalis, Alcea nudiflora, A. rosea, Abutilion theofrasti, Hibuscus thronium, Malva sylsestris,* which were partitioned on the chromatograph column. Qualitative and quantitative composition was determined using HPLC, HPTLC and chromato-mass-spectrometer.

Qualitative and quantitative composition of the sum of the polyisoprenoids, isolated from different sorts and types of *Malvaceae* plants, will be compared. Results on study of accumulating dynamics in plants vegetation, methods of their analysis and their biological activity described.

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ON THE PHARMACOLOGY OF CYCLOBUXINE D

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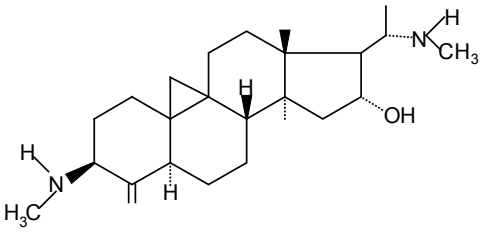
Steroidal alkaloid cyclobuxine D isolated from several species of Box tree (*Buxaceae* fam.). According to literature, LD_{50} of cyclobuxine D at per os, s.c. and i.v. administrations subsequently were 137, 100 and 20 mg/kg accordingly. On narcotized cats in doses 3–5 mg/kg the alkaloid decreases arterial pressure for 20–40 mm. Hg during 30 min. Cyclobuxine D possess by myorelaxant activity. It revealed antimicrobial, antiprotosoa and anticancer activities. This compound diminished the alterative changes in myocard at partial occlusion of myocardial vessels. According our studies, the compound in dose 1 mg/kg didn′t influenced, while at dose 3 mg/kg increased locomotor activity of white mice. In this dose the compound prolonged duration of soporific action of sodium pentobarbital. It deleted the seizures caused by strychnine, but didn't influence on pentetrazole seizures. Like atropine the cyclobuxine D abolished arecoline tremor and salivation, negative chronotropic activity of acetylcholine on narcotized rats. In these experiments cyclobuxine D revealed comparatively high M-cholinoblocking activity. On isolated rat ileum cyclobuxine D revealed low activity, approximately only 0.25% of atropine activity. Summarized finding are presented in the Table.

Studied compounds	ED_{50} and EC_{50} of M-cholinoblocking activity of alkaloids			
	On heart, mg/kg	On ileum, g/mL	Salivary glands, mg/kg	CNS Arecoline tremor, mg/kg
Atropine	0.015 (100%)	$2.2 \cdot 10^{-9}$ (100%)	0.59 (100%)	0.79 (100%)
Cyclobuxine	0.078 (19.2%)	$5.4 \cdot 10^{-7}$ (0.18%)	1.9 (32.2%)	2.4 (30.4%)

Thus, the studies of cyclobuxine D have revealed some degree of sedative and high degree of M-cholinoblocking activity on heart, secretory organ and CNS, but comparatively low activity on ileum. Chemical structure of cyclobuxine D is presented below.



ON PHARMACOLOGICAL ACTIVITY OF SEVKORIDININE

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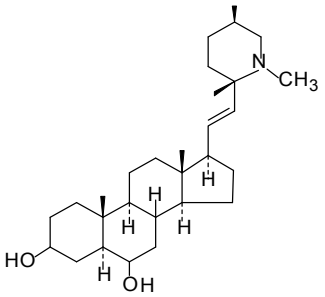
Aminospirit sevkoridinine isolated for the first time in Institute of Chemistry of Plant Substances from endemic Central Asian plant *Korolkowia sewertzowi*. Pharmacological studies have showed the excitatory effect, concomitant with exophthalm, increased reflectory excitation on sound and pain stimuli. Seizures, like pentetrazole attacks, sometimes took place. LD_{50} was 44 (36÷53) mg/kg i.v. Sevkoridinine increased the seizures caused by pentetrazolum and strychnine.



In experiments on narcotized cats the alkaloid in dose 3.0 mg/kg called sharp and short lasting hypotension, bradicardia, and decreasing of respiration frequency, that altogether may be qualified as Bezold-Jarish reflex. At another part of experiments moderate hypotension revealed after latent period of 20–45 min. took place. In third parts of experiments arterial pressure isn't changed, of even some increased. In these experiments decrease of force and frequency of heart contraction took place. In mentioned dose the alkaloid reveal vagolytic activity of different character. In some vagolytic activity soon after drug administration experiments took place, at another part the vagolytic activity appeared after latent period 30–45 min. Duration of vagolytic effect lasted 90–240 min. On isolated rat heart the alkaloid in concentration 10^{-5} g/mL call decreasing of contractility force, frequency of contractions and arrest it. Sevcoridinine reveal antiarrhythmic activity on aconitine arrhythmia model on anesthetized rats. In dose 3 mg/kg the alkaloid didn't influenced on neuro-muscular conduction. On isolated rat ileum the alkaloid in concentration 10^{-5} g/mL abolished the contraction of intestine called by acetylcholine and $BaCl_2$ after 20 min. exposition. Abolition of the mentioned effect took place after 30 min. of washing. On isolated frog sartorius muscle sevkoridinine changed the character of veratrinic effect of veratroylzygadenine. Veratrinic postcontraction become short or sometime disappeared, but the typical contraction height increased considerably. Sevcoridinine in 1% concentration revealed the anesthetic activity on rabbit cornea. On rabbit the intradermal injection of 0.1% solution called anesthetic activity, that passed until nerve death.

Thus, pharmacological studies of sevcoridinine revealed contradiction of it pharmacological activity. This compound revealed as excitation, as blocking activity, and may be considered as a partial agonist and partial antagonist for different receptor species.

ANTIOXIDANT ACTIVITY AND HEMODYNAMIC EFFECT OF POLYSACCHARIDES OF HIGHER PLANTS IN BLOOD LOSS

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Polyfunctional phytopolysaccharides are widespread in nature and have a high diverse physiological activity and specific physical features. For the targeted usage of polysaccharides in different sectors of the economy resolving a number of issues of biopolymer′s structural peculiarities and interrelation of biological activities in "structure–activity" system is needed.

The purpose of the research is investigation of structural peculiarities of different groups of polysaccharides in promising local plants and revealing their antioxidant features and hemodynamic effect under acute blood loss.

With this purpose, galactomannans, galactan-comprising polysaccharides isolated from plants of the local region were selected and indicated as K_1, K_2 and K_3.

Galactomannanes and glucogalactans are referred as branched polysaccharides. The backbone of the galactomannan consists of 1,4-β-*D*-mannopyranose residues and some mannose residues are substituted with α-*D*-galactopyranose residue at O-6 position, glucogalactans-polysaccharides with 1,6 α-*D*-galactopyranose units, in which glucose oligosaccharide fragments are attached to C-2 atom of the galactopyranoses main chain.

Antioxidant activity of these polysaccharides in free-radical oxidation of polysaccharides was studied on the model system with Na-nucleate as oxidation substrate and Fe^{2+} as oxidation activator.

To study the hemodynamic effect of polysaccharides a model of acute blood loss was applied. The experiments were carried out on 60 chinchilla rabbits (weight 2.2 ± 0.2 kg), blood loss caused by portioned bloodletting, reducing blood pressure till 40 mm Hg in 1 h. The results shown, that polysaccharides possess by antioxidant activity, the tested blood substituents effectively protected isolated cells against free radical oxidation. The degree of antioxidant activity of blood substituents, containing K_1, K_2 and K_3 are directly dependent on the concentration of iron and time of action in the biological system. New blood substituents containing polysaccharide complexes with metabolites K_1, K_2, K_3 have a pronounced hemodynamic effect of acute blood loss.

ARABINOGALACTANS OF TWO *Ferula* SPECIES

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The genus *Ferula* belongs to the family *Apiaceae* and comprises about 150 species. It is known from the literature, that aerial part of this genus is rich for biologically active substances, generally represented by flavonoids.

The purpose of our research is to study the polysaccharides of aerial part of two *Ferula* species: *F. varia* and *F. kuhistanica* from the local region and their specific biological activity. Water-soluble polysaccharides (WSPS), pectins (PS), and hemicellulose (HC) ere isolated by well-known methodologies. The presence of WSPS in aerial part of *F. varia* and *F. kuhistanica* were established in quantities 16.5% and 9.1%, respectively.

By fractional precipitation of WSPS with alcohol the homogeneous fractions of arabinogalactan with with yield 14.3 (*F. varia*) and 24.8 (*F. kuhistanica*) and with Gal–Ara 1.2:1.0 proportion were obtained. It should be noted, that arabinogalactan (AG) from *F. kuhistanica* contained insignificant amount of glucose together with the abovementioned monosaccharides.

In IR-spectrum of arabinogalactans the following characteristics of absorption band were identified: 878; 1255; 1418; 1597; 1731; 2957–3363 cm^{-1}.

Chemical structure of AG were studied using chromium, periodate oxidation and methylation methods. The results of AG oxidation with chromic anhydride indicated the presence of β-glycosidic linkage between monosaccharides residues.

The results of AG periodate oxidation and methylation analysis indicated, that galactopyranosic residues linked by 1→3 types of linkages.

In this way, the isolated polysaccharides of *F. varia* and *F. kuhistanica* are appeared to be arabinogalactans, and their main chain consists of β-1→3 linked galactopyranosic residues. The results of chemical experiments were supplemented with methodologies of ^{1}H and ^{13}C NMR spectroscopy, that identified putative arabinogalactan main chain as: β-*D*-Gal*p*1→3-β-*D*-Gal*p*1→3-β-*D*-Gal*p*1→3-β-*D*-Gal*p*1→3-β-*D*-Gal*p*1…

The study of biological activity of WSPS of two *Ferula* types revealed, that they possess by immunostimulationg activity.

ALKYLATION OF ANILIDE-2 BENZIMIDAZOLYL-THIOCARBONIC ACID

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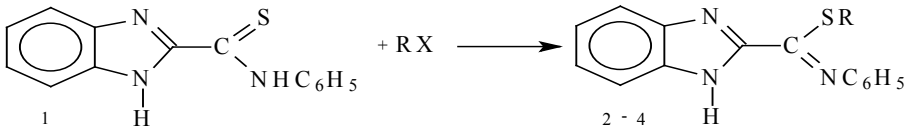
Benzimidazoles are widespread in nature (e.g., vitamin B) and possess by a wide spectrum of biological activity. More than twenty of their derivatives are used in medicine, veterinary and agrochemistry (albendazole, actamizole, benomyl, dibazol, medamin, thiobendazol etc.) [1]. The systematic synthesis of novel benzimidazole compounds is being already by the fifth or sixth generation of chemists and is very complicated. This task can be simplified by the introduction of previously known preparative methods for their new reagents already containing benzimidazole fragment, especially those with active reaction centers. Previously unknown anilides of benzimidazolyl-2-thiocarbonic acid (**1**) may be used as such substrates. As they are interesting from the theoretical standpoint, they have multiple reaction sites (thioamide group, carbon and nitrogen atoms of the heterocycle). In this aspect, we decided to use our previously synthesized benzimidazole-2-tioanilid [2]. In order to find biologically active substances we carried out the alkylation of **1** with methyl, butyl iodides and benzyl chloride in alcoholic solution in the presence of sodium hydroxide. It was founded, that the reaction is proceed at room temperature or under heating, and leads to the formation of products alkylation of the sulfur atom, i.e. benzimidazolyl-2-alkyltioformamidines (**2–4**).



R = CH_3; C_4H_9; $C_6H_5CH_2$; X = Cl, J

Progress of the reaction on the sulfur atom exclusively explained "softness" as compare to its nitrogen atoms N^1 и $N_1{}^3$. The structure products of acylation were studied and confirmed by the IR, NMR ^{1}H spectrometric data bases.

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THE PERSPECTIVE OF GEROPROTECTIVE REMEDY DEVELOPMENT ON THE BASIS OF PLANT SUBSTANCES OF DIFFERENT CLASSES

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The creation of geroprotectors affecting to the hormonal, metabolic and immunological changes in the body is actual direction of modern gerontology. In this respect the use of plant drugs is promising. A complex of plants with the code-named gerophytol was developed in ICPS of AS RUz on the basis of *Astragalus siversianus, Ajuga turkestanica, Medicago sativa* and flavonoid quercetin. It was experimentally established, that long-term introduction of this complex to the short-lived animals (mice) increased the average duration of their life. In these animals the indicators of protein, carbohydrate and lipid metabolism improved, antioxidant status of the organism normalized, lipid peroxidation processes decreased. The study of macroscopic state of the internal organs showed the lack of obvious pathological changes (in contrast to the control group of animals). Gerophytol stimulated metabolic processes during two weeks of introduction to rats of different ages (5 and 18 months), more significantly in animals of 18 months old. The investigated complex of plans showed the hepatic protective (under experimental toxic hepatitis) and antiulcer (in gastric pathology caused by butadiene) action. It was seen an increase physical performance of white mice of 2 and 8 months old (estimated on forced swimming test with the load constituted 5% of body weight) under the influence of single and multiple administration of gerophytol, and noted, that gerophytol largely increased capacity of 8 month old mice. Positive influence of preparation was also observed in rather development of difficult motive-food reflex in white outbred rats in Small′s labyrinth. Rats applied gerophytol for a long time, faster reached to the necessary temporal criterion, than intact animals (on 5 days) and rats, applied Pyracetamum (on 3 days), and had a greater amount of individuals attaining a temporal criterion and slower, than intact animals (on 4 days), forgot a way to the feeding in lack of food reinforcement. Thus, we can conclude, that the metabolically-active components of the new plant complex from the local flora (gerophytol) improves metabolism, physical and mental abilities of the organism, influences on duration of the life of aging laboratory animals.

The experimental data allow make conclusion, that gerophytol represents practical interest as new geroprotective remedy.

EVALUATION OF STIMULATING EFFECT OF TOTAL EXTRACTIVE PREPARATIONS FROM DIFFERENT CLASSES OF PLANT COMPOUNDS ON PERFORMANCE EFFICIENCY

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In this paper we studied the effect of the total extractive preparations isolated from *Silene brahuica*, contained phytoecdysteroids: ecdysterone, sileneosides A. C, D. E, etc.), and *Zygophyllum oxianum*, contained the sum of triterpene glycosides of chinovic acid, the main one being the Zygophyloside E, on dynamic performance efficiency in laboratory animals. It was established, that their administration at the doses 5–10 mg/kg orally increases duration of mice running (males, 18–20 g) in the "infinite" rope for climbing already after 1 h. The effect of total ecdysteroids was 46%, and sum of triterpene glycosides – 28% ($p < 0.05$). A similar pattern was also observed in experiments with swimming animals. Repeated administration of these drugs to mice (within 7 days) resulted in a greater stimulatory effect. Under the influence of total ecdysteroids of *S. brahuica* the duration of mice running on a tightrope increased by 72.4%, swimming – 48.6%, corresponding effect of total triterpene glycosides from *Z. oxianum* increased to 52.6% and 39.4%, respectively ($p < 0.01$). Quite significant from a practical point of view results was obtained in experiments with animals (male rats, 150–180 g), which was forced to swim until complete exhaustion twice – before and 1 h after administration of the testing substance (rats swam with a load of 6% of total body weight). Analysis of the results showed, that recommencement swimming time in the control rats after one hour of rest period was 32.4% from baseline taking as 100%, then on the background of effect of total ecdysteroids from *S. brahuica* and *Z. oxianum* the duration of the recommencement swimming to the first reached 72.4–56.8% ($p < 0.01$). Such a pronounced stimulatory effect on the performance of the total test preparations may be, on one hand, due to expressed stimulation of myofibrillar protein biosynthesis, shown by the example of m.tibialis anterior, m.extensor digitorum longus and m.soleus, and, on the other hand, by adaptation of the organism to physical stress due to a number of favorable metabolic changes, aimed to maintaining the homeostasis of energy production in the working muscles and a high level of total reserve carbohydrates and less accumulation of lactic acid, which is one of the main factors, limiting their performance. Both total preparations are non toxic, don′t possess by hormonal side effects and represent a significant interest for the development of new high-performance preparations on their basis for use in reduced work capacity, fatigue and rapid recovery after exhausting exercise.

The investigated preparations, especially the sum of ecdysteroids from *S. brahuica* surpass other none doping pharmacological herbal drugs, widely used in sports and medical practice asactoprotective remedies: Ginseng Extract, Saparal, Tribestan.

OBTAINING A SMALL DISPERSED ANTIHELMINTIC PREPARATION AZINOX

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Azinox is the antihelmintic preparation widely applied to treatment of trematodosis and cystodosis. The purpose of our work was to develop a rational technology of azinox, obtain its small disperse form and simplify technological process. The terms of purification and solvents were selected. The most available and widely used solvents chosen.

TABLE 1. **Solubility of Azinox**

Solvent	Purification temperature,°C		Amount of solvents g/100 mL	
Water			Not soluble	Not soluble
Ethanol			10	12
Methanol			5	8
Acetone	room	boiling	4	5
Chloroform			8	10
5%, 10% solutions of hydrochloric and sulfuric acids			Not soluble	Not soluble

Experimental data shown, that technical azinox substance is expedient to carry out purification by ethanol, the subsequent sedimentation - by water (Table 1). For determining of optimum purification conditions for azinox the influence of a number of factors, such as a ratio of initial reagents, temperature and process duration were studied.

Experiment results are provided in the Table 2.

TABLE 2.

Ratio of initial reagents Prep.–EtOH–water	Temperature, °C	Time, min	Yield, %	Purity, %
1:5:20	70–75	15	90	95
1:10:20	-//-	15	92	98.5
1:15:20	-//-	15	90–92	96
1:20:20	-//-	15	90	94
1:5:30	-//-	15	90	95
1:10:50	-//-	15	90–92	98.8

Optimum condition of the preparation purification was the ratio azinox–ethanol–water 1:10:20, temperature 70–75°C, time 15 min. The analysis of the preparation was carried out by TLC, HPTLC and spectrophotometer methods. Influence of temperature of reprecipitation, yield and dispersion of the preparation is also studied. It is established, that reprecipitation temperature practically doesn't influence to the product yield, and dispersion depends on reprecipitation temperature, i.e. with temperature increasing the size of particles of the preparation increases. Thus, optimum conditions of purification founded and the technology for azinox obtaining have developed. On the basis of the received results the technological scheme of azinox purification have developed.

PHARMACOLOGICAL PROPERTIES OF 1-ARYLTETRAHYDROISOQUINOLINE HYDROXYETHYL DERIVATIVES

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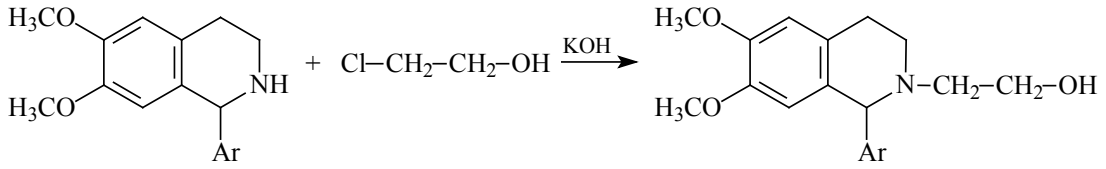
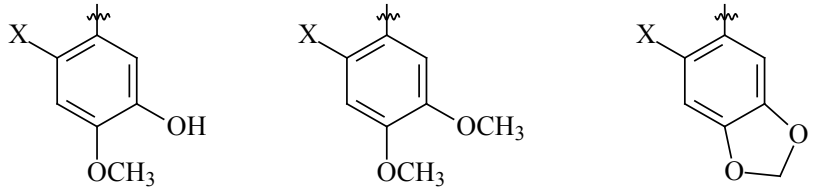
The reaction of substituted 1-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline **1a–h** and ethylenchloroethanol (**2**) provided 1-aryl-2-hydroxy-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline **3a–h.**



1 a-h **2** **3 a-h**

Ar =



a: X=H
b: X=Br

c: X=H
d: X=Br
e: X=NO_2

f: X=H
g: X=Br
h: X=Cl

In experiments on animals on analgesic and local anesthetic activity of these substances has been studied. Compounds **3 a, b, d, f** displayed analgesic activity, while substances **3 e, g, h** showed no reliable analgesic activity.

The study of local anesthetic activity of compounds on the model of terminal anesthesia of rabbit cornea had been shown local-irritant properties of **3 d, f, g, h**, and **3 b, e,** and absence of local anesthetic activity.

The study of the resorptive effect of substances in sub-toxic doses showed different trends of their impact on the central nervous system:

- Substances **3a, b, g** were CNS depressants.
- Compounds **3 c, d, f, h** excited the central nervous system.

TERPENOID COUMARINS FROM *Ferula ovina*

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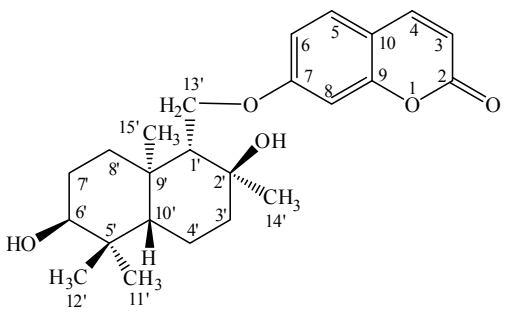
Continuation of chemical research on the roots of *Ferula ovina*, collected during the flowering period in Surkhandarya region of Uzbekistan. From the alcoholic extract by column chromatography on silicagel, eluting with hexane–ethyl acetate were isolated two terpenoid coumarins.

One of which is identical as samarcandine (**1**), the second our isolated compound were identical with isosamarcandine (**2**).

Identification samarcandin and isosamarcandine have been established on the basis of their physical and chemical properties and the analysis of their spectral data IR, UV, ^{1}H, ^{13}C NMR, DEPT, HMBC, COSY, NOESY, X-Ray structural analyses and compared with literature data.

Samarcandine and isosamarcandine have been isolated from *Ferula ovina* for the first time.



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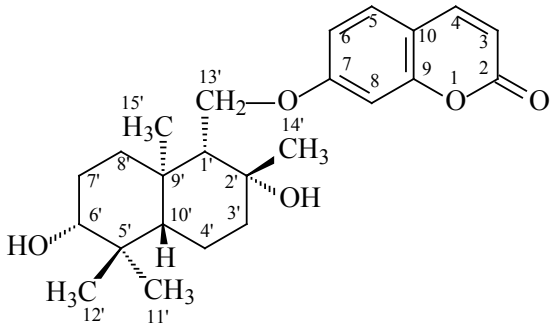

2

RESOURCES OF PLANT *Silybum marianum* IN UZBEKISTAN

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Milk Thistle – *Silybum marianum* (L.) Gaertn. is an annual or biennial thorny plant with a height 1–1.5 m. Flowering and fruiting time is July–August. Country of origin of this plant is Mediterranean. On the territory of Uzbekistan it grows in Surkhandarya and Kashkadarya regions. *Silybum marianum* grows in weedy places as a wild plant and sometimes breeds in the gardens and vegetable gardens.

Milk Thistle *S. marianum* used as a folk remedy in liver cirrhosis, acute and chronic hepatitis, jaundice, diseases of the biliary colic. The main active ingredients are flavonoids and flavonlignans (silybin, silikristin, silidianin). Also it contains alkaloids, saponins, fatty oils (until 25%), proteins, vitamin K, resins, mucus, tyramine, histamine, and macro - and microelements.

During the 2012–2013 we investigated the distribution and reserves of *Silybum marianum* in Kashkadarya and Surkhandarya regions of Uzbekistan (Table 1).

TABLE 1. **Square Shrubs and Feedstocks of *Silybum marianum* in South of Uzbekistan**

Main area	Area, ha	Density of reserves, kg/ha	Biological reserves, ton (as air dried)
Kashkadarya region			
neighbourhood of Kitab town	6.5	0.40	2.6
neigh. of Shakhrisabz town	2.7	0.70	2.0
neigh. Lyangar village	1.0	0.40	0.4
neigh. Guzar	1.5	0.46	0.7
Surkhandarya regions			
neigh. Pulkhakim village	0.5	0.25	0.2
neigh. Altinsay village	2.2	0.45	1.0
neigh. Denau town	2.5	0.60	1.5
neigh. Khandiza village	2.0	0.70	1.4
neigh. Shargun village	5.0	0.50	2.5
neigh. Sari-Asiyo village	1.0	0.55	0.5
neigh. Sarimas village	2.6	0.75	2.0
Total	25.3		14.8

Thereby the identified area of shrubs of *Silybum marianum* in Uzbekistan is 25.3 ha and biological reserve is 14.8 ton.

EVALUATION OF ANTIOXIDANT ACTIVITY OF PROANTHOCYANIDINS SUM OF *Polygonum coriarium*

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Search and development of antioxidants and antihypoxants is still an urgent problem, since many disease processes in the human body caused by the development of oxidative stress, resulting from the impact of adverse factors damaging agents and oxygen. Similar work is being done in our Institute. In this regard, a number of polyphenolic compounds isolated from various domestic plants, are investigated. Suffice expressed antihypoxic and antioxidant activity showed the amount of proanthocyanidins with an average molecular weight of 7800 D, isolated from the roots of ram tanning (*Polygonum coriarium*), which we call "k*atatsin*e."

The purpose of this study was to investigate the possible antioxidant activity of katatsin in the experiment. Experiments were carried out on rats weighing 180–210 g, drug was administered orally in the form of an aqueous solution in doses of 50 and 100 mg/kg for 10 days. "*Actovegin*e" ("Nycomed Austria GmbH", Austria) drug was used as standard. The antioxidant activity of the test drug was evaluated to determine their effect on key EPA enzymes: catalase and superoxide dismutase (SOD), as well as the intensity of lipid peroxidation (LPO), which was determined by the change in the level of malondialdehyde in liver and serum.

Studies have shown, that 10-day administration of the study drugs in experimental animals resulted in an increase antioxidant protection compared to intact animals. SOD and catalase activity in the serum by the action *katatsine* 50 mg/g did not change substantially, but the untreated group – 100 mg/kg increased for 12–8%, while under the influence *aktovegine* (150 mg/kg) for 7–9.4%, respectively. At the same time, also reduction of lipid peroxidation products took place – the level of MDA in serum under action of katatsine (50 and 100 mg/kg) decreased for 18.8 and 28.2%, and on aktovegine – 26.5%, respectively.

Similar changes were observed in the liver, both the antioxidant system and the intensity of lipid peroxidation. Under the action of catalase *katatsine* (50 and 100 mg/kg) was increased slightly for 6–7%, whereas the level of SOD increased for 10.2–19.35%. Introduction of aktovegin in this case contributed to the increase of catalase and SOD for 10.7% and 19.1%. It should be noted the more pronounced inhibition of lipid peroxidation processes in the liver as compared to the action of the test drugs in serum. Introduction of katatsine decreased hepatic MDA level for 36.6% and 43.2% (in the introduction of 50 and 100 mg/kg, respectively). Effect of aktovegine (150 mg/kg) in this case was 39.2%.

Thus, these results suggest, that the sum of proanthocyanidins from the roots of *Polygonum coriarium* (katatsine) increasing the antioxidant defense of the body, inhibit the intensity of lipid peroxidation. The study *katatsine* activity in the optimal dose was quite comparable to the effectiveness of the drug "Actovegine".

PHYTOECDYSTEROIDS OF *Stachys hissarica* PLANT

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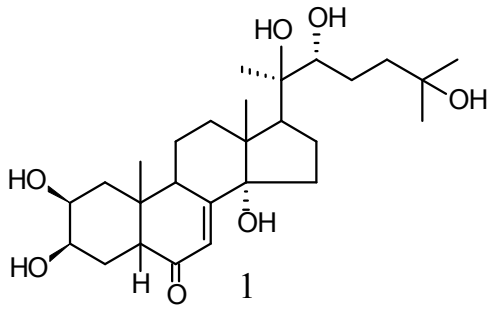
Ecdysteroids are widespread and numerous family of steroid compounds in the plant and animal world, and they are involved in the life of almost all classes of organisms, performing multiple functions. Phytoecdysteroids are natural substances that enter the body with plant food and can control the vital functions of the body on the integral level, tie into one whole the functioning of nervous, sensory, endocrine, cardiovascular and digestive system, metabolism and energy, immunity and reproduction. Activation and efficient operation of ecdysteroids in the body is possible only in their outside efflux in the form of complex systems with a stress proteins, vitamins and metal ions, trace elements.

We studied the plant *Stachys hissarica* (Fam. *Lamiaceae*) in order to find new sources of the ecdysteroide-containing raw materials. The dried and crushed plant was extracted 5 times with MeOH. The extract was concentrated and diluted with the equal volume of water. The resulting precipitate was removed by filtration, and MeOH evaporated. The aqueous portion was sequentially extracted with chloroform, then 1-butanol. After evaporation of the solvents under vacuum BuOH fractions were obtained. Fractions were separated from the buthanol extract of the methanol extract by chromatographiy on a silica gel column, eluting with the systems chloroform–methanol 50:1, 40:1, which contained original samples of 20-hydroxyecdysone (**1**), polypodine B (**2**), and mixtures of BAS. These ecdysteroids were founded in this plant for the first time.



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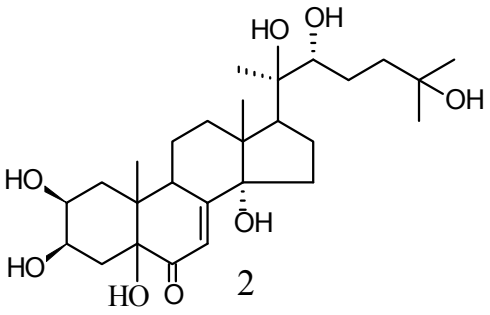

2

Isolated individual ecdysteroids were identified on the basis of IR and NMR spectroscopy, as well as by comparison with standard samples.

INTERACTION OF KONVOLVIN TO ACID ANHYDRITES. SYNTHESIS OF KONVOLVIN *N*-ACYL DERIVATIVES

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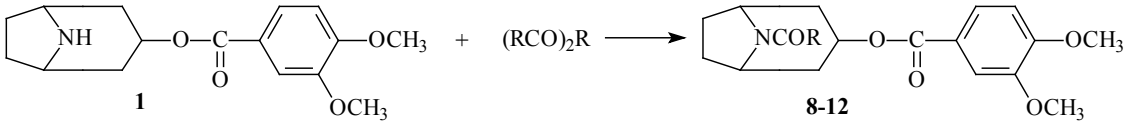
Konvolvin (**1**) is the main alkaloid of *Convolvulus subhirsutus* and *C. pseudocanthabrica*. Depending on the vegetation period its content reaches in the aerial parts to 0.3%, and roots – 0.7% [1, 2].

Previously some chemical conversion of compound **1** had been studied. A number of syntheses with alkyl halides made and konvolvin alkyl derivatives obtained [3].

In this work, we studied the interaction of **1** with aliphatic (acetic, propionic, butyric), cyclic (amber, glutaraic) anhydrides of aliphatic and aromatic (phthalic) dibasic acids (**2–7**). This acylation might be expected in NH-group, as well as the possibility of 3,4-dimethoxybenzoic residue re-acylation with formation the new acyl derivatives. Reaction was conducted in a solution of absolute benzene. It was founded, that acylation with acetic, propionic and butyric anhydride run at room temperature. For succinic, glutaric and phthalic anhydride the heating of the reaction mixture for 70–80°C is required. In the case of the first three anhydrides *N*-acetyl (**8**), propionyl (**9**) konvolvins were obtained. In the reaction with cyclic acid anhydrides (**5–7**) *N*-(ω-carboxyalkyl,-phthaloyl) konvolvins (**10–12**) yielded. In this case the formed carboxyl group does not enter into further reaction.



2. R=CH_3, **3**. R=C_2H_5, **4**. R=$CH_3CH_2CH_2$. **5**. R=$(CH_2)_2$, **6**. R=$(CH_2)_3$, **7**. R=C_6H_4.
8. R=CH_3, **9**. R=C_2H_5, **10**. R=CH_2CH_2COOH, **11**. R=$(CH_2)_3COOH$, **12**. R=C_6H_4COOH

The reaction was monitored by high performance thin layer chromatography (HPTLC). Chromatographic plates «Whatmann Paper LTD», Germany used in the analysis.

The structure of the synthesized compounds was proved by IK and ^1H NMR spectroscopy.

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COMPARATIVE CHARACTERISTIC OF ALBUMINS AND GLOBULINS FROM THE SOFT AND HARD WHEAT CULTIVATED IN UZBEKISTAN

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Last years the increasing attention of researchers is involved with soluble fraction of proteins of the wheat. Representing the heterogeneous fraction consisting of various enzymes and their inhibitors, proteins of protoplasm can render essential influence on balance S-S bonds and SH-groups in gluten and, hence, on its properties.

The purpose of the present work was revealing features of protein spectrum of albumins and globulins fractions from various kinds of the wheat, which were cultivated in Uzbekistan, and establishment of the possible reasons of wheat distinction in quality.

For research 4 grades of wheat, a crop of 2012, grown up on irrigation fields of the Kashkadarya area have been selected: a grade "Karlik" hard wheat, kind *Triticum durum*; the grade «Krasnovodopadskaya», kind *Triticum aevestum*, soft red seed wheat deduced in Kazakhstan, but cultivated in Uzbekistan, grades «Ravi» and «Ok marvarid», kind *Triticum aevestum*, soft white seed wheat. Soluble fraction of wheat proteins was extracted by phosphate buffer pH 7 with 1 M NaCl at 40°C with the subsequent dialysis. Protein dried at the low temperature in high vacuum fractions, was analyzed by HPLC on column Zorbax GF-250; 4.6 × 250 mm, 4 μm, as a mobile phase initial 0.1 M the phosphatic buffer pH 7, containing 0.1 M NaCl used.

Results are presented on Figs.1, 2 (the molecular weight of proteins components, kDa is resulted from the right party of figures).

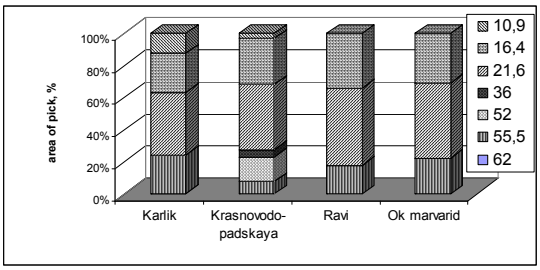

Fig 1. The quantity of proteins components, % in albumin fractions of wheat of various grades

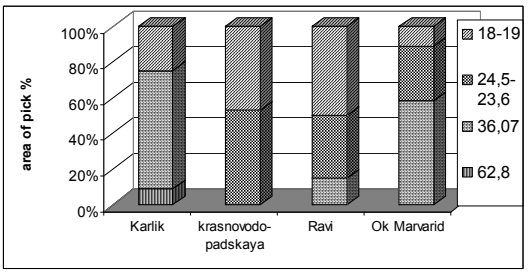

Fig. 2. The quantity of proteins components, % in globulin fractions of wheat of various grades.

Apparently from the resulted data, albumin and globulin fractions of soft grades white seed wheat «Ravi» and «Ok marvarid» are characterized by identical componential structure, but a various parity of proteins components. Componential structure of hard wheat of a grade "Karlik" and Kazakhstan wheat «Krasnovodopadskaya» considerably differed from the investigated grades of soft wheat by presence of high-molecular components with molecular weight 62 kD, 52 kD and 36 kD and low-molecular components with molecular weight 10.9 kD.

Considering, that investigated grades of wheat, had gluten with II groups of quality (100–90 unit of apparatus of on determination of index of gluten deformation), except for a grade «Ravi», quality gluten of which was 110 unit of gluten deformation index (III group), it is possible to conclude, that the presence at soluble protein fraction of high-molecular components, as well as their quantity may be an additional criterion of the estimation of the wheat quality.

FLAVONOIDS OF *Geranium saxatile*

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Previously we isolated and elucidated a structure of a number of phenolic compounds from aerial part of medicinal herb *Geranium saxatile* (*Geraniaceae*) [1, 2].

Continuing studying of this plant, we investigated composition of flavonoids and their glycosides of ethylacetate extraction from aqueous-alcoholic extract.

Column chromatography of ethylacetate extraction was performed with silica gel with the subsequent gel-filtration of received elution on Sephadex LH-20. It was isolated **3** substances.

For identification of the isolated substances characteristics of ^{1}H, ^{13}C NMR spectra including 2D experiments and results of the analysis of the optical – IR, UV-spectra used. The isolated substances identified as luteolin (**1**), luteolin-4′-*O*-β-*D*-glucopyranoside (**2**) and quercetin-5-*O*-β-*D*-glucopyranoside (saxifragin) (**3**).

Thus, saxifragin (**3**) for the first time isolated from the genus *Geranium*, and luteolin (**1**) and its glycoside luteolin-4′-*O*-β-*D*-glucopyranoside (**2**) for the first time from aerial part of *Geranium saxatile*.

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LIPIDS OF *Punica granatum* FLOWERS

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Punica granatum L. (*Punicaceae*) is widely known food and herb plant. Its fruits, seeds and a peel are used in pharmaceutics and cosmetics. The chemical composition of flowers practically has not been investigation. It is known, that this plant contains dye-stuffs.

We investigated compositions of lipids of this plant flowers. The total lipids were extracted from previously dried-up and pounded flowers by chloroform–methanol (2:1, v/v). The yield of lipids was up to 1.5%. For establishment the group composition the total lipids were divided by column chromatography on silica gel, the neutral lipids (NL) was eluted by chloroform, glicolipids (GL) – by acetone, and phospholipids (PL) – by methanol. The yields of NL, GL and PL fractions were up to 13.3, 74.5 and 12.2%, respectively. The qualitative structure of lipids was defined by TLC on silica gel and silufol plates using systems of solvents and indicated developments for the indicated groups of lipids [1].

It was established, that hydrocarbons, triacylglycerols, free fatty acids (FFA), aliphatic alcohols, triterpenols and their esters with FA were by components of NL fraction.

Fraction of GL consisted of sterilglycosids and their esters with fatty acids, monogalaktosyl, digalactosyldiacylglycerols and cerebrosides. Besides, in the GL fraction phytosterols and triterpenol acids were founded. The last components were founded earlier in the *Punica granatum* leaves, where their contents reached 0.2%.

Phospholipid fraction was presented by phosphotidilholines, phosphatidilethanolamines, phosphotidilinosites and phosphatidic acids.

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USE OF THE ENZYME COMPLEX OF MOLD FUNGI FOR THE HYDROLIYSIS OF POLYSACCARIDES OF *Sorghum sacchartum* STALKS

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The plant *Sorghum sacchartum* (sorghum), unlike other grains has the juicy stalk containing, in dependence of the variety and conditions of farming, 10–30% sugars, including 0.6–1.0% pectin, 11–25% sucrose, 7.3% cellulose, 5.2% starch. Juice of sorghum stalks is a valuable raw material for the production of bioethanol as a renewable energy source.

Stem juice is inside the plant cells and in intercellular spaces and held firmly by plant tissue. Therefore, an important factor affecting on the completeness and the speed of extracting the juice, is the destruction of the integrity of the cell structure of the stalks and the hydrolysis of pectin, which prevents the escape of juice due to easy formation of gel.

We studied the stalks of "Kattabash" sorghum variety grown in soil and climatic conditions of the Tashkent region. The ground mass of stalks (1 kg) with size of pieces of 3.0–10.0 mm was diluted with water (25% by weight of raw materials), acidified with sulfuric acid to pH 3.5–6.0 and subjected fermentation. Enzymatic treatment of the pulp was treated by complex enzymes of dry fungi *Aspergillus oryzae* and *Aspergillus awamori* biomass (10–12% of the volume of the grounded raw) at a temperature of 50–80°C and processing time 60 min. In the end of hydrolysis the juice was separated by pressing of the pulp on an expeller. The concentration of sugars in the juice was determined by the known method [1].

To determine the optimal degree of crushing of stalks and optimum temperature multifactorial experiment carried out, in which the juice obtained from the stalks, was crushed to particles of 3.0, 5.0 and 10.0 mm size at temperatures of 50°C and 60°C, 70°C and 80°C. As a result, it was founded, that the optimal particle size is 3.0–5.0 mm, and the optimum temperature 60–70°C. In this case, the high juice yield (1.24 kg) with high sugar content (24.8%) is observed at fermentation of raw materials in optimal conditions, and at pH of 4.5–5.0. Isolation of juice from the stalks, chopped to an optimal particle size, a direct compression without enzyme treatment gave the juice yield 0.96 kg with sugar at a concentration of 20.4%.

0.1 kg of ethanol was obtained from the juice by fermentation and 0.08 kg of ethanol – in the case of direct compression.

Thus, the hydrolysis of the crushed stalks of sorghum with the enzyme complex of dry biomass of fungi *Aspergillus oryzae* and *Aspergillus awamori* allows increase in the concentration of sugars in the juice for 4.4%, and for22% increase in ethanol yield per unit of weight of the treated stems.

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THE STUDY OF TOXICITY AND ANTIALCOHOLIC ACTIVITY OF CYTISINE AND ITS DERIVATIVES

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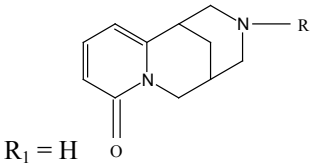
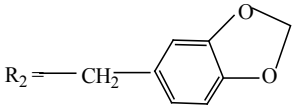
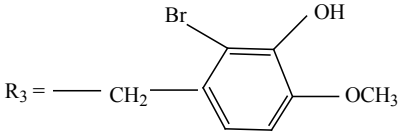
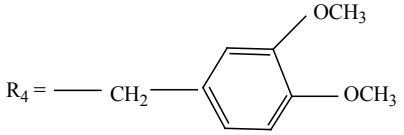
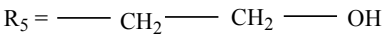
Acute alcohol intoxication is a serious problem of practical medicine that requires a range of therapeutic interventions, one of the most important is the restoration of violation respiratory apparatus in a comatose state, accompanied by aspiration-obstructive type, which gives the greatest number of deaths in the prehospital phase. Acute alcohol intoxication is widely used respiratory analeptic agents – cytisine, bemegride etc.

We have investigated the effect of four cytisine derivatives, which were obtained by the condensation of substituted benzaldehydes with cytisine, on acute alcohol intoxication, as well as their acute toxicity.

Compounds	Structure
Cytisine	
N-(3,4-Methylenedioxybenzyl) cytisine hydrochloride – $C_{19}N_{20}O_2N_2$	
N-(2-Bromo-3-hydroxy-4-methoxybenzyl)cytisine hydrochloride – $C_{19}N_{21}N_2O_3Br$	
N-(3,4-Dimethoxybenzyl) cytisine hydrochloride – $C_{20}N_{24}N_2O_2$	
N-(β-Hydroxyethyl) cytisine hydrochloride – $C_{13}N_{18}N_2O_2$	

It was founded, that *N*-substituted derivatives of cytisine were in the 2–60 times less toxic, than cytisine. By antitoxic activity in acute alcohol intoxication, among the tested compounds *N*-(3,4-methylenedioxybenzyl) cytisine hydrochloride had the greatest anti-drug activity, which shortened the duration of narcotic state of experimental animals compared to the control group by more than 2 times, being superior to cytisine.

SEARCH FOR BIOLOGICAL ACTIVE SUBSTANCES IN A SERIES OF BENZIMIDAZOLES. SYNTHESIS AND BENZOYLATION OF 2-METHYL(ETHYL)-BENZIMIDAZOLES

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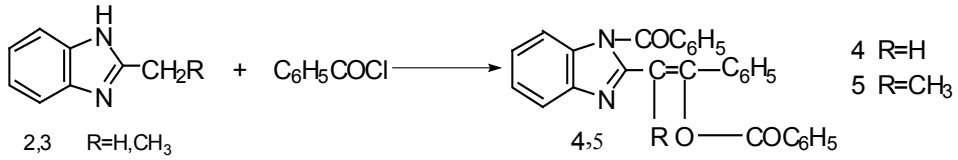
Compounds with benzimidazole ring were founded in many natural products. Among the derivatives of benzimidazole some drugs for the medicine (dibazol), fungicides for agriculure (Olgin, benomyl), anthelmintic (medamin), and other drugs founded.

It is known, that 2-substituted benzimidazoles are prepared by condensation of *o*-phenylenediamines with aliphatic or aromatic acids, as well as lactones [1]. To study the acylation of 2-alkyl (aryl, benzyl) benzimidazole we realized synthesis of 2-methyl-ethylbenzimidazole (**2**, **3**) by condensation of *o*-phenylenediamine (**1**) with acetic or propionic acids alloying mixture of reagents in the absence of solvents.

Acylation reaction of compounds **2**, **3** may run on a nitrogen atom and a methyl (methylene) group. Those manner *N*-acyl products or their further acylation products with a second or third acyl residues may be prepared. We developed a method for the acylation of 2-methyl(ethyl)-benzimidazole with benzoyl chloride (BC) under mild conditions (60–65°C) in the presence of triethylamine. It was founded, that the reaction of **1** with BC proceeds with the formation of the product (**4**, **5**) with three acyl groups.



Triple benzoylation of **1** may occur: to the *N*-1 atom, on the α-carbon atom to form 1-benzoyl-2-benzoylmetylbenzimidazole, further benzoylation of oxygen atom of the enol form of another molecule BC is gives the product **4**. Acylation of **1** BC under more severe conditions also gives the product **4** [2]. In the case of 2-etylbenzimidazol BH use the reaction is run similarly, and 1-benzoyl-2-(β-benzoyloxy-β-phenylpropenyl) benzimidazole (**5**) formed.

The structure acylation products were studied and confirmed by the IR, NMR, ^{1}H and mass spectrometric data bases.

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CHROMATO-SPECTROPHOTOMETRIC METHOD FOR THE QUANTITATIVE DETERMINATION OF GALANTAMINE IN LEAVES OF UNGERNIA VICTORIS

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On the basis of Pilot manufacture of the Institute of Chemistry of Plant Substances serial production of the drug substance Galanthamine hydrobromide from the leaves Ungernia Victoris organized. Galanthamine hydrobromide is widely used in medical practice as an anticholinesterase agent [1].

Chromatocolorimetric method for the quantitative determination of alkaloid galantamine in the plant material is well known [2]. The method required a long time.

We developed a new chromato-spectrophotometric method for the quantitative determination of galantamine in the plant material, which consists of the extraction of alkaloids from plant material, chromatographic separation of galantamine hydrobromide from impurities on the plates «Merck UV-254" (chloroform–ethyl acetate–methanol–ammonia 16:16:1:1 system).

On the absorption spectrum of the solution prepared at the concentration of galanthamine hydrobromide 0.1–0.02 mg/mL in the range of 240–350 nm wavelength the band with an intense absorption peak at 285 ± 2 nm appeared. The eluate solution of the control strip used to make a comparison.

The quantitative content of galanthamine was calculated for raw material dry mass in % using the formula:

$$x = \frac{D \cdot m_0 \cdot 0{,}05 \cdot 2 \cdot 10 \cdot 0{,}819 \cdot 100 \cdot 100 \cdot C_0}{D_0 \cdot 2 \cdot 10 \cdot m \cdot 0{,}1 \cdot (W - 100) \cdot 100}$$

in which D – optical density of the test solution; D_0 – optical density of the solution of the working standard sample (RSO) of galantamine hydrobromide; M_0 – galantamine hydrobromide weight in grams; m – mass of raw material, in grams; W – raw material humidity in %; C_0 – the content of the main substance in the working standard sample of galantamine, in %; 0.819 – scaling factor equal to the ratio of molecular weights of galantamine base and galantamine hydrobromide: 368.28 : 449.18 = 0.819

The metrological characteristics of the method of Ungernia Victoris leaves analysis is provided in the Table.

n	f	x	S	f	p	Σ	Σ, %
6	5	0.087	$2.7 \cdot 10^{-3}$	2.57	95	$5.9 \cdot 10^{-3}$	0.9

The metrological characterization shown, that the accuracy of a single determination is 0.9%.

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COMPARATIVE CHARACTERISTIC OF INULIN AND PECTIN SUBSTANSES OF TWO TOPINAMBUR TYPES

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Topinambur for a long time is used to produce fructose syrup and are characterized by a high content of polyfructanes, one of them is inulin, which promotes the excretion of heavy metals and the absorption of calcium and iron, *L*-inulin has immunomodulatory properties. In this regard, the goal of our research is to select promising inulin and pectin-containing raw materials. We have isolated and identified the compositions of water-soluble polysaccharides (WSPS), pectin (PC), hemicellulose, inulin, from two varieties of topinambur *Faiz barracks* and *Muzhiza.*

Physico-chemical properties and the quantity of carbohydrates and proteins in the two study varieties were established. Their monosaccharide and amino acid compositions identified. A comparative analysis of the content of inulin in two studied varieties established, that grade *Faiz barracks* contains the higher inulin in raw material. While content PC and WSPS prevailed in grade *Muzhiza*. Among the product of acid hydrolysis of pectin mainly galacturonic acid and neutral sugars founded. The molecular weight of PC is 9000 and 9500, respectively. Their qualitative characteristic has studied. Based on these dates we can see, that the PC in two varieties of topinambur belong to the low-esterified pectin, so as a degree of etherification of the grade *Muzhiza* –39.3%, *Faiz barracks* – 36.3%.

Note, that the analyzed *Muzhiza* grade of topinambur has higher protein content (19.2%) compared with a grade *Faiz barracks* (6.45%). Comparison of the amino acid composition of two types determined, that the grade *Muzhiza* differed in quantity of methionine, and higher quantity of lisine and isoleucine. The last amino acid determines the nutritional value of the protein.

It is known, that the source of fructose is plant material containing the polysaccharide inulin. In this regard, a cultivated variety of *Faiz barracks* could be raw materials for production of fructose in the Republic of Uzbekistan, and high-protein variety *Muzhiza* can be a source of pectin substances.

GRAIN QUALITY MARKERS OF THE LOCAL VARIETIES OF WHEAT

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Functions of proteolytic enzymes inhibitors in plants are not limited by their ability to inhibit the activity of splitting enzymes of proteins and peptides. The simplest variants are so-called bifunctional inhibitors. The physiological importance of amylases and proteases from seeds of cereals and fabaceous attracted close attention to their study. The regulation of the activity of these enzymes is associated with protein inhibitors in the seed – notably with bifunctional inhibitors. The share of proteins – inhibitors in wheat is one third of the total grain albumins. From technological point of view, they may be of interest as the "auxiliary" proteins involved in the formation of gluten, thereby contributing to improving of the baking quality of flour. Furthermore, the lack of inhibitors of this type can cause so-called "pre-harvest sprouting" seed associated with premature activation of α-amylase.

In this regard, in our studies of local varieties of wheat we carried out isolation and characterization of the bifunctional inhibitors, proteases and α-amylase (BIF) as a measure of quality grade, as well as nutritional value. We have investigated the bifunctional inhibitors of more than 20 varieties of hard, medium, low wheat which is cultivated in Uzbekistan and revealed correlation between the sort of wheat and content (activity) of bifunctional inhibitor of proteases (BIF). Until now, the proteinase inhibitors of plants viewed as substances that reduce the nutritional value of plant foods. Obviously, these views do not take into account the values of inhibitors for the plants themselves as a factor in increasing their biological stability.

When comparing healthy and damaged "bug" (*Eurygaster integriceps*) of "Kupava" wheat variety in response to the failure observed decrease in BIF from 13.5% to 1.4%, indicating that the performance of the protective function of inhibitor in plant. Also, we have obtained evidence that the unstable variety "Matonat" characterized by low value of BIF (6%), which indirectly indicates the susceptibility of the variety to disease. It is shown that high-protein varieties "Andijan 4R" with a protein content – 22% and the "Andijan 2R" – 20% were significantly different in content of BIF, amount of which were – 2.9% and 9.51%, respectively. In this high-protein "Andijan 4R" variety was more susceptible to disease, than "Andijan 2R".

Thus, the total protein content is not the main criterion for the quality of wheat grain, especially of such index as its resistance to various diseases and pests.

RELAXANT ACTIVITY OF THE DITERPENOID ALKALOID TALATIZAMINE AND THEIR DERIVATIVE 14-*O*-BENZOYLTALATIZAMINE

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Diterpenoid alkaloid talatizamine isolated from the plant *Aconitum talassicum R.* posses curare-like action and caused muscle relaxation similarly to nondepolarizing miorelaxant agents. Recently we founded, that 14-*O*-benzoiltalatizamine, a derivative of talatizamine, produced more potent relaxation in comparison with the talatizamine. In order to further characterize relaxant action of these alkaloids we have studied their effects on contractile activity of smooth muscle of rat aorta. Studies were carried out on thoracic aortic preparation isolated from white rat (200–250 g). The thoracic aorta was removed, cleaned of adventitia, cut into ring segments (3–4 mm in length), mounted on stainless steel hooks and suspended in a 5 mL jacketed tissue bath with Krebs′ physiological salt solution aerated with 95% O_2-5% CO_2. The contractile activity of the preparation, induced by high KCl or norepinephrine, was recorded under isometric conditions using Grass FT03 force-displacement transducer and chart recorder (Endim 621.02).

In preliminary experiments talatizamine and 14-*O*-benzoiltalatizamine in wide range of concentration had no effect on basal tone of aortic preparation, but at concentration-depended manner relax preparations pre-contracted by 50 mM KCl. In these conditions talatizamine started the relaxation only at a concentration of 50 μM and produced maximum of relaxation of 92 ± 1.5% at 750 μM. In contrast, the relaxant effects of 14-*O*-benzoiltalatizamine first occurred at 40 μM and maximum of relaxation of 64.2 ± 3.2% achieved at a 200 μM. These effects of alkaloids on contraction induced by high KCl, which mediated by activation of *L*-type voltage-operated Ca^{2+} channels, could be attributed to inhibition of extracellular Ca^{2+} entry. However, talatizamine and 14-*O*-benzoiltalatizamine with similar efficiency and potencies produced relaxation of aortic preparation pre-contracted by norepinephrine. These results suggest that studied alkaloids relaxed the rat aorta by suppressing the Ca^{2+} entry into smooth muscle cells through both voltage- and receptor-operated calcium channels. The more potent relaxant activity of 14-*O*-benzoiltalatizamine apparently is due to presence in its structure of benzoyl group at carbon atom C_1 instead of hydroxyl group of talatizamine.

IR-SPECTRUM GLYCOPROTEIN COMPLEX «BIOVIT»

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Jenus *Gleditsia* belongs to the family *Caesalpiniacea* and has 12 species, of which 8 introduced into the Botanical Garden to them. FN Roussanov Academy of Sciences of Uzbekistan (Tashkent).

In the study of carbohydrate content (water-soluble polysaccharides, pectin, hemicellulose) found that the endosperm of seeds *Gleditsia* contains in its composition 17% carbohydrates (5.4% – VRPS, 1.2-ae, 7.6% GC A.3 2% GC-B).

It is water-soluble polysaccharides derived from endosperm seeds honey locust, contain nitrogen, whose presence is associated with the presence of protein substances. Furthermore, found that water-soluble polysaccharides are galactomannans, which are known from the literature have growth promoting activity [1].

Continuing our study received IR spectral data of the complex "Biovit" protein fraction and water-soluble polysaccharides from the complex. A common feature of glycoproteins – the presence of a carbohydrate-protein bond. In plants, the oligosaccharide groups are usually attached to oksilizinu or hydroxyproline. Distributed communication, when the 4-arabinose is attached to the glycoside bond hydroxyproline. In some plant glycoproteins to oksilizine can also join the *D*-galactose. [2].

When comparing the IR-spectrum of the sum of the initial samples have observed the greatest change in the absorption 1143–980 cm^{-1} responsible for the stretching vibrations of C-O groups (ester bond-glycoside bond). Reducing the intensity of the absorption bands in the region, and their offset in the short region may indicate a new ester linkage, characterized by the electronic structure of the original ester (glycoside) in the primary communication connections.

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HPLC INVESTIGATION OF METABOLIC CHANGES IN THE WHEAT UNDER THE INFLUENCE OF BIOVIT PREPARATION

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The effect of preseeding treatment with preparation «Biovit» on the protein composition of wheat grain was studied by HPLC.

Column Zorbax GF-250, 4.6 × 250 mm, 4 μm using precolumn Zorbax diol; 4.6 ×12.5 mm 5 μm. Mobile phase: 0.1 M sodium phosphate buffer pH 7, flow rate 0.25 mL/min, column temperature control at 28°C, the concentration of proteins in solution – 1 mg/mL, peaks detection at 210 nm. Quantity of protein applied to the column was 5 μL.

To determine the molecular weight of proteins the column was previously calibrated using solutions of standard proteins with known molecular weights: immunoglobulin (160 kD), bovine serum albumin (67 kD), ovalbumin (45 kD), trypsin inhibitor (20 kD). The molecular weight was determined by constructing a calibration curve using as parameters the logarithm of protein molecular weight (ordinate axis (y) of their retention volume, defined as the product of the retention time on the flow speed (the axis of abscissas (x)).

The protein isolated from wheat grain control untreated variant consisted of five protein components with molecular weights of 120 kD, 46 kD, 24 kD, 18.5 kD, 14.8 kD. In quantitative ratio the protein components with molecular weight 46 kD and 14.8 kD dominated, which percentages were 28.5 and 30.4%, respectively. The content of high molecular weight component with molecular weight 120 kD in the untreated wheat was 3.04%.

The protein isolated from wheat grain subjected to preliminary treatment with bioregulator Biovit in the rate of 50 g per a thousand of seeds, consisted of three protein components with molecular weights of 120 kD, 47.3 kD and 19 kD, corresponding to the major protein components of the untreated wheat. In the treated by Biovit wheat the fraction with a molecular weight of 19 kD dominated, the percentage of which was 77%.

The disappearance of the protein components with molecular weights of 24.6 kD and 14.8 kD, presented in the untreated wheat in total quantity 53.3%, and the significant increase in the protein component with a molecular weight of 19 kD, indicating the changes taking place in the process of protein synthesis under the influence of Biovit, promoting change in the protein spectrum and low molecular weight components synthesis.

CYTOSTATIC AND CYTOTOXIC ACTIVITY OF TAMIRINE

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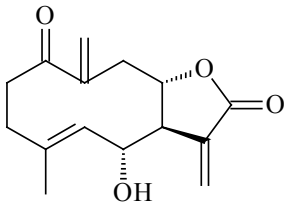
Sesquiterpene lactone tamirine is produced in plants of *Tanacetum* and *Tanacetopsis* genii. Tamirine molecule contains activated double bonds (exocyclic methylene of γ-lactone cycle and α,β-unsaturated ketone, three substituted double bond). It is known, that such sesquiterpene lactones possess with expressed antitumor activity, and some of them used in medicine. So, the investigation of cytostatic and cytotoxic activity of tamirine on 60 cancer cell lines on DTP anticancer drug discovery program in the National Cancer Institute, USA had been carried out.



Tamirine displayed moderate cytostatic activity on cell lines of leukemia (K0562, MOLT-4, SR), colon (COLO 205, HCT-116, HCT-115, HT 29, SW-620), kidney (ACHN, CAKI-1, RXF 393, TK-10, UO-31), ovarian cancer (OVCAR-3, OVCAR-8), melanoma (LOX IMVI, UACC-62). Cytotoxic concentrations of tamirine were relatively high (LC_{50} in diapason 10^{-5}–10^{-4}), excepting COLO 205 line, LC_{50} for which was 7.04×10^{-6}.

SECONDARY METABOLITES OF *Artemisia sogdiana*

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Artemisia sogdiana Bunge is semi-shrub plant of 40 cm height with wood perennial part of 10–15 cm lenght. This *Artemisia* species is wide spread in Uzbekistan, predominantly in Fergana valley, foothills of Kuramin, Alay, Turkestan, Nurata, Zeravshan, and Hissar ranges.

There is no any information related to volatile compounds composition of *Artemisia sogdiana* Bunge.

By method of chromato-mass-spectral analysis we have studied compounds composition of benzene extract of aerial parts *Artemisia sogdiana*, gathered in stage of buds forming and bloom begin in Dzhizak region of Uzbekistan, and spur of Nurata range. In the benzene extract we identified following in table compounds:

Component	R_t, min	Area, %	Component	R_t, min	Area, %
m-Xylene	4.16	1.79	(–)-β-Thujone	10.56	3.18
1-Vinyl-1,3-cyclohexadiene	4.63	0.38	(+)-β-Thujone	10.92	2.69
Nonane	4.73	0.58	α-Isophoron	11.06	1.05
1*R*-α-Pinene	5.54	1.61	2-Pinen-7-one	11.19	5.23
Isoterpinolene	5.90	0.53	*trans*-Pinocarveol	11.64	1.50
4,4-Dimethyl-2-buten-4-olide	6.03	17.99	Camphor	11.81	8.65
β-Pinene	6.63	1.14	(1*R*)-(–)-Myrtenal	13.57	0.79
p-Cymene	8.01	0.99	ψ-Limonene	16.78	0.60
Eucalyptol	8.19	28.13	Filifolide A	17.66	4.05
γ-Vinyl-γ-valerolactone	8.51	8.71	(*Z*)-Jasmone	20.26	0.81

In need to note, that all presented in the table compounds are identified for the first time.

TECHNOLOGY OF PRODUCTION OF ALKALOID ACONITINE FROM *Aconitum karakolicum* AND *Aconitum soongaricum*

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It is known, that the major alkaloid aconitine is used in scientific practice for an experimental modeling of cardiac arrhythmias on laboratory animals, when looking for effective ways to treat arrhythmias and other serious heart disease. In the Central Asia, two types of plants of the genus *Aconitum* – *Aconitum karakolicum* and *Aconitum soongaricum* growing, that contained aconitine alkaloid. Aconitine is the main alkaloid in the total alkaloids of these plants. But depending on the type of plant material, from their place of growth, from the soil and climatic conditions the related alkaloids may be different, such as karakoline, mesaconitine, songorine, disoxiaconitine etc.

We have developed a method for producing aconitine alkaloid with a purity of at least 96% from these plants by extraction of raw materials with 80% aqueous ethanol or with weak solutions of mineral or organic acid with further purification. By experimenting with the different solvents the system selected for the technical purification of related aconitine alkaloids, on column with alumina sorbent with varying Brockmann activity. The purity of the product was determined by HPLC.

DEVELOPMENT OF ANALYTICAL METHODS FOR STANDARDIZATION OF DIHYDROATISINE HYDROCHLORIDE

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Currently, the Institute is working on a new anti-arrhythmic drug dihydroatisine hydrochloride, derived from the aerial parts of *Aconitum zeravschanicum* Steinb., the buttercup family (*Ranunculaceae*), growing on the territory of the Republic of Uzbekistan.

The aim of this work is to develop methods for standardization of plant material, substance and dosage form of the drug. The main alkaloids atisine and isoatosine contained in the aerial parts of *Aconitum zeravschanicum* Steinb. were the raw material for the preparation of dihydroatisine hydrochloride.

To determine the content of atisine and isoatosine in the plant material we have proposed chromato-spectraphotometric method. In contrast to the raw materials, spectrophotometric method proposed for the determination of the active substance in the substance and dosage form of the drug dihydroatisine hydrochloride. As comparison solution working standard sample of dihydroatisine hydrochloride was used. The measurement was made at a wavelength of 220 nm.

The results showed that the content of atisine and isoatosine in the raw material is at least 0.2% by weight of air-dried raw materials, the content of dihydroatisine hydrochloride substance should be at least 98%. Also it was founded, that the dosage form of the preparation (2 mL of 1% solution for injection) should contain at least 0.019–0.021 g of active substance.

SYNTHESIS OF 3,4-DIHYDRO-6,7-DIMETHOXY-1 (2-*H*)-IZOQUINOLINON

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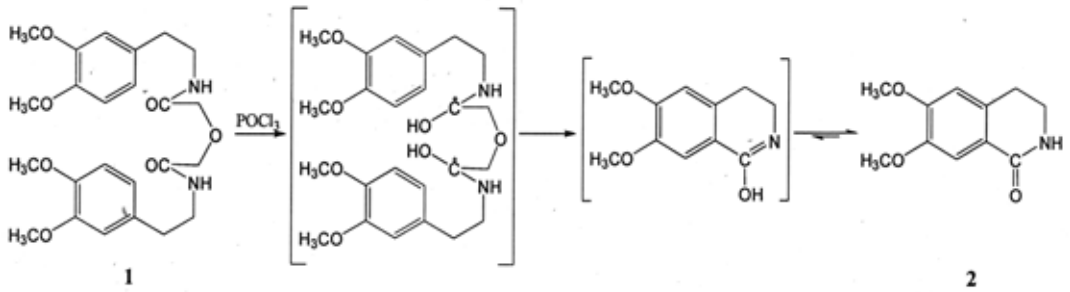
There are several methods of substituted isoquinolines′ preparation [1]. However, the Reaction of Bischler-Napieralski remains still now as the most applicable due to the availability of reagents. Cyclization of diamide **1** with $POC1_3$ was carried out on boiling in benzene. The end of reaction was controlled by TLC. The reaction mixture consists of three substances. The main compound **2** was separated by column chromatography with yield 15%, mp 174–175°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm): 2.9, 3.6 (Ar-CH_2-CH_2-N), 3.95 (OMe), 6.72 (5-H), 7.62 (8-H), 7.7 (NH).



The substance **2** was identified with known alkaloid coridaldine, extracted from the plant Berberis baluchistanica [2], and its structure is confirmed by the RSA.

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PREPARATION OF POLYMER COMPLEX OF ALBENDAZOLE WITH PECTIN

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All currently known antihelmintic drugs are not active enough for a complete care of infected animals and humans. Moreover, they are highly toxic substances.

The aim of this work is to obtain a polymeric form of albendazole with pectin in order to create new drug with high biological activity and, simultaneously, low toxicity.

Albendazole is practically insoluble in water and known organic solvents. Therefore the step of dissolution of the active biological component is the important point of the preparation of albendazole polycomplex. We have founded the method of albendazole dissolution and the optimal conditions for producing the polymer complex with pectin. Various samples (in form of solution, gels, films and dry powder) of the albendazole complex with pectin have been obtained.

IR-spectroscopic analysis of the samples had shown the presence of shifts both in high and low frequency of characteristic absorption bands of the functional groups of the initial components. Thus, there is a significant low frequency shift of the band 3421 cm^{-1} (NH- of albendazole) to the 3231 cm^{-1} (NH- of the complex). There is a shift of the band 3336 cm^{-1} (OH- of pectin) to the 3231 cm^{-1} (OH- of the complex). The band 3564 cm^{-1} (OH- of pectin) is deleted. High-frequency shift is observed for the C=O groups of pectin (1747 cm^{-1}) and 1753 cm^{-1} (complex), as well as carboxymethyl group band 1633 cm^{-1} (albendazole) and 1641 cm^{-1} (complex). All this facts indicates the interaction between NH-groups of albendazole and C=O and OH-groups of pectin with the formation of polymer complex “albendazole–pectin”.

The preliminary biological tests had shown the high activity and low toxicity of the polymer form of albendazole.

LIPIDS OF TWO *Primula* SPECIES

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In the continuation of our research on the lipids of *Primulaceae* family we have investigated the seeds, roots and leaves of two *Primula* species – *Primula capitellata* Boiss. and *Primula fedschenkoi* Rgl. Plants of the *Primula* genus are characterized by containing of Δ6-polyunsaturated fatty acids.

The lipids from the studied objects were extracted with chloroform–methanol (2:1, v/v) and analyzed by thin layer chromatography. Yield of the lipids from three parts of two plants is presented in the Table. The fatty acid composition of all lipid samples was established by GLC and GC-MS in the form of their methyl esters. Fatty acids were identified by comparison of their retention times and mass-spectra with standards and Δ6-polyunsaturated fatty acids isolated earlier by us from *Cortusa turkestanica* seeds [1].

TABLE. **Yield of Lipids from Two Species of *Primula***

Plant	Parts of plant	Yield of lipids, % from dry weight
Primula capitellata Boiss.	Seeds	10.3
	Roots	1.7
	Leaves	5.0
Primula fedschenkoi Rgl.	Seeds	11.2
	Roots	1.7
	Leaves	4.8

The resulting dates indicate that the lipids content of the roots was founded to be lower than the leaves and seeds (Table). The lipid compositions from three parts of *P. capitellata* were very close to that of *P. fedschenkoi*. Δ6-polyunsaturated fatty acids were founded in the lipids of both investigated plants. The contents of these fatty acids were different in the studied parts of plants.

Lipids from seeds, roots and leaves contained octadeca-6*Z*,9*Z*,12*Z*,15*Z*-tetraenoic (stearidonic) acid. Amount of this unusual fatty acid in the leaves lipids of *P. capitellata* and *P. fedschenkoi* was higher (8.9 and 9.8%), than in the roots (2.6 and 4.4%) and seeds lipids (3.1 and 3.3%), respectively.

The octadeca-6*Z*,9*Z*,12*Z*-trienoic (γ-linolenoic) acid was also detected in the leaves lipids of *P. capitellata* and *Primula fedschenkoi* in amount of 0.8% and 1.5%, respectively. These dates showed that fatty acid composition of photosynthetic tissues of the *Primula* species represents interest for their chemotaxonomic studies.

The lipids of the wild species of *Primula* genus growing in Uzbekistan were studied for the first time.

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STRUCTURE AND PROPERTIES OF QUINAZOLINE-4-ONE DERIVATIVES FROM INVARIOM MODELLING

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New quinazolone derivatives based on natural products were synthesized [1], purified and crystallized to investigate possible biological activity. As part of the investigation we have also carried out single-crystal X-ray diffraction experiments to elucidate their solid-state structure. Fig. 1 shows the chemical composition of the compounds. In order to derive more accurate molecular geometries beyond the use of the independent atom model the new crystal structures of 2-chloroacetyl)-2,3,3a,4-tetrahydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**1**) and 4-(2-diethylamino)acetyl-2,3,3a,4-tetrahydropyrrolo[2,1-b]quinazoline-9(1*H*)-one (**2**) (see left Scheme in Fig. 1) were further refined with aspherical scattering factors from the Invariom database [2] to take into account valence electron density (Fig. 1).

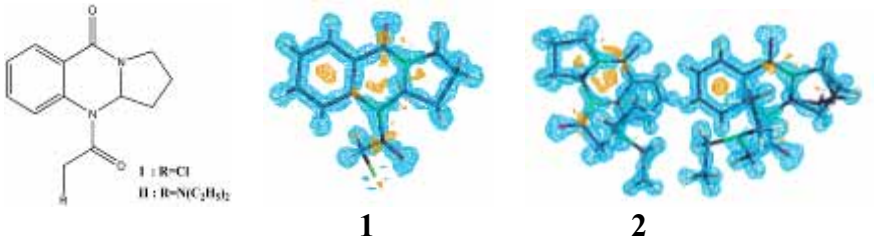

Fig. 1. Three-dimensional deformation electron density (0.1 eE^{-3} isosurface) from fast Fourier transform with *MolecoolQt* [3] for the **1** and 2.

A strenght of the invariom model is that it predicts the distribution of valence electron density in crystals already on the basis of conventional diffraction experiments with normal resolution (sinи/L around 0.7 E^{-1}). The so-obtained structural data and the electron-density model then allows to predict electronic properties that can be correlated with molecular reactivity.

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STUDY OF NEW LIGNIN ENTEROSORBENT BIOEQUIVALENCE WITH A FOREIGN ANALOG – "FILTRUM-STI"

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Nowadays, enterosorption is gaining higher popularity both among medical clinicians, and among the public. Entersorbents are the medicines intended for clearing the body of residues, toxins and poisons: both the ones which got from outside and the ones arisen in it under the influence of various pathological processes. One of the prospective enterosorbents is the sorbents based on hydrolytic lignin. Being macroporous and soft-structured (unlike activated carbon and other hard-structured medicines), they do not injure intestinal mucosa and are capable of macromolecules and bacterial cells sorption.

Objective: Study of cotton hydrolytic lignin based entersorbents, developed in UzKFTI compared to wood hydrolytic lignin based Filtrum –STI medicine (produced by "STI Med-Sorb" Corp, Russia).

Methods: the study of an acute toxicity was conducted on 36 white mice of both genders, weighted 18–21 g. 10–25% suspension was prepared from the study medicine by adding Tween-20 and orally injected into mice in an amount of 0.8 mL. After one-time injection of the medicine, observations were carried out hourly on the day of injection, 3 times/day on the second and third days, and once/day during the following five days. The study of specific antidiarrheal activity was carried out on male rats, weighted 180–220 g. Diarrhea was caused by adding lactose into the ration. Study medicines were injected by atraumatic probe in dose of 50 mg/kg once a day.

Results: the results indicated that injections of both medicines in doses of 2500 mg/kg, 5000 mg/kg and 10000 mg/kg do not cause considerable changes in the behavior of mice. Cases of death were not observed during the 7 days.

Animals fed by lactose-containing diet were observed having diarrhea, accompanied by the change of stool form (loss of feces solidness), the moisture in which made up 69.5% against 50.7% of intact rats′ ones. Under the impact of lignin enterosorbent (UzKFTI), the share of moisture in stool dropped to 30.8%. Unidirectional activity was also ascertained under the impact of Filtrum-STI – 29.6%, that indicates identical antidiarrheal effect of both medicines.

Outcomes: new lignin enterosorbent developed in UzKFTI and Filtrum-STI, as dosed 10000 mg/kg, do not cause fatalities and are identical in action. According to the toxicity classification, they may be referred as substances of class 5 – almost nontoxic. Both medicines are also identical in terms of entorosoption activity on models of diarrhea.

DETERMINATION OF FLAVONOIDS CONTENT IN "HEPAFIL" PREPARATION

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In the Tashkent Pharmaceutical Institute on the Pharmacognozy chair "Hepafil" preparation on the base of flowers *Achillea filipendulina* Lam., aerial part of *Artemisia absinthium* L. and *Stigmata maydis* was created. The preparation exhibits the expressed cholagogic activity. Phytochemical investigation of dry extract, from which "Hepafil" is obtained, showed that there are more flavonoid compounds and also rutin among various biologically active substances. In order to standardize "Hepafil" substance the content of rutin is determined by spectrophotometric method.

One gram (precise weighing substance) of preparation is put into the measured flask of 50 mL and 30 mL of 95% ethyl alcohol is added. After that the solution is put into the ultrasonic bath for 10 min, diluted with 95% ethyl alcohol to reaching the mark and filtrated.

1 mL of filtrate is put into the measured flask of 25 mL, add 5 mL of 95% of ethyl alcohol, 5 mL of 5% aluminium chloride solution in 70% ethyl alcohol, after 10 min add 2 mL of 5% acetic acid solution in 70% ethyl alcohol, lead to volume of 70% solution with alcohol to the mark and then mix.

After 30 min the optic density of the obtained solution on spectrophotometer at the curve length of 408 nm in the ditch with layer thickness of 10 mm, using as the compensatory solution, which consists of 1 mL of the preparation, 5 ml of 95% alcohol and 2 mL of acetic acid solution in 70% alcohol is measured, placed in the measured flask of 25 mL and led with 70% alcohol to the mark.

Simultaneously, after 30 min, the optic density of compared solutions is measured (solution of standard sample of rutin), prepared similar to the tested solution with the use as compensatory solution, the solution consisting of 1 mL of compared solution and 2 mL of acetic acid solution in 70% alcohol, placed into the measured flask of 25 mL and led with 70% alcohol to the mark.

The content of flavonoids sum (x) in the preparation on the account to rutin in mg in 1 mL is calculated according to the formula:

$$X = \frac{D_1 \cdot m_0 \cdot 50 \cdot 1 \cdot 25 \cdot P \cdot 100}{D_0 \cdot m_1 \cdot 100 \cdot 25 \cdot 1(100 - W)},$$

where D_1 – optic density of the investigated solution; D_0 – optic density of solution WSS (rutin), m_0 – mass of weighing substance (rutin in g); m_1 – mass of weighing substance in g; P – content of rutin in WSS in per cent (99.40); W – loss of mass in drying raw material in per cent.

It was ascertained by the spectrophotometric method, that the content of flavonoids accounted to rutin in "Hepafil" preparation is no less than 4.45%. The obtained results will be used in standardization of this preparation.

ISOMERIZATION OF FATTY ACIDS IN MODIFICATION OF OILS AND FATS

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Quality and food safety of catalytically modified fats depends on triglycerides composition of used fatty raw materials and an arrangement of fatty acids in TAG acyls. In our researches Nisosel-800 catalyst made by Engelkhard firm in Holland used as the most effective powdery catalyst.

For the first time process of continuous technology of cotton oil catalytic modification using the powdery Nisosel-800 catalyst is developed. In order to decrease the contents of the *trance*-isomers of monoenoic fatty acids in catalytically modified food fats, improve their quality, physiological and nutrition value continuous hydrogenation of cotton oil on the production autoclave using the regenerated catalyst carried out. In the conducted pilot researches it was interesting to obtaine the low-melting and high-melting food fats used for production of margarine production and confectionery fats.

Volume speed of oil supply, m^3/h	Quality			Nutrition value	
	Iodine number, % I_2	Melting point, °C	Hardness, g/cm	Contents of trance acids, %	Content of hard glycerides, %
5.0	68.4	33.1	280	13	47
5.2	70.8	32.6	240	7	43
5.5	72.6	31.4	200	5	34

The provided data testified that catalytic modification proceeds with insignificant decrease in iodine number of oil. Under the specified conditions of catalytic modification the insignificant accumulation of trance-isomers of monoenoic fatty acids in the hydrogenated fats is observed. However, a consistence of the received fatty production is very hard. Thus, technological ways of improvement of quality and ensuring food safety of catalytically modified food fats on catalysts of new generation are developed.

STUDYING OF VITAMIN A VALUE IN ENRICHMENT OF FOOD OIL

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Nutritional value of fat depends both on fatty acid composition and contents of various additives (vitamins, phosphpolipids etc.).

Vitamin A is stable and assimilated by an organism only in fat solutions. This vitamin plays an important role in the metabolism and especially in activity of the growing organism. Considering these facts, in our researches degree of safety of vitamin A in enriched by vitamines cotton oil and influences on it the food phospholipids being biologically active agents and natural antioxidants, stabilizers, an emulgators were studied. As a control fat the butter and melting butter containing vitamin A were taken. For vitaminization the food refined cotton oil obtained by a method of pressing and not containing phospholipids was taken. As a source of vitamin A its concentrate was used, that was added to cotton oil in quantities 26, 43, 46 and 92 IU in 1 g of fat. The samples of oils containing 26, 43 and 46 IU of vitamin, had identical organoleptic indicators (color, smell, taste), peculiar to cotton oil, with imperceptible smack of vitamin concentrate. At addition of vitamin A to oil in concentration of 92 IU in 1 g only insignificant smack and a smell of vitamin concentrate was noted. In addition to the vitaminized samples of cotton oil phospholipids in concentration of 0.7 and 1% the small shade of smack of sunflower oil was noted, but taste and a smell peculiar to cotton oil generally remained. All samples of the vitaminized oil were exposed to heat treatment which is usually carried out in the course of cooking, i.e. warming up to 160°C and "calcinating" to 240°C. Obtained samples of oil gained pleasant organoleptic properties, smack of a concentrate of vitamin A disappeared, and a concentrate of phospolipids remained in the form of insignificant traces. Results of the conducted researches established the possibility of vitaminization of cotton oil by vitamin A in a combination with food phospholipids. Probably, safety of this vitamin B combination with phospholipids may be explained by high content of antioxidant tocopherol (from 86 to 110 mg %) in the oil.

AROMATIC COMPOUNDS FROM HERBAL RAW MATERIALS FOR DETERGENTS

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The synthetic detergents (SD) are intended for use in living conditions, and in the industry. Rapid development of their manufacture is caused by possibilities for creation of the detergents suitable on the properties and appointment in various fields. Synthetic detergents are manufactured in the form of powder, pastes or liquid. All raw materials for production of SD are subdivided into two groups - useful additives of an inorganic and organic origin; surface-active washing substances. Such salts belong to useful additives, as technical sodium tripolyphosphate, sodium tetrapyrophosphate, hexametaphosphate sodium, trimetaphosphate sodium, sodium silicates. Besides, neutral inorganic salts (sodium sulfate and sodium chloride), and also sodium perborate and sodium percarbonate used. All types of raw materials previously analyzed, then in accordance with data of analyses a compounding of this or that type of SD make. Taking into account the above, the compounding and components of some types of the universal synthetic detergents developed by us is given below.

Components	Without bleaching	With bleaching	With bleaching in washing machines
Washing substances (in terms of 100% substance) Including	20	17	15
Alkylbenzenesulfonates	+	+	+
Alkylsulfonates	+	+	+
Alkylsulfates primary	+	+	+
Oxyetylated alcohols or alkylphenols	+	+	2–3
Soap	–	–	6
Sodium tripolyphosphate	40	45	40
Sodium silicate (in terms of solid)	3-8	3-8	5
CMC (in terms of 100% substance)	1.0	1.0	0.9
Sodium perborate	–	20	25
Stabilizer of peroxide salts (trilon B or magnesium chloride)	–	0.3–2.0	0.4–2.0
Sodium toluolsulfonat	0–2	0–2	–
Optical bleach	0.3–0.4	0.3–0.4	0.3–0.4
Perfumery fragrance	0.1–0.3	0.1–0.3	0.1–0.3
Sodium and impurity sulfate	to 25.6	to 9.3	to 9.3
Water	10	5	5

GERMACRENES AND OTHER CONSTITUENTS OF *Seseli korovinii*

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Seseli korovinii Schischk. is the perennial polycarpic plant of 70 cm height. It grows on an altitude 1600–2900 m above-sea level on the slope of Turkestanic, Nurata, and Zeravshan ridges. According to reference data, the plant roots contain coumarin derivative bergaptene and chromones gamoudol and gamoudol acetate. Composition of aerial part of *Seseli korovinii* was not studied earlier.

Chromato-mass-spectral analysis method was applied to study the composition of hexane and benzene extracts of *Seseli korovinii* aerial parts collected in the slope of Nurata rang in Uzbekistan at the beginning of blooming.

The following constituents are identified in hexane extract: (*E*)-2-methyl-2-butenoic acid (4.89 min; 0.19%), isopropylmethylthiophene (12.51; 0.41), α-terpinene (18.27; 9.84), α-cubenene (19.47; 1.96), 2,2-dimethyl-3-methylene-bicyclo[2.2.1]heptane (20.28; 0.41), *trans*-β-caryophyllene (20.85; 4.74), α-caryophyllene (21.92; 5.66), (–)-germacra-1(10),4(15),5-triene (22.80; 14.08), bicyclogermacrene (23.27; 5.00), γ-elemene (23.54; 4.99), α-terpinolen (24.09; 14.89), (–)-isoledene (24.44; 1.73), eudesma-3,7(11)-diene (24.64; 4.95), germacrene B (25.08; 2.81), endo-1-bourbonanol (25.72; 2.66), 1,7,7-trimethyl-2-vinylbicyclo[2.2.1]hept-2-ene (26.22; 0.47), α-bisabolol (29.13; 5.60).

The following compounds were identified in benzene extract: pinene (5.55 min; 2.49%), (+)-sabinene (6.57; 2.60), β-myrcene (7.05; 1.98), *1*-phellandrene (7.42; 0.85), (+)-3-caren (8.14; 0.80), *trans*-α-ocimene (8.44; 0.32), *cis*-β-ocimene (8.76; 1.36), *m*-cresol (9.94; 1.00), isopropylmethylthiophene (12.73; 1.86), α-terpinene (18.25; 5.79), α-cubenene (19.46; 0.57), [3a*S*-(3aα,3bβ,4β,7α,7a*S**)]-octahydro-7-methyl-3-methylene-4-(1-methylethyl)-1*H*-cyclopenta[1,3]cyclopropa[1,2]benzene (19.95; 0.93), *trans*-β-caryophyllene (20.84; 3.86), aromadendrene (21.59; 1.43), α-caryophyllene (21.92; 5.66), germacra-1(10),4(15),5-triene (22.79; 11.97), bicyclogermacrene (23.26; 3.97), α-terpinolen (24.09; 11.88), (4AR-*trans*)-1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-(1-methylethylidene)-naphtalene (24.63; 6.39), germacrene B (25.08; 2.63), endo-1-bourbonanol (25.70; 1.87), 1,7,7-trimethyl-2-vinylbicyclo[2.2.1]hept-2-ene (26.21; 0.34), 2-isopropyl-5-methyl-9-methylene-bicyclo[4.4.0]dec-1-en (27.09; 1.93), α-bisabolol (29.10; 4.17), angelicin (= isopsoralen) (31.82; 2.80).

All of the reported compounds were identified in aerial part of *Seseli korovinii* Schischk. for the first time.

ISOPRENOIDS OF *Tanacetopsis karataviensis*

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Tanacetopsis karataviensis Kovalevsk. is perennial plant of 30–60 cm height, blossoming in June–August and fruiting in July–September. It grows on a crushed rocky slope of mountains in median and overhead zones: in Samarqand and Dzhizak regions (Nuratau mountains and west ridge of Zeravshan range).

Constituents of aerial part of *Tanacetopsis karataviensis* weren′t studied earlier.

Applying method of chromato-mass-spectral analysis we have studied compounds composition of hexane and benzene extracts of *Tanacetopsis karataviensis* aerial parts. Plants were collected at the beginning of blossoming in the slope of Nurata range at the height of 1600 m.

In the hexane extract we identified following compounds: geraniol acetate (19.69 min; 0.15%), *cis,trans*-farnesol (27.53; 15.08), α-bisabolol (29.07; 1.07), nerolidyl acetate (34.65; 4.67), nerolidol (36.09; 1.53), caryophyllene (37.68; 11.02).

In benzene extract following components were identified: α-phellandrene (7.42; 0.24), 1-(4-methyl-3-cyclohexen-1-yl)ethanone (11.42; 0.14), (+)-(*R*)-limonene (19.67; 0.14), geraniol acetate (21.03; 0.17), 2-isopropenyl-5-methyl-4-hexenyl acetate (23.71; 0.30), *cis,trans*-farnesol (27.50; 8.65), α-bisabolol (29.02; 0.49), farnesyl acetate (34.56; 3.07), (*E*)-β-farnesene (35.99; 0.88), caryophyllene (37.60; 9.35), (*Z,E*)-α-farnesene (35.99; 0.88).

All of the reported compounds were identified for the first time in aerial part of *Tanacetopsis karataviensis*.

SESQUITERPENES AND OTHER COMPONENTS OF *Lepidolopha komarovii*

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Lepidolopha komarovii C. Winkl. is subsrub of up to 1 m height, blossoming in June–July and fruiting in August–September. It grows on stony slopes of low and median zones of mountains in Tashkent (Pskem and Ugam ranges), Samarqand (Zeravshan range), Surkhandar′ja (Hissar range) regions. Secondary metabolites of this species of plant′s genus *Lepidolopha* had not been studied earlier.

Chromato-mass-spectral analysis was applied to study the composition of hexane and benzene extracts of aerial parts *Lepidolopha komarovii,* collected at the beginning of blooming in the slope of Central zone of Nurata range at height of about 1600 m.

In hexane extract the following compounds were identified: eucalyptol (8.21 min; 0.68%), (+-)-linalool (10.43; 1.47), chrysanthenyl acetate (15.79; 33.37), 2,6-dimethyl-1,7-octadiene-3,6-diol (16.39; 0.91), 1,7,7-trimethylbicyclo[2.2.1] hept-2-yl acetate (16.57; 0.85), 2-isopropenyl-5-methyl-4-hexenyl acetate (16.77; 1.82), geraniol acetate (19.79; 7.65), 10s,11s-himachala-3(12),4-diene (22.84; 8.09), nerolidol A (30.58; 1.20).

In benzene extract the following compounds were identified: *o*-xylene (4.64 min; 0.07%), nonane (4.74; 0.31), santolinatrien (4.92; 0.65), (+)-α-pinene (5.55; 1.09), camphene (5.92; 0.30), (+)-sabinene (6.57; 0.83), eucalyptol (8.21; 3.76), 4-thujanol, stereoisomer (9.35; 0.37), (+-)-linalool (10.43; 2.27), (+-)-camphor (11.83; 0.73), chrysanthenyl acetate (15.85; 37.95), 2,6-dimethyl-1,7-octadiene-3,6-diol (16.35; 1.11), 1,7,7-trimethylbicyclo[2.2.1] hept-2-yl acetate (16.57; 1.12), 2-isopropenyl-5-methyl-4-hexenyl acetate (16.78; 2.06), 2,2-dimethyl-3-methylene-bicyclo[2.2.1]heptane (18.39; 0.90), geraniol acetate (19.80; 5.93), vulgarole (20.37; 2.49), *trans*-β-caryophyllene (20.84; 0.51), geraniol formate (21.02; 1.36), 10s,11s-himachala-3(12),4-diene (22.84; 4.63), geraniol butyrate (23.77; 1.10), (1*R*,4*R*,6*R*,10*S*)-4,12,12-trimethyl-9-methylene-5-oxatricyclo[8.2.0.04,6]dodecane (25.87; 1.03).

All of the reported compounds were identified in aerial part *Lepidolopha komarovii* for the first time.

EFFECT OF RONCOLEUKINE ON SERUM CYTOKINES IN LEUKEMIC RATS

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Objective: to study contents of cytokines IL-1β, IL-6 and TNF-α in blood serum of rats with experimental leukemia (EL) in pharmacotherapy dynamics.

Material and Methods. 157 male rats were subcutaneously injected with 40% oil solution of benzyl (0.01 mL per 100 g of body weight) within 8 months. Development of leukemia was assessed by changes in peripheral blood and bone marrow. 20 rats were intact. After 5 months 126 rats with leukemia signs were divided into 4 groups: 1st group (33 rats) received physiological solution 0.5 mL/100 g; 2nd (31 rats) – hydrae 0.06 mg/100 g intraperitoneally; 3rd (31 rats) – roncoleukine 0.006 mg/kg intraperitoneally 3 times per a day within 10 days; 4th (31 rats) – hydrae + roncoleukine at the same doses. Stage-by-stage treatment was carried out in 10 days within 3 months. Animals were sacrificed under slight anesthesia, according to the rules of the European Convention for the Protection of Vertebrate Animals. Contents of IL-1β, IL-6 and TNF-α in blood serum (pg/mL) were determined by immunoenzymatic method. The data obtained were processed using methods of variation statistics.

Results and Discussion. At 6 month, in rats with EL serum contents of IL-1β, IL-6 and TNF-α were increased for 3.36 ($P < 0.001$); 2.43 ($P < 0.001$) and 1.61 ($P < 0.01$) times, respectively. At 7 month, contents of IL-1β and IL-6 remained at the same values, while TNF-α progressively increased in 2.35 ($P < 0.01$) times. By final term, contents of IL-1β, IL-6 and TNF-α continued increase, significantly exceeded the values of intact rats in 3.99; 4.42 and 2.44 times, respectively. Stage-by-stage chemotherapy for EL with hydrae reduced high levels of the investigated cytokines. Probably, this was connected with damaging effect of hydrae on DNA synthesis, resulting from inhibition of ribonucleotidereductase and DNA-polymerases in cells of bone marrow. Combination of hydrae and roncoleukine more significantly decreased the levels of cytokines, especially TNF-α. The same changes, but to a lesser extent, were observed at use of roncoleukine without cytostatic. This may be connected with apoptosis induction by roncoleukine, resulting from increase of level of proapoptic protein Bad and decrease of levels of antiapoptic proteins Bcl-2 and Bcl-x1, as well as activation of T- and B-cells of central and peripheral lymphoid organs and macrophage functions. In our experiments the drug induced antitumoral effect of hydrae that was manifested by decrease of animals' mortality and inhibition of leukosogenesis progression.

Conclusions. EL induced by prolonged introduction of benzyl is manifested by increase of serum levels of IL-1β, IL-6 and TNF-α, depending on terms of experiment. Pharmacotherapy for EL with hydrae decreased the levels of proinflammatory cytokines because of damaging effect on lymphoid tissue, and decrease of functions of T- and B-cells. Introduction of roncoleukine in pharmacotherapy of EL sharply reduced contents of cytokines, especially IL-6 and TNF-α.

HYPOCHOLESTEROLEMIC AND HYPOCOAGULATORY PROPERTIES OF SULFAPORIN IN HYPERCHOLESTEROLEMIA

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Objective was to study hypocholesterolemic and hypocoagulatory properties of sulfaporin on the model of experimental hypercholesterolemia (EHC).

Sulfaporin is chitosan sulfate, which formation was identified by elemental analysis; the degree of sulfation was determined by conductometric titration. IR spectroscopy and X-ray analysis established the structure of sulfaporin. EHC was reproduced in 46 rabbits by introduction of cholesterol diet for 3 months. Development of EHC was judged by the change in lipid and lipoprotein spectrum of blood serum. By the final deadline, morphologically atherosclerotic changes developed in aorta. Animals by this time were divided into 5 groups: 1st group received placebo (8 rabbits), 2nd – heparin in standard doses (7 rabbits), 3rd – hypocholesterolemic drug hemfibrasil 100 mg/kg, 4th – sulfaporin at a dose of 500 IU/kg, 5th – sulfaporin 1000 IU/kg parenterally within 1 month. At 90 and 120 days of experiment, we determined total cholesterol (TC), high-density lipids (HDL), low-density lipids (LDL) and very low-density lipids (VLDL) in blood serum, as well as the main parameters of platelet-vascular coagulation and hemostasis. The digital material was processed by variation statistics.

Correction of EHC with hypocholesterolemic drugs for 2 months had a positive effect on lipid metabolism. The content of TC significantly reduced in 1.35 ($P < 0.05$), 1.75 ($P < 0.01$) and 2.29 times ($P < 0.001$), respectively in the groups treated with hemfibrasil, sulfaporin-500 and sulfaporin-1000, compared with control group. The levels of LDL decreased for 1.36 ($P < 0.05$), 1.65 ($P < 0.05$) and 2.19 ($P < 0.01$) times, respectively. VLDL contents also decreased for 1.45 ($P < 0.05$), 2.13 ($P < 0.01$) and 2.52 times ($P < 0.001$) respectively, while the levels of HDL increased for 1.72 times ($P < 0.05$) at use of hemfibrasil, and in 1.49 ($P < 0.05$) and 1.92 times ($P < 0.01$), at use of sulfaporin-500 and 1000, respectively, in comparison to control animals. Thus, hemfibrasil had a weaker positive effect on serum lipoprotein spectrum.

Hypercoagulatory syndrome developed in rabbits with EHC. Pharmacotherapy with heparin significantly improved platelet-vascular coagulation and hemostasis. Application of sulfaporin for a long time reduced platelet count to $237.8 \pm 6.2 \times 10^9$/L, significantly prolonged time of blood coagulation (beginning 155.48 ± 5.55 sec, end – 231.28 ± 5.9 sec) and thrombin time to 11.4 ± 0.86 sec, as well as reduced PTI on 17.1% and fibrinogen on 39.1%. After treatment with heparin the following parameters were observed: $248.1 \pm 15.7 \times 10^9$/L; start – 176 ± 13.2 sec. and finish – 253 ± 15.9 sec.; 10.8 ± 3.2 sec; 16.5% and 46.9%, respectively, in comparison with untreated group.

Sulfaporin has a strong hypocholesterolemic effect, lowering TC, VLDL, LDL, and increasing HDL. Its hypocholesterolemic properties depend on the concentration and are better than those of fibrates. Pharmacotherapy of EHC with sulfaporin decreases the number of platelets, prolongs time of blood coagulation, thrombin time, and reduces the concentration of fibrinogen and PTI. Sulfaporin is proved to be an effective anticoagulant of direct action and by its effect is not inferior to heparin.

USING OF GEL FORMS OF CHITOSAN IN THE TREATMENT OF THERMAL BURNS

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Objective was to study some mechanisms of regenerative action of chitosan (CS) on the model of thermal injury.

We used gels of *Bombyx mori* chitosan, crosslinked by glutaraldehyde (GA) and filled with 0.5% furacilinum (F). Model of thermal burns of III degree with area of 18–20 cm^2 was reproduced on 120 male rats by immersion of depilated skin area in boiling water for 10 seconds under light ether anesthesia. After 2 hours after burns modeling, rats were divided into 4 groups and topical treatment was conducted: 1st group (25 rats) were treated with CS, 2% acetic acid + GA + F; 2nd group 2 (25 rats) – CS, 2% acetic acid + GA; 3rd group (25 rats) – levomikol; 4th group (25 rats) – saline; 5th group – 10 intact rats. We conducted preliminary assessment of regenerative activity planimetrically, calculated recovery rate (Rr), the value of regression of regeneration (RR), as well as inclusion of ^{3}H-thymidine into DNA and ^{14}C-uridine into RNA in the skin. The number of pulses per minute was measured by counter «Beckman». The digital material was processed by variation statistics.

More pronounced reduction of the wound area was observed in the animals of the 1st group. The drugs in the 2nd and 3rd groups coincided, whereas in the 4th group regeneration decreased that was proved by the dynamics of the rate of wound healing. Thus, in the 1st group it decreased by 10 day from 14.08 ± 0.66 cm^2 to 9.47 ± 0.41 cm^2; in the 2nd group – from 13.26 ± 0.65 cm^2 to 10.90 ± 0.52 cm^2. The least regeneration was observed in the 3rd and 4th groups of animals. The calculation of the rate of healing in the 1st group showed progressive increase in this index since 3 days by the 7th day, and at 10 day it slightly reduced. At 3 day, the speed of healing exceeds parameters of control for 3-5-fold, and 4-fold at 7 day. Proof of this was the Rp index, the values of which were significantly higher in the 1st group. At 3 day, in the 1st group inclusion of ^{3}H-thymidine into DNA was 52%, at 7 day – 72%, at 11 day – 94%, whereas in the 4th group it was 48%; 27.8% and 25.5%, respectively. Inclusion of ^{14}C-uridine into RNA was more intensive in the 1st and 2nd groups: 40% and 38% at 3 day, 67.2% and 57.4% at 7 day, 80% to 90% at 10 day of experiment, respectively. In the 3rd group, these values were 32%; 50% and 70%, in the 4th group – 35%; 27.3% and 20%, respectively.

Chitosan gels, especially in combination with furacilinum, significantly accelerated the rate of healing of the affected areas, increased the regeneration rate, contributing to earlier reduction in burn surface. Speed of inclusion of ^{3}H-thymidine into DNA and ^{14}C-uridine into RNA during treatment with CS + GA + F was substantially higher than values of treated with levomikol and, especially, untreated animals, apparently, due to more complete recovery of the native DNA structure and gene expression.

STUDY OF LIVER ENERGY-PRODUCING AND DETOXICATION FUNCTIONS IN EXPERIMENTAL LEUKEMIA

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In hemoblastosis, liver is often involved in the pathological process due to liver leukemic infiltration, toxic effects of drugs, as well as viral, fungal and bacterial infections.

Objective is to reveal features of impairment of liver energy-producing and detoxication functions in rats with experimental leukemia (EL).

157 male rats were subcutaneously injected with 40% oil solution of benzyl (0.01 mL per 100 g of body weight) within 8 months. Common mortality was 40.1%. Development of leukemia was assessed by changes in peripheral blood and bone marrow. EL developed in 50; 77.4 and 86.4% of rats by the end of 6; 7 and 8 months. 20 rats were intact. At these terms, animals with signs of leukemia were sacrificed under Rausch-anesthesia, according to the rules outlined by the European Convention for the Protection of Vertebrate Animals. Subcellular structures were isolated from liver homogenate. In liver mitochondrial fraction we determined activity of succinate dehydrogenase (SDH), rotenone-insensitive cytochrome C reductase (RI-cytochrome C reductase), succinate-cytochrome C reductase, cytochrome oxidase (CCO); in microsomal fraction – contents of cytochromes P-450, b_5, P-420, activity of amidopyrine *N*-demethylase (*N*-AP), aniline hydroxylase (AH), and NADPH-cytochrome C-reductase (NADPH-cyt. C-red.). The data obtained were processed by using statistical computer program Statistica 5.

At 6 month, activities of SDH, RI-cytochrome C reductase and succinate-cytochrome C reductase significantly ($P < 0.001$) decreased in 3.25; 3.68 and 3 times, respectively, whereas activity of CCO increased in 2.59 times. At 7 month the activities of complexes II and III of the respiratory chain increased, however, these values still remained lower ($P < 0.05$) values of intact rats (in 1.73; 1.43 and 1.29 times, respectively), whereas activity of CCO remained high in 2.46 times ($P < 0.001$). By final term, activities of SDH, RI-cytochrome C reductase and succinate-cytochrome C reductase re-inhibited in 2.3; 2.12 and 2 times ($P < 0.001$), respectively. Activity of CCO also sharply reduced, but still remained high in 1.51 times ($P < 0.05$). Prolonged introduction of benzyl significantly ($P < 0.001$) inhibited contents of cytochromes P-450 and b_5 in liver, the levels of which were progressively reduced with strengthening of liver leukemic infiltration: at 6 month – in 2.3 and 3 times; at 7 month – in 2.5 and 3.2 times; at 8 month – in 2.9 and 3.87 times, respectively. Activity of *N*-AP also decreased in 5.1; 5.7 and 8.1 times, AH – in 5.13; 5.2 and 7 times, NADPH-cyt. C-red. – in 3.4 ($P < 0.001$), 3.82 and 5.22 times, respectively, in regard to terms.

In dynamics of EL activities of liver mitochondrial enzymes of rats reduced at 6 months. At 7 months, we could determine compensatory activation of complexes II and III of the respiratory chain, and transition to decompensation stage by final term. Activity of complex IV remained high. We observed progressive reduction of contents of cytochromes P-450 and b_5, activities of *N*-AP, AH and NADPH-cyt. C-red. in liver of rats with EL.

IMPORTANCE OF ABU ALI IBN SINA'S WORKS FOR DEVELOPMENT OF NEUROLOGY AND PSYCHOLOGY

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Abu Ali Ibn Sina (Avicenna) belongs to a number of greatest scientists in history of humankind, who enriched world science with achievements of vital importance. As the original scientist, Abu Ali Ibn Sina successfully worked in all areas of knowledge. In sources, more than 450 names of his compositions are mentioned, and number of works came up to us is about 240. They cover such areas of the science, as philosophy, medicine, logic, psychology, natural sciences (physics), astronomy, mathematics, music, chemistry, ethics, literature, linguistics, etc. However, Abu Ali Ibn Sina became famous, mainly, due to the works on philosophy and medicine.

Ibn Sina′s merits are especially great in the field of medicine. His main medical work is "Canon of medical science". This is the original medical encyclopedia, which covers with logic harmony the questions of prevention and treatment of illnesses.

Ibn Sina gave the certain concepts of medicine, resulted in the doctrine about juices and nature (temperament), anatomic descriptions of organs and systems, including the nervous system, considered the reasons, symptoms, and both classification of illnesses and general rules of their treatment. He enabled to familiarize with national medicine of his time. Many medicines offered by Ibn Sina strongly have come in pharmacopeia and have been applied until today. He gave especial attention to the doctrine about feed, lifestyle and preservation of health in all periods of life (general and private hygiene). By the main conditions of health prevention, he named physical exercises, regime of nutrition and rest. The descriptions of manifestations of diseases are evidence of his extraordinary observation, talent and experience.

Ibn Sina′s works represent the certain interest in neurology and psychology. He interested in mental and neurologic disorders not only from only medical point of view, but also as the object of psychological research. Apparently, he in detail expounded the insights into their nature and reasons of psychoneurologic disorders. He for the first time made the large step to materialism, trying to connect separate kinds of mental activity of a human with the certain parts of the brain. It is enough to recollect, for example, Ibn Sina′s instruction that bruises and traumas, destroying separate parts of the brain, defeat sensitivity and cause loss of some functions. He considered that the direct reason of psychological disorder was influence of environmental conditions or corporal damages. Thus, apparently, Ibn Sina interested in finding-out interrelations and interconnection between psychological and somatic. Therefore, "Canon" contains the instructions on possibility of psychosis occurrence in acute feverish diseases, connection of gastrointestinal diseases with the nervous system, etc. Until now, the developed by Ibn Sina pharmacological, physical, psychological and other methods of treatment have been used in rehabilitation of neurologic patients and prevention of more dangerous complications, for example, stroke.

Thus, Abu Ali Ibn Sina left enormous knowledge and ideas connected with struggle for protection of human health. His creativity played the great role in medicine not only in Central Asia, but all over the world.

STRUCTURE OF ESSENTIAL OILS OF *Artemisia annua*, GROWING IN HIGH MOUNTAINS OF FERGANA

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Leaves of high-mountainous samples of plant *Artemisia annua*, the settlements Yardan of Fergana area collected in vicinities were object of research. The essential oil fraction was received by distillation with water steam. The composition was obtained by chromato-mass spectrometry method on capillary column HP-5 MS, 0.25 mm × 30 m, column temperature 40–270°C (4°C/min), gas – helium on device NR-5972 series II with chromatograph HP-5890 series II. The bibliography of mass-spectra is NBS 75 K.L. (P. K. Igamberdieva, B. Y. Abduganiev, A. A. Ibragimov, 2009).

Chemical components of essential oils and their relative maintenance are identified in the table. 12 main substances make up 99.97% of total mixture weight. Among them most the maintenance is for eucolyptol (32.09%) and camphor (29.79%). There are more 22peaks of minor components on chromatogram, but their content is too small (in the sum of 0.05 %).

Chemical components	Substance index	Content in the mixture, %
2,5-Cyclohexadien-1-one, 4-ethyl-3,4- dimethyl-	1000	11.49
Benzene, 1,3,5-trimethyl-	1405	1.61
Benzene, 1-methyl-3-(1-methylethyl)-	1554	1.78
α-Thujone	1776	2.04
6-Oxabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 1,8-dimethyl-7-oxo-methyl ester	1883	2.16
Camphene	1975	2.27
2,4-Hexadiene,-2-methyl	2364	2.71
Camphor	2595	29.79
3,5,5-Trimethylcyclohex-2-en-1-one	2650	3.04
Eucolyptol	2795	32.09
β-Thujone	4747	5.45
Limonene	4828	5.54

According to other authors (I. Burzo, 2008; Zhengwen Yu, 2011; S. Cavar, 2012), the leaves of *Artemisia annua* grown in Romania, China and Bosnia, contain other substances in a differ proportion. All they allocated 74 substances containing more than 0.3%. As the main components vary: Artemesia-ketone 30.7–60.2%, camphor 6–15.8%, eucolyptol 5–16.11%, β-myrcene 20–37.7%. So, the comparison shows, that the quantitative content of substances in the composition of essential oils of *Artemisia annua* of Yardan and other countries had many differs.

Cousinia umbrosa IN THE TASHKENT REGION

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Cousinia umbrosa Bge is a perennial polycarpic herbal plant of ephemerides mesoxerophites from *Asteraceae* family. This species unlike other *Cousinia* Cass species is characterized by wide natural habitat. In Uzbekistan it is widely distributed in Tashkent, Samarkand, Surkhandarya and Fergana regions. This plant mainly grows in foothills and lowlands, in the shade places.

Cousinia umbrosa is not only forage, honey and oil plant, but promising source of inulin in domestic flora. As our preliminary investigations have shown, the content of inulin in roots of *Cousinia umbrosa* is 27–28%. Latter, as it is known, is widely used in food supplements of special use for normal carbohydrate metabolism, increasing of bifidobacterium in the intestinal tract and as immune modulator and absorbent. Inulin has also holagogic and hepatoprotective activity, prevents symptoms of bone diseases, inhibits tumours development, decreasing levels of cholesterol, triglycerides and phospholipids, atherosclerosis and cardiovascular diseases. Taking into consideration the above-mentioned, there is a great interest to study the possibility of gathering *Cousinia umbrosa* for working out the inulin-containing food supplements and remedies.

In 2012–2013 we described plant communities and took into account reserves of *Cousinia umbrosa* subterranean organs in Tashkent region in the Large and Small Chimgan place. It was ascertained, that *Cousinia umbrosa* grows chiefly in barley-cousinia-polyherbal communities, often in other cenosis with prevalence of ethemers and ethemerides, scattered in the barley-polyherbal and Lucerne-barley-polyherbal associations.

The productivity of crops *of Cousinia umbrosa* in the registration area (10 mL) of the investigated territory varied from 4 to 6 kg, and on average was 5 t/ha. Taking into account the revealed area of fields, which are 3500 ha, the reserve of *Cousinia umbrosa* roots is 17500 tons of raw material of dry or more than 1700 tons of air-dry mass.

The obtained results show the opportunity for using the *Cousinia umbrosa* roots as a source of inulin due to the sufficient raw material base.

POTATO DISEASE OF BREAD AND METHOD OF ITS PREVENTION

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Potato, or so-called, "viscous" disease of bread is evinced that bread crumb under influence of microorganisms causing this disease, becomes viscous (at breaking even of stale bread such crumb stretches with mucous, very thin, cobweb threads) and gains sharp, rather specific, unpleasant smell and taste. Activators of this disease are the cryptogamous microorganisms, concerning to Bacillus mesentericus form (potato stab). In occurrence of potato disease of bread also can be the reason Bacillus subtilis form microorganisms (hay stab). These microorganisms widespread in the nature (in air, on soil, on plants), and also meet in different quantity on any grain and in any flour.

They look like stabs in length from 1.6 to 6.0 microns and thickness about 0.5 microns. Disputes of Bacillus mesentericus have oval-roundish shape, and concern to thermophile type. So, for example, to destroy these disputes, it is necessary to influence them with water steam in temperature of 100°C during 5–6 h, they sustain temperature of 109–113°C up to 45 min, and 122–123°C – up to 10 min. At temperature of 130°C disputes perish instantly.

It is necessary to notice that if temperature in the centre of a crumb of bread by the end of a batch is 96–97°C, disputes of Bacillus mesentericus can remain in bread without losing the viability.

Microorganisms start actively breeding and functioning in 12 h after the batch. Optimum conditions for their viability are temperature from 35 to 45°C and raised humidity.

The potato stab possesses a complex of active starch-splitting (dominates alpha-amylase) and proteoclastic (proteinase, polypeptidase) enzymes which action causes specific changes of a crumb of bread at potato disease.

Specific taste and smell of the bread affected with potato disease attribute to products of deep proteolysis of albuminous components of a crumb. Proteinase of potato stab is active in a wide range of pH – from 5 to10 and has an activity maximum at pH 7–9.

The major factor causing possibility and rate of potato disease in bread is acidity. At pH lower than 4.8–5.0 there is practically no disease of bread. Increase of acidity of the pastry is one of the basic methods of prevention of potato disease of bread. For this purpose is recommended addition of lactic ferments, liquid yeast, parts of the ripe pastry (or leaven) of the previous production or adding into the dough. Acidity of bread is the factor which inhibits activity of causative agents of potato disease.

Effective remedy of preventive maintenance of given disease is addition of bio additives, in particular wheaten ferments. A particular interest represent polystrain ferments of spontaneous fermentation, for example the peas-anise tree, traditionally used in baking of Uzbek bread. Its advantage concerning other ferments consists that the technology of preparation is fulfilled and approved by centuries, in diluting cycle do not apply pure cultures of yeast and bacteria, and created conditions for development of natural micro flora of a flour.

SUPPRESSING EFFECT OF FLAVONOIDS ON THE THYMOCYTE VOLUME REGULATION INVOLVES SWELLING–ACTIVATED ANIONIC TRANSPORT

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When subjected to a hypoosmotic stress, rat thymocytes first passively swell in accordance with Van′t–Hoff′s low, and then actively regulate their volume back to a nearly normal level, the process called Regulatory Volume Decrease (RVD). We have recently demonstrated that thymocytes express swelling-activated anion channels, which are involved in their robust volume regulation. However, the pharmacology of the RVD process in general and of the volume-regulated anion channels in particular, is very poor at present. We have recently tested effects of a number of flavonoids on RVD of rat thymocytes and identified several of them, which had a distinct suppressing effect at micromolar range of concentration. However, the inhibiting effect of these substances could be accomplished via modulation either of the following three key components of the RVD process: (i) the swelling induced increase of plasmalemma calcium permeability, (ii) concomitant activation of potassium and (iii) anion channels. In order to identify the component of the RVD process affected by the flavonoids, we have worked out experimental conditions in which the membrane cationic conductance was increased by gramicidin D (which is known to form nonselective cation channels) and all the monovalent cations were replaced by a large organic cation, *N*-methyl-*D*-glucamine (NMDG). We have demonstrated that under these conditions (termed NMDG-GrD), the regulatory volume decrease is controlled mainly by the level of anionic permeability of plasmalemma.

When four of the RVD-suppressing flavonoids were tested in NMDG-GrD conditions, all of them exhibited a profound inhibiting effect of RVD. Thus, the half-maximal effect (IC_{50}) of pulicarin was 20.2 ± 1.4 μM with a Hill coefficient (h) of 1.4 ± 0.2 (n = 6), which is close to the parameters of its effect on the RVD under normal sodium containing hypotonic conditions (IC_{50} = 20.4 ± 1.9 μM; h = 1.2 ± 0.1). Similar result was obtained for pinocembrin (IC_{50} = 52.4 ± 1.6 μM; h = 3.3 ± 0.2) and hispidulin (IC_{50} = 94.4 ± 4.5 μM; h = 2.1 ± 0.3). These data are also reminiscent of those obtained in normal Na^+-containing conditions.

Previously we founded, that lemanin produces a biphasic effect on RVD in normal Na^+-containing conditions. Consistently, in NMDG-GrD conditions, RVD was 18.8 ± 3.1% at 50 μM and 97.1 ± 0.8 % at 100 μM. The half-maximal effect for the first phase was observed at 11.4 ± 0.5 μM with Hill coefficient of 2.1 ± 0.2 (n = 6). This is close to the parameters of RVD suppression effect of lemanin observed earlier in normal Na^+-containing hypoosmotic conditions.

In conclusion, our results suggest that the suppressing effect of the four most effective flavonoids on the volume regulation of rat thymocytes is likely to be mediated via inhibition of the volume-regulated anionic transport of thymic plasma membrane.

COMBINED DRYING OF AGRICULTURAL PRODUCTS

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It is known that fruits and vegetables, as well as their by-products, are in steady demand both in domestic and in foreign markets.

Improving food security of the population is based, humidity, on the production of high-quality canned foods by improving the processing of agricultural raw materials, the intensification of production, development and introduction of new high-performance systems, saving energy resources.

One of the main methods of processing is the drying of products, which is an energy-intensive process. The analysis shows that the existing dryers are expensive, energy consuming and sometimes ineffective. Vegetables and fruits are subjected to drying, are an indispensable source of important biologically active substances – vitamins, carbohydrates and minerals necessary for normal human life.

The solution of the problems of the intensification of the drying process requires the development and implementation of new efficient methods of processing plants and technology with the best technical embodiment.

Combination method of drying fruits and vegetables is a promising method of dewatering includes a pulse – the acoustic processing moist material in the infrared convection drying.

The advantage of the combined method of drying is to intensify the process, improving performance of the machine by reducing the duration of the process.

When drying the product is subjected to external diffusion of moisture from the surface of a dried product. The larger surface of the product and the speed of hot air lead to the faster evaporation of moisture from the boundary layer of the product. The further course of drying depends on the movement of moisture in the product, there is moisture rushes into the outer layers of the product. This concentration of moisture in the inner and outer layers seeks alignment.

To ensure the necessary residual moisture of dry product required for its further processing, the product is processed in the acoustic field. In the acoustic field at the liquid solid – milking the body by the action of the source of the sound of high intensity is devastating effects.

One of the known effects of acoustic influence is cavitation – the formation of gaps in the liquid or on the border liquid and solid state physics.

Under the influence of the variable acoustic pressure in the liquid phase in the negative pressure ruptures occur, that instantly filling by steam and dissolved gases. In the cavitation bubbles slam the shock waves of high amplitude pressure appeared. These mechanical forces are the cause of the ravages of acoustics.

CONDENSATION OF HOMOVERATRILAMINE TO GLYCOLIC ACID

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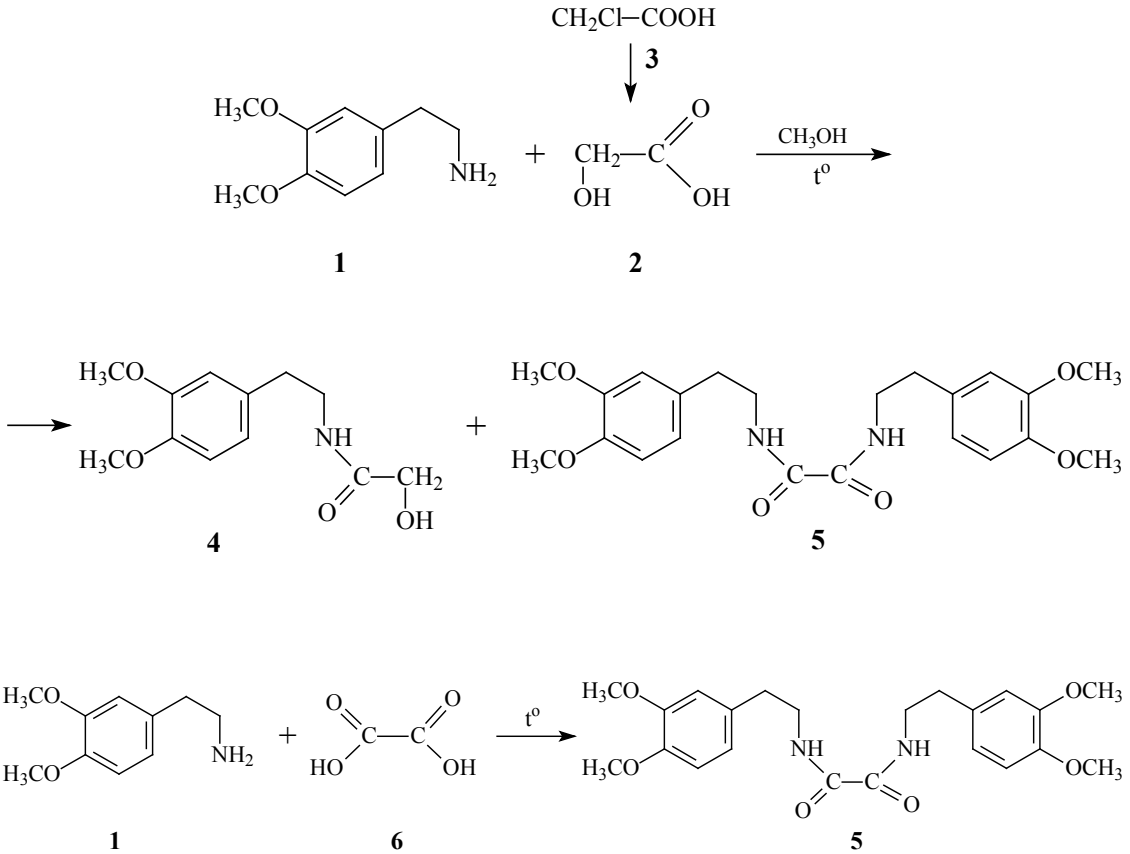
Condensation of homoveratrilamine (**1**) and glycolic acid (**2**), obtained from monochloroacetic acid (**3**), provides the mixture of two amides: glycolic acid amide (**4**) and oxalic acid diamide (**5**).

Obtaining of oxalic acid diamide (**5**) was confirmed by the counter synthesis on the basis of oxalic acid (**6**) and homoveratrilamine (**1**).



The structures of the compounds were proved by spectroscopic techniques (IR and ^{1}H NMR).

IMIDAZOLIUM AND BENZIMIDAZOLIUM SALTS OF LUPANE SERIES

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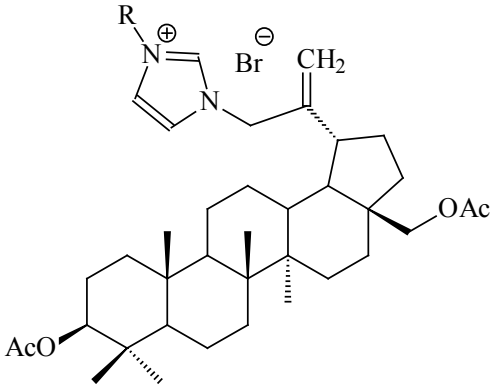
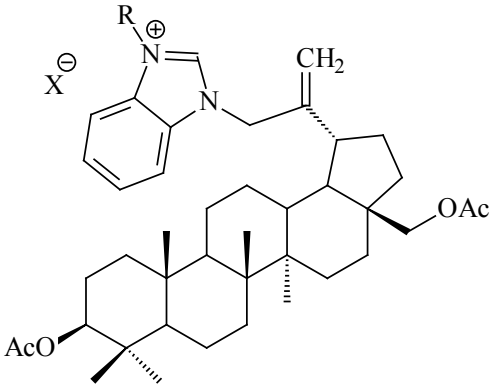
In light of our sustained interest to the 30-amino-substituted lupanes [1], we report on synthesis of new imidazolium and benzimidazolium salts **1**–**3** of lupane series.



1 R = H (a), Me (b), Vin (c), *i*-Pr (d), *t*-Bu (e) ,Bn (f), Ph (g), 2-MeC_6H_4 (h), 2,6-$Me_2C_6H_3$ (i), 2,4,6-$Me_3C_6H_2$ (j)



2 R = Me, X = I; **3** R = Bn, X = Br

Reaction of 30-bromo-3β,28-diacetoxy-lup-20,29-ene with substituted imidazoles afforded compounds **1a–j** used as *N*-heterocyclic carbene ligands in Suzuki-Miyaura reaction [2].

Treatment of 30-benzimidazolyl-3β,28-diacetoxy-lup-20,29-ene with iodomethane in toluene at room temperature gave rise to compound **2** (yield 78%). Salt **3** (43% yield) was obtained by the reaction of 30-benzimidazolyl-3β,28-diacetoxy-lup-20,29-ene with excess of benzyl bromide. Structure of compounds **1**–**3** was confirmed by NMR ^{1}H and ^{13}C spectra.

Citotoxicity of compounds **1–3** is under investigation.

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CHEMICAL COMPOSITION OF *Lonicera* SPECIES FROM KAZAKHSTAN

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The genus *Lonicera* (*Caprifoliaceae*) comprises of 200 species with 21 growing in Kazakhstan. The genus includes shrubs with both climbing and non-climbing sprouts. The fruits of most species are either inedible or poisonous (**1**).

The present work aimed to investigate two *Lonicera* species, *Lonicera iliensis* Pojark. and *L. altaica* Pall. ex DC collected in different vegetation stages for chemical composition of the essential oils. These species belong to subsection of blue honeysuckles *Caeruleae* Rehd. (section *Isika* Rehd.), both of them have edible fruits (**2–4**).

Flower, leaf at blooming and fruiting stages and fruits of two *Lonicera* species were hydrodistilled with Clevenger type apparatus to obtain essential oils. Chemical compositions of the oils were investigated by GC-FID and GC/MS techniques. Detected constituents were classified as monoterpenes, sesquiterpenes, alkanes, phenylpropanoids, fatty acids, aldehydes and alcohols.

Quantitative and qualitative diversity depending on species, organ and phase of development of the plants have been detected. A high abundance of alkanes (17.1–44.5%) was detected in the volatiles of all the *L. iliensis* organs investigated. In the flowers, leaves at blooming stage and fruits of *L. altaica* alkanes were found as dominating group. However, alkanes have not been detected in the leaf oil of *L. altaica* collected at fruiting stage. Polycyclic aromatic hydrocarbons were the distinguishing characteristic in the volatiles of *L. altaica* leaves at fruiting stage while oxygenated monoterpenes were in high percentages in the leaves at blooming stage. The flowers of *L. iliensis* and *L. altaica* have been found to be rich by oxygenated sesquiterpenes (21.0 and 15.0%, respectively) with hexahydrofarnesyl acetone as the major representative.

The present work is the first contribution into chemistry of volatiles of *Lonicera* species growing in Kazakhstan.

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HERBOLIDE A FROM *Artemisia karatavica*

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Artemisia karatavica Krasch. et Abol. ex Poljak. is endemic species, growing in stony, and clay slopes of low-hills in the South Kazakhstan region, Republic of Kazakhstan. *Artemisia karatavica* Krasch. et abol. ex Poljak. species is close to *Artemisia porrecta* Krasch. ex Poljak. Naturally these species grow together, but develop out of step, as *A. porrecta* Krasch. ex Poljak. blossoms and fructifies slightly earlier than *A. karatavica* Krasch. et abol. ex Poljak.

We carried out the chemical studying of an aerial part of *A. karatavica* Krasch. et abol. ex Poljak., growing in the South Kazakhstan region, Republic of Kazakhstan [1].

0.400 Kg of aerial part (leaves, flower baskets, buds) of *A. karatavica* Krasch. et abol. ex Poljak., collected in a flowering phase in Arpaozen ravine near Karatausky National Park of the South Kazakhstan region, extracted three times by chloroform, are as a result was received 54.1 g sum of extractive substances. The received concentrated extract was processed by aqueous–alcoholic (1:2). Thus, filtrate was processed by chloroform (1:1). The received sum of extractive substances (26.20 g) was chromatographed on silica gel column КСК (sum–carrier 1:20).

At elution of column with mix petroleum ether and ethyl acetate (95:5) was isolated colourless crystal substance (**1**), mp 169–171°C. Yield was 0.061 g (0.015% on air-dried raw material). R_f 0.33 (petroleum ether–EtOAc 2:3).

By data of IR-, UV-, ^{1}H and ^{13}C NMR, mass spectra, substance (**1**) was sesquiterpene lactone 9β-acetoxy-6β,7,11α(*H*)-germacr-1(10),4(5)-dien-12,6-olide (herbolide A), isolated before from *Artemisia herba–alba subsp.* valentine [2].

Thus, at chemical studying of aerial part of *A. karatavica* Krasch. et abol. ex Poljak. was isolated germacrane sesquiterpene lactone herbolide A, identified from this species for the first time.

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1β(10β),3β(4β)-DIEPOXY-5α,7α,6β(*H*)-GUAI-11(13)-EN-12,6-OLIDE FROM *Tanacetopsis pjataevae*

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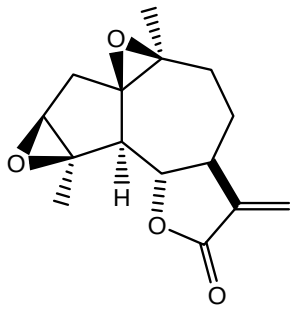
For studying of chemical composition of *Tanacetopsis pjataevae* (Kovalevsk.) Karmyscheva – endemic species of Kazakhstan [1], was made chloroform extraction of the air-dried crushed raw material (0.7 kg, leaves, flower baskets, buds), collected in the flowering phase, May 2012, in Arpaozen ravine, Karatau, the South Kazakhstan region.

The received sum of extractive substances (44.0 g) was chromatographed on silica gel column KCK in ratio of sum–carrier 1:20.

Elution of column by mix petroleum ether–ethyl acetate (92.5:7.5) was received colourless substance (**1**), mp 149–152°C (from diethyl ether), $C_{15}H_{18}O_4$. Yield of compound (**1**) was 0.057 g (0.008 % on air-dried raw material).

On the basis of the spectral data (IR-, ^{1}H and ^{13}C NMR-, mass) and results of X-ray analysis for molecule (**1**) was determined the structure 1β(10β),3β(4β)-diepoxy-5α,7α,6β(*H*)-guai-11(13)-en-12,6-olide.



(**1**)

By literary data, 1β(10β),3β(4β)-diepoxy-5α,7α,6β(*H*)-guai-11(13)-en-12,6-olide (**1**) was synthesized before on a basis of sesquiterpene lactone arglabin [2], then was received as a result of multiphasic synthesis [3] and from plant source was isolated for the first time.

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COMPOSITION OF ESSENTIAL OILS OF TWO SPECIES OF *Artemisia* L.

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The analysis of the essential oils from *Artemisia valida* Krasch. et Poljak. and *Artemisia saissanica (*Krasch.) Poljak ex Filat. was made by GC-MS for the first time.

Artemisia saissanica (Krasch.) Poljak ex Filat. grows in meadow saline lands. It can be met in East low land and Zaisan. It is endemic species.

Artemisia valida Krasch et Poljak grows in deserted zone in saline lands. It can be met in Turkestan and Karatau as endemic species [1].

Raw material of *Artemisia* species was collected at budding stage in August 2013 near the Balkhash lake. Essential oils were produced by hydrodistillation for 3 h using a Clevenger type apparatus. The yields of the essential oils were 1.39% and 0.28% for *Artemisia valida, Artemisia saissanica* respectively. Essential oil of *Artemisia valida* contained 40 compounds, 28 of which were identified. The major constituents were found to be camphor (27.65%), 1,8-cineole (9.55%), β-thujone (6.06%) and camphene (4.15%). Essential oil of *Artemisia saissanica* contained 11 compounds, 8 of which were identified. The major constituents were found to be camphor (61.96%), β-thujone (19.18%), 1,8-cineole (5.93%).

The qualitative composition of essential oils and their quantitative content was analyzed by the chromatography-mass spectrometry method on gas chromatograph with mass-selective detector Agilent 7890/5975C. Components were identified on mass spectra and hold-up times, with using library Wiley GC/MS.

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POLYPHENOL COMPOUNDS OF *Polygonum aviculare*

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Polygonum aviculare L. grass shows styptic, anti-inflammatory, blood-stopping and diuretic action. Substances from this plant possess some hypotensive properties, are low toxic.

To isolate polyphenol compounds we studied an aerial part of *Polygonum aviculare* L., collected in flowering phase. Extraction by ethanol was carried out at various temperatures 24–26°C and 60–70°C.

The qualitative composition and quantitative content of polyphenol compounds in the received extracts were defined on chromatograph Hewlett Packard Agilent 1100 Series in isocratic mode. By results of HPLC analysis were defined resveratrol, quercetin and rutin. The data on quantitative content of polyphenol components are in Table 1.

TABLE 1. **The Quantitative Content of Resveratrol, Quercetin and Rutin in *Polygonum aviculare* L. Extracts**

Extracts	Quantitative content on HPLC analysis, %		
	resveratrol	quercetin	rutin
Polygonum aviculare L. at 24–26°C (aerial part)	not found	0.001	0.06
Polygonum aviculare L. at 60–70°C (aerial part)	0.027	0.026	0.112
Polygonum aviculare L. at 24–26°C (roots)	0.0007	0.028	0.029
Polygonum aviculare L. at 60–70°C (roots)	0.0002	0.135	0.005

According to the received data, extraction with ethanol at temperature 60–70°C provides the high quantitative content of resveratrol, quercetin and rutin from *Polygonum aviculare* L.

7-METHOXYCOUMARIN FROM *Matricaria chamomilla*

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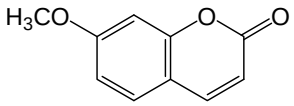
After isolation of essential oil, *Matricaria chamomilla* L. raw material was extracted by chloroform.

Extraction was made with chloroform three times, in result sum of substances was obtained. Then water–alcohol (1:2) processing of the received extract was made and residue was filtered. Further filtrate was processed by chloroform (1:1). The received sum of extractive substances (13 g) was chromatographed on silica gel column (sum–carrier 1:20). Results of the chromatomass spectrometry analysis of chloroform extract of *Matricaria chamomilla* L. are resulted in Table 1.

TABLE 1. **Results of the Chromatomass Spectrometry Analysis of Chloroform Extract of *Matricaria chamomilla* L.**

Compound	RT, min	Content, %
Unidentified component	5.160	0.65
trans-β-Farnesene	26.657	3.44
Unidentified component	29.659	0.69
Bisabolol oxide B	31.401	15.37
Bisabolone oxide	32.042	7.59
7-Methoxycoumarin	32.893	11.03
Chamazulene	33.066	0.85
Bisabolol oxide A	33.393	30.36
2-(2,4-Hexadiynylidene)-1,6-dioxaspiro[4.4]non-3-ene	36.159	30.02

The colorless crystal substance with mp 116–119°C was isolated at elution of columns with petroleum ether–ethyl acetate (98:2). Structure of isolated compound (**1**) was proved by GS-MS.



1

The absorption bands are in IR-spectrum, which characterizing for groups C=O (1703 cm^{-1}) and C=C (1613 cm^{-1}).

7-Methoxycoumarin was isolated first from *Matricaria chamomilla* L.

NEW ARYLDERIVATIVES OF GERMACRANOLIDE ARGOLIDE AND THEIR ANALGETIC ACTIVITY

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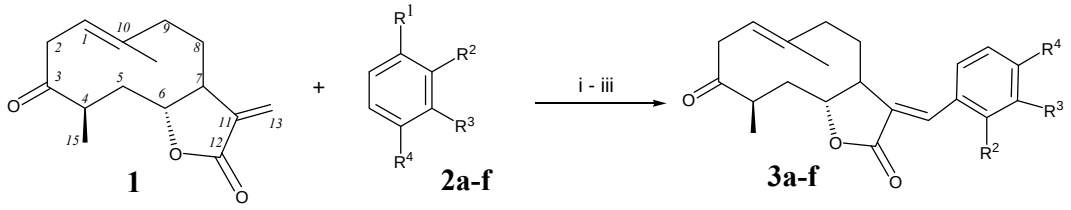
Germacrane sesquiterpene lactone argolide **1** was isolated for the first time from aerial part of *Artemisia glabella* Kar. et Kir. [1]. The Heck reaction on a basis of argolide **1** with arylhalogenides **2a–f**, catalyzed by system $Pd(OAc)_2$-(*o*-tolyl)phosphine, in dimethylformamide with various bases (conditions i-iii) is resulted.



i) - $Pd(OAc)_2$, (*o*-Tol)$_3$P, Et_3N, DMF, 120°C, 12 h;
ii) - $Pd(OAc)_2$, (*o*-Tol)$_3$P, Et_3N, DMF, 120-130°C, 10-36 h;
iii) - $Pd(OAc)_2$, (*o*-Tol)$_3$P,Cs_2CO_3, DMF, 120-130°C, 32 -36 h

2a,3a: R_1=I, R_2=R_3=H, R_4=OCH_3; **2b,3b**: R_1=I, R_2=R_4=H, R_3=CF_3;
2c,3c: R_1=I, R_2=R_3=H, R_4=F; **2d,3d**: R_1=I, R_2=R_3=H, R_4=Cl;
2e,3e: R_1=I, R_2=SCH_3, R_3=R_4=H; **2f,3f**: R_1=Br, R_2=CH_3, R_3=R_4=H;

Composition and structure of the received compounds **3a–f** were confirmed on the basis of the data of the element analysis, mass, IR-, UV-, NMR ^{1}H and ^{13}C spectra. For definition of analgetic activity of samples **3a,f** was used the test "acetic writhing". By results of bioscreening was determined that derivatives **3a, 3f** possess analgetic activity comparable with action of preparation "Diklofenak".

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GEMOSTATICAL MEDICINES ON THE BASE OF LAGOHILINE AND ACETYLCELLULOSE DERIVATIVES

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Nowadays the great attention is devoted to obtain of haemostatic preparations in polymeric form by chemical bonding of highmolecular haemostatic preparations owing to introduction in structure of polymer (matrix) with aim of prolongation of their action at minimal concentration of medicine substance. Also the polymeric form of the melien preparation has ensured its using as *in vivo* and *in vitro*.

Derivatives of Lagohiline obtained from plant *Lagohilus* as low-molecular haemostatic preparates and the oxidized water-soluble acetylcellulose were used as polymeric matrixe.

The reaction of Lagohiline derivatives to oxidized water-soluble acetylcellulose has been investigated. This reaction was carried out at intensive mixing at 60–70°C during 6 h in dimetylformamide. The product reaction was isolated by precipitation in acetone.

The structures of obtained compounds were proved by comparison of their IR-spectra with initial compounds. In IR-spectrum of the initial oxidized water-soluble acetylcellulose the adsorbtion band corresponding to aldehyde group has appeared at 1740 cm^{-1}. In IR spectrum of the product intensity of this band has decreased sharply, that has proved aldehyde group of the oxidized water-soluble cellulose substitution by alcohol group of the Lagohiline derivatives.

Also investigations were carried out by obtain of medicine form (water-soluble films) of the synthesized compounds. Solutions containing diterpenoids and water-soluble acetylcellulose were filtrated for removal of insoluble particles and impurities. Obtained solution was subjected to de-aeration. Films were obtained from solutions on the horizontal polish surface. Horizontality was determined using polish surface with stable legs. Drying was carried out under room temperature.

The acute toxicity was determined on white mice in intraperitoneal introduction of films containing 5% Lagoden. Obtained results have shown that LD_{50} was equaled more than 1500 mg/kg.

Investigations were carried out by the influence of films, containing 5% of Lagoden, on the duration of parenteral haemorrhage of rats and rabbits.

Obtained results have shown that initial film from water soluble acetylcellose didn′t influenced on the parenchymatous haemorrhage, but the same film with content of 5% of Lagoden has decreased a duration of above-mentioned process on 34% (for rats) and on 38% (for rabbits) in comparison to the control.

Thus, our investigations have shown some advantages of proposed styptic polymeric water-soluble preparations in comparison with known preparations by decreasing of parenchymatous haemorrhage duration.

MODELING OF CHEMICAL COMPOSITION OF COMPOSITE FLOUR MIXES WITH PROGRAMMING LANGUAGE «DELPHI»

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Works in nutrition bases, human needs for food nutrients and energy, as well as the study of the biological value of bread showed that in this product the rate-limiting acid is lysine (only 23.1% of daily needs) – an amino acid, the most deficit in the nutritional balance. Alternative sources, which include multi-functional mixture, contain high amounts of food and minor biologically active substances are needed. However, now they are unreasonably little used in the production of functional food.

We have developed software on «Delphi» language for the calculation of composite of flour blends. The resulting solution algorithm takes into account the data of the chemical composition of the mixture ingredients. The program for the calculation of the formulation of the following indicators: the components percentage in the mixture, the content of functional components in a composite mixture. Optimization of the parameters of the developed product is carried out by simulation using the integral formulation of the criterion of balance on the content of lysine. Simulation of recipes is to find a domain G-factorial *n*-dimensional space R_n, corresponding to the limits put to the design. In the particular case, as the multi-dimensional space can be a linear form like this:

$$F(X_1,\ldots,X_n) = \sum_{i=1}^{m} \sum_{k=1}^{n} C_i X_k,$$

where *n* – number of ingredients in the formulation; m – number of components in the i – th product ingredients; xk - k- th component in the formulation.

In the creation of the composition of the mixture wheat flour of first grade, non-traditional bakery cereal, flour milling by-products and canning industries, powders of medicinal plants were used. As the products of processing of raw materials powdered semi-finished products selected as the most convenient form for use in composite flour blends.

Thus, functional food enriched with bioactive nutrients from non-traditional sources of environmentally friendly raw materials is virtually unlimited resources in terms of volume and diversity of physiological effects that are now especially important and has great socio – economic importance.

CHEMICAL TRANSFORMATIONS OF GOSSYPOL AT TECHNOLOGICAL PROCESSING OF OIL-CONTAINING RAW MATERIALS

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In this work the technology of partial refining of cotton oil in oil-containing raw materials improved using solutions of the caustic soda and calcium chloride in the various concentrations, previously activated in an electromagnetic field with optimum intensity 1.6 A/m.

As a result of the offered technology use the quality indicators of oil, cake and meal increase due to the enrichment of them by calcium salts of fatty acids is reached.

Influence of concentration of the caustic soda and calcium chloride activated solutions on decreasing of free fatty acids content, free and connected gossypol, and also phosphatide is studied.

Free fatty acids form sodium soaps, and gossypol and its derivatives – sodium gossypolate, which are transferred further to calcium salts under the influence of calcium chloride solutions. Sodium and calcium salts, passing to composition of cake and meal, provide their increased fodder value.

Value of intensity of an electromagnetic field is estimated at partial refining of cotton oil in raw materials and final refining the received crude oil. It is established, that the most essential results turn out at the intensity of an electromagnetic field equal to 1.6 A/m.

Optimal technological parameters of processing of low-grade and non-standard cotton seeds are determined. Reliability of the established optimum parameters is provided by methods of statistical processing and optimization of experimental data, which were recommended for carrying out experimental-manufacturing tests.

Processes of extraction of the cakes containing calcium salts of fatty acids, and also calcium gossypolat are studied. It is shown, that extraction of the cakes enriched with calcium salts, proceeds in compliance in industrial technology.

Influence of raw materials processing by the activated solutions of the caustic soda and calcium chloride on the maintenance of a protein in the cake and meal is studied, improvement of their fodder advantages reached.

FEATURES OF TECHNOLOGY OF CRUDE COTTON OIL REFINING

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In processes of crude cotton oil refining the interaction of accompanying substances insoluble in oil with soluble in water chemical reagent happens on fat-water phases bound and depends on an effective area of contacting phases.

For improvement of quality of the refined cotton oil and improvement of its physical-chemical indicators due to deeper removal of free fatty acids the alkaline (NaOH) solution, sodium aluminate salt $NaAlO_2$ and preliminary prepared water. During neutralization of free fatty acids under influence of reagents, in particular NaOH water solution, on triglycerides of oil the by-product the soap stock being difficult colloidal system, and on bound of phases of system soap stock – neutral free fatty acids the complexes and associates are formed. On the researches it was established, that used alkaline solution promotes more accurate separation of phases of soap stock – neutral oil system and intensified the process of removing of neutralized oil.

Laboratory researches of free fatty acids neutralization technology were carried out by a standard technique in addition to the crude cotton oil of necessary quantity and concentration of alkaline solution at the temperature of 25 … 35°C. For an assessment of the obtained results the control sample of crude cotton oil refined with NaOH solution using traditional technology (Fig. 1).

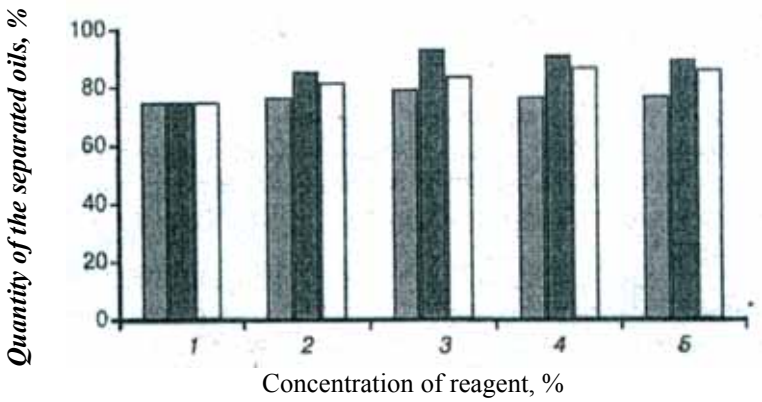

Fig. 1. Efficiency of separation of emulsion at concentrations of alkaline solution: *1* – control; *2* – 15 %; 3 – 25 %; 4 – 35%; 5 – 45 %; temperature: ■ – 25°C; ■ – 30°C; □ – 35°C

Apparently, the best results received at the temperature of 25°C with addition of 15% alkaline solution of sodium aluminate of the oil weight. Thus, the quantity of separated neutralized oil increased for 18% and reached 92% of total volume of the system soap stock – neutral oil. It is necessary to note, that the separation of soap stock from neutralized oil occurs twice quicker (in 25 min), concentration of the general fat in soap stock decreases for 12% at improvement for two times the ratio of saponified and neutral fat.

PTP1B ACTICITY STUDY OF EXTRACTS OF THE *Echinops integrifolius*

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From ethanolic (70%) extracts by column chromatography isolated and identified several individual substances: lupeol, lupeol acetate, umbelliferone, β-sitosterol glucopyranoside, chrysoeriol, apigenin, jaceidin, centaureidin, hispiduli and axillarin.

PTP1B reaction system contained 5mM pNPP, 0.09 μM his-PTP1B$_{1-321}$ and buffer containing 20 mM HEPES, 150 mM NaCl, and 1 mM EDTA. After incubation of extracts for 5 min, the reaction was initiated by addition of pNP. The amount of produced pNP was measured by detecting absorbance at 405 nm using microplate spectrophotometer (SpectraMax M5/M5e, America). IC_{50} value was calculated by fitting data with Origin software.

PTP1B Activity Inhibitory Research Results

Extracts	IC_{50}, μg/mL
Whole plant boiled in water 2 h	15.42 ± 2.38
Whole plant boiled in 93% ethanole 2 h	3.19 ± 0.25
Whole plant boiled in 70% ethanole 2 h	No effect
Aerial part boiled in water 2 h	27.14 ± 2.10
Aerial part boiled in 93% ethanole 2 h	4.40 ± 0.25
Aerial part boiled in 70% ethanole 2 h	9.01 ± 0.96
Roots boiled in water 2 h	7.94 ± 1.10
Roots boiled in 93% ethanole 2 h	9.35 ± 0.40
Roots boiled in 70% ethanole 2 h	36.42 ± 0.77
Roots petroleum ether in 3 days	27.44 ± 0.32
Roots extract CH_2Cl_2 in 3 days	47.49 ± 2.96
70% ethanolic extract fractions result	
Petroleum ether fraction	863.43
Butanolic fraction	17.5
Ethylacetate fraction	34.97
Aqeuous residue	916.95

93% ethanol extract from whole plant and aerial parts was shown good PTP1B inhibitory effect.

Among the isolated substances umbelliferone and lupeol acetate in concentration 100mg/ml show low antimicrobial activity against SA.

Acknowledgment. Thanks for financial support of Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

N-MONO -,-*N*, C-DI-N-, C-, *O*-BENZOYLATION OF THREE 2-BENZYLBENZIMIDAZOL

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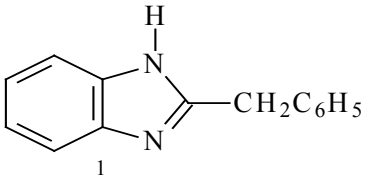
It is known that benzoylation of 2-methyl benzimidazole with benzoyl chloride (BCl) in diglyme in the presence of triethylamine provides products of N-, C-, O-, poly-, or -C, O - dibenzoylation [1, 2]. In the literature there is no information about acylation of the 2-benzyl benzylbenzimidazol (**1**, **2**) with chloranhydrides of acids. Compound **1** is interesting because it has a methylene group with the benzyl′s character, and mobility of protons in it is more, than in 2-methylbenzimidazole.

Recently we have shown, that the benzoylation reaction of 2-methyl-5*H* (chloro, nitro) benzimidazoil going by different ways [3]. Continuing of these studies in this manuscript, we present our results on benzoylation of the benzylbenzimidazol 2-benzoyl chloride (HD) under the mild conditions.

The results shows, that in ratio 1.2: BCl *N*-benzoyl-2-benzyl-benzimidazole (**2**), *N*-benzoyl-2-benzoylethylidenbenzimidazole (**3**) and *N*-benzoyl-β-2-(benzoyloxy-β-phenylethylidene)-benzimidazole (**4**), i.e. products of mono-, di-and tribenzoilation are formed.



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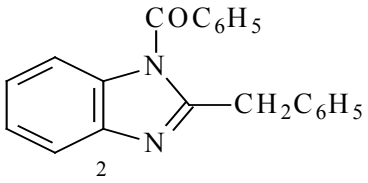

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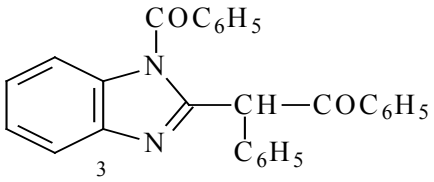

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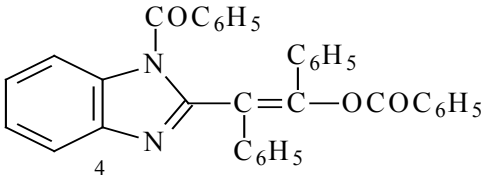

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Ratio 1: BCl 1:1 leads to the formation only of compound **2**. In case of 1:2 ratio formation of 2,3 mixture occurred. The reaction in ratio 1:3 provides the mixture of compounds **2**, **3**, **4**.

In case of the reactants ratio 1:4, only product of three acylation (**4**) obtained.

The mutual conversions of compounds **2**, **3**, **4** are investigated.

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IDENTIFICATION LACTONE AND DBP FROM THE *Echinops integrifolius*

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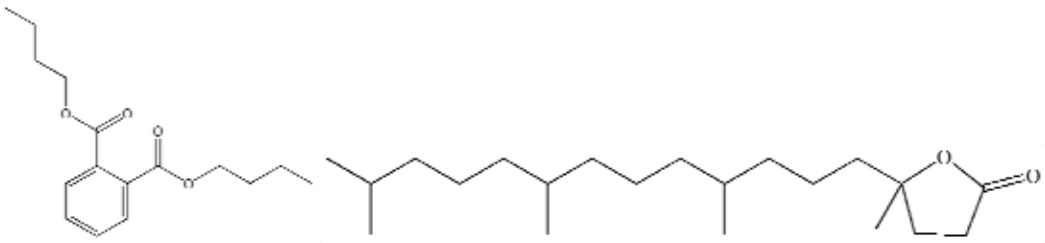
Continuing study of the ethanol extract of the plant *E. integrifolius* by column chromatography isolated colorless, oily substance, which with methods ^{1}H, ^{13}C NMR and GCMS was identified as dibutylphthalate. Dibutylphthalate (DBP) was also isolated from the plant *Echinops grijisii*. Identification of substances by GC-MS was carried out by comparing the mass spectra with those of digital libraries NIST, Wiley.

Continuing chromatography from the silica gel column fraction was isolated, a mixture of DBP (RT = 87.29 (15.7%)) and 4,8,12,16-tetrametilheptadecan-4-olide (R_T = 106.96 (53.3%)).

Dibutylphtalate (1). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.97 (6H, q, J = 7.31, 7.31, 7.43, H-5′, 5″), 1.44 (4H, dd, J = 7.39, 7.39, 7.33, 14.70, H-4′, 4″), 1.72 (4H, m, H-3′, 3″), 4.31 (4H, t, J = 6.72, 6.72, H-2′, 2″), 7.51 (2H, dd, J = 3.31, 5.72, H-3, 4), 7.71 (2H, dd, J = 3.34, 5.69, H-2, 5). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 13.7 (C-5′, C-5″), 19.2 (C-4′, C-4″), 30.6 (C-3′, C-3″), 65.5 (C-2′, C-2″), 128.8 (C-2, C-5), 130.9 (C-3, C-4), 132.2 (C-1, C-6), 167.6 (C-1′, C-1″).

4,8,12,16-Tetramethylheptadecan-4-olide (2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.1 (C-2), 32.9 (C-3, C-8, C-12), 25.9 (C-18, C-14), 40.1 (C-15), 41.4 (C-5), 29.6 (C-6), 38.8 (C-7, C-9, C-11, C-13), 19.7 (C-19), 25.9 (C-10), 29.5 (C-16), 22.8 (C-20, C-17), 19.9 (C-21).



Acknowledgment. Thanks for financial support of Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

CHEMICAL COMPONENTS OF THE ROOTS *Echinops integrifolius*

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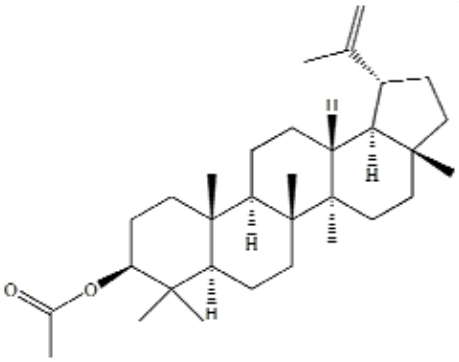
In previous studies has reported the constituents of volatile compounds of various fractions of ethanol extract of the plant *E. integrifolius*, and on the allocation of four triterpenes, six flavonoids and one coumarin.

Extraction of plant roots with diethyl ether was conducted for 2 hours in a Soxhlet apparatus. The extract was chromatographed on a column of silica gel. During chromatography solvents hexane, chloroform, hexane–chloroform (10:1–1:10) isolated and established patterns for lupeol (**1**), lup-20(29)-en-3-ol acetate and lup-19(20)-en-3-ol acetate (**2**), by NMR spectroscopy and GCMS identified dibutylphtalate, alkanes, fatty acids.

Lupeol acetate sample were analyzed on GC-MS. Mass-fragmentation was show 2 compounds with lupan type molecular signals, which were identified on ^{13}C NMR spectra as lup-20(29)-en-3-ol acetate and lup-19(20)-en-3-ol acetate.



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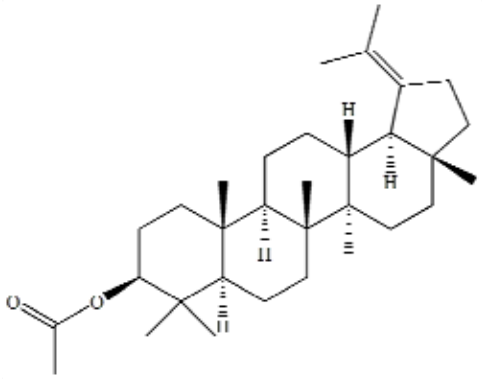

2

Lupeol-acetate tautomers: 1) lup-20(29)-en-3-ol acetate; 2)lup-19(20)-en-3-ol acetate

Acknowledgement. Thanks for financial support of Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

SYNTHESIS OF THE DERIVATIVE OF TROPANE ALKALOIDS

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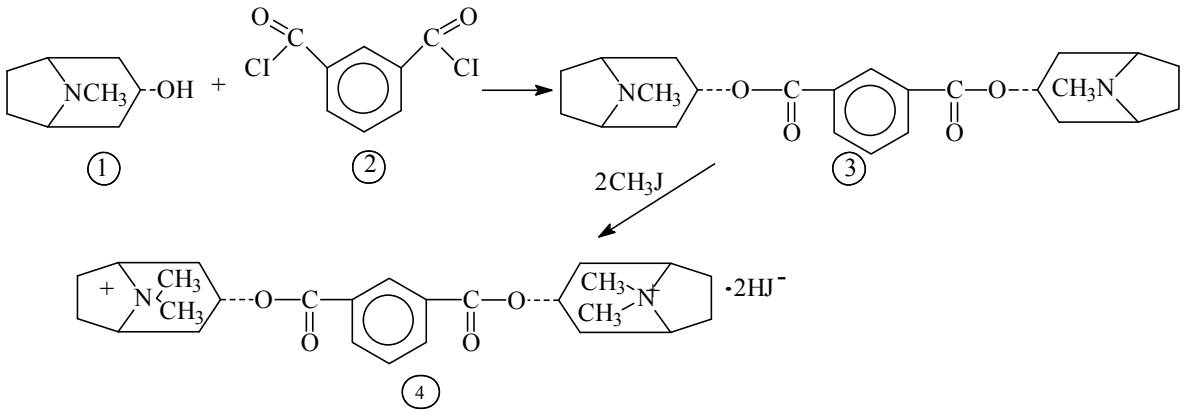
Chemical modification of natural bio-regulators is one of the most promising ways of synthesis of biologically active compounds. Both natural and synthetic tropane alkaloids possess by a wide spectrum of biological activity.

Consequently, we synthesized a derivative based on the amino alcohol of tropine (**1**) and isophthalic acid (**2**).



Dichloranhydride of isophthalic acid (**2**), obtained by reaction with $SOCl_2$, was etherificated with tropin-base (**1**) in toluene solution in presence of triethylamine. The product **3** was purified by column chromatography on alumina, mp 85–87°C.

Compound 3. IR spectrum (cm^{-1}): 1730 (O-CO), 1605, 1585, 1270, 1245, 1040, 945. NMR spectrum (δ, ppm): 6.85 (1H, c), 6.55–6.40 (2H, m), 5.95–6.03 (1H-Ar, m), 2.47 (4H, m, C-1, 1′; 5, 5′); 1.80 (6H, c, $2NCH_3$), 1.38–1.72 (16H, m, $8CH_2$).

The synthesized compound **3** reaction to methyl iodide provided diiodomethylate (**4**), mp 290–292°C.

TO THE PHARMACOLOGY OF COMPOSED DRUGS DERIVED FROM *Glycerhizae glabra*

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Previously studied pharmacological properties of individual flavonoids isolated from *Glycerrhiza glabra* have showed expressed anti-inflammatory and anti-ulcerogenic activity [1, 2]. In order to create favorable for technological production drug, samples of flavonoid fractions were obtained from total sum of aerial parts of plant.

Purposes of Study. Investigation of presented glacembrin and flavonoids fractions obtained by different methods for pharmacological activity.

Used Methods. Determination of acute toxicity of presented glacembrin and fractions conducted on white mice at per os administration. Compounds were introduced in 1–3% solution in doses 500–1500 mg/kg. Anti-flogistic activity was studied on white rats legs by formalin injection (exudative model of inflammation); proliferative model called by subcutaneous implantation of cotton ballet on rats back; alteracive process studied on skin of rats by necrotisation. Most active anti-flogistic fraction was revealed by method of formaline swelling of mice legs.

Results. Conducted study has show, that glacembrin and fraction 4 revealed most expressed antiflogistic activity on mice legs with formalin swelling. The compound at per os administration in dose 1500 mg/kg didn′t influenced on mice behaviour as at single injection, so at administration during 14 days. This fact displayedlow toxicity of compound. It was observed Glacembrin retards development the exudative process on rats beginning from dose 10 mg/kg, but doses 25 and 50 mg/kg were most optimal. Mechanism of antiflogistic activity of Glacembrin consists from depression of granulation forming around implanted cotton ballet, stimulation of regeneration of skin at necrotic zone on rats back.

Thus, conducted study has show, that there is easy available and high active antiflogistic compound called “Glacembrin” in flavonoidal sum of *Glycerrhiza glabra*, revealing specific antiflogistic activity at several models of inflammation on rats and mice. Glacembrin principally may be accepted as perspective easy approachable antiflogistic compound.

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ALKALOIDS OF *Delphinium longipedenculatum* AND *Rosa canina*

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Delphinium longipedenculatum Nevski is perennial herbaceous plant growing in dry loess, gravelly and rocky slopes of the foot-hills and lower mountains of the Tashkent, Ferghana, Samarkand, Kashkhadarya and Surkhandarya regions of Uzbekistan.

Alkaloids composition of the plant has not been investigated. We have studied the alkaloids content in this plant collected on the slopes of the Hissar mountains in the Yakkabog district of Kashkadarya region during the flowering period.

Air-dried aerial parts of the plant (884 g) were extracted with 80% ethanol. After 7 drains and usual treatment 0.25% (2.2 g) of total alkaloids was obtained. The total alkaloids were separated on weakly basic (pH 8) and strongly basic (pH 12) factions. From the weakly basic fraction the alkaloid $C_{26}H_{41}NO_7$, with mp 200–202°C (methanol) was isolated.

The IR spectrum showed an absorption band of hydroxyl groups (3512 cm^{-1}) and ether linkages (1090 cm^{-1}).

The PMR spectrum show the signals of *N*-ethyl group (7.05 ppm, 3H, t), four methoxyl groups (3.28, 3.33, 3.42, 3.20 ppm, each 3H, s), a methylenedioxy group (5.05 and 5.12 ppm, each 1H, s) and signal of geminal proton to C-6 β-hydroxyl group (4.25 ppm, 1H, s).

The melting point and reduced spectral data agree with the same for alkaloid delkorine.

In order to confirm the structure and stereochemistry of the alkaloid X-ray diffraction study was made, which confirmed the earlier identified structure (Fig. 1).

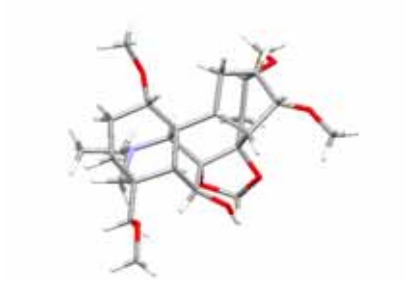

Fig. 1. Spatial structure of delkorine.

Rosa canina L. is large, up to 3 m tall shrub. It grows at the waterside of mountain rivers and streams, at gardens, in walnut and juniper forests in the lower and middle zones of the mountains. In Uzbekistan it grows in Tashkent, Ferghana, Samarkand, Kashkadarya and Surkhandarya. It is flowering in May–July, fruiting in July–October.

Alkaloid composition of the plant has not previously been investigated. We investigated the alkaloids of the fruits of this plant collected in the Tashkent region during fruit ripening to employees Pilot Production Plant Chemistry Institute of the Academy of Sciences RUz.

Crushed dry fruits of *Rosa canina* (100 g) were extracted with 80% aqueous ethanol. Alcohol was distilled till water residue. 12 drains made and treated in the same manner. The combined aqueous solutions were basified to RN8 soda and extracted with chloroform. The chloroform extract was dried over sodium sulfate and, after stripping and removal of the solvent gave 0.1 g of total alkaloids (0.1% by weight of dry plants).

SYNTHESIS OF SPIN LABELED SUCCINATES DERIVATIVES OF α-TOCOPHEROL AND TROLOX

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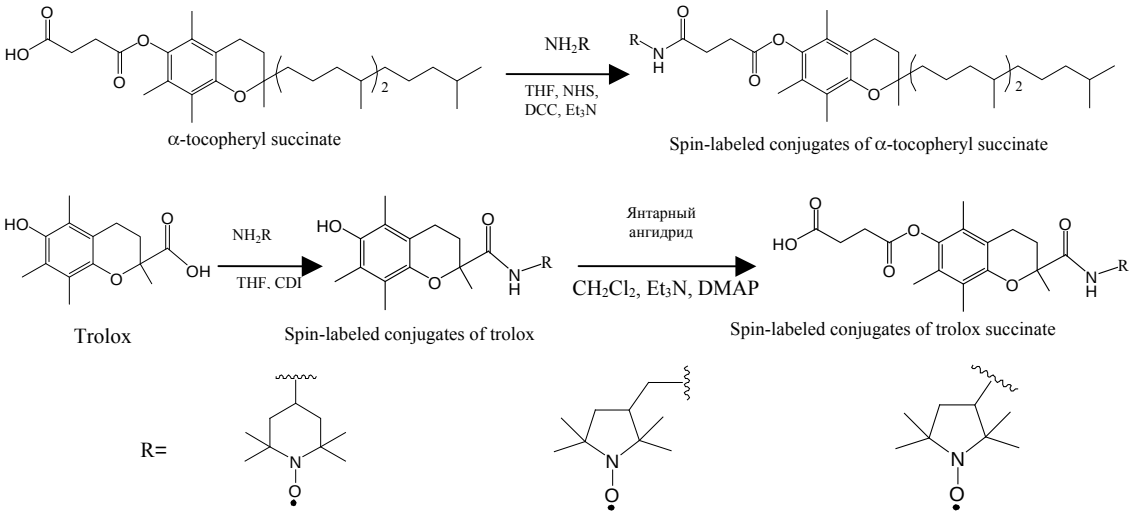
Modern medicinal chemistry actively uses synthesis of polyfunctional active hybrid compounds based on natural biologically active substances for drugs creation as priority direction. Among pharmacologically active compounds, the chromane core type of compounds such as α-tocopherol (vitamin E) and its structural analogs can be identified.

In this work, the following "molecule-leaders" were chosen as biologically active substances for hybrids creation: acid Trolox – synthetic water-soluble analogue of α-tocopherol and α-tocopheryl succinate (α-TC), contained in the group of ‘mitocans’ – mitochondrial-targeted anticancer drugs. They possess pronounced antioxidant activity, membrane protective features. Besides, α-TC possesses high cytotoxicity and selectivity with respect to different types of tumors, non-toxic to healthy cells and tissues.

We have carried out the synthesis of spin-labeled succinated derivatives of α-tocopherol and trolox containing fragments of nitroxyl radicals (NR) of piperidine and pyrrolidine types– ternary hybrids containing three biologically active fragments.



We suppose that paramagnetic polyfunctional conjugates synthesized on the basis of biologically active succinates of α-tocopherol and trolox – the so-called “molecules-leaders”– are highly likely to reveal various types of pharmacological activity with low general toxicity and high selective toxicity against pathological targets. It makes the synthesized compounds rather useful and perspective “candidates” for the further development of modern mitochondrial-targeted anticancer drugs. Besides, the presence of a free radical fragment in the molecules makes them perspective contrasting agents for biomedical magnetic resonance tomography (MRT) research.

BIOLOGICAL ACTIVITY AND COMPOSITION OF THE ESSENTIAL OIL OF *Ferula halophila*

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The genus *Ferula* (*Apiaceae*) comprises more than 180 species and it is widespread throughout the Mediterranean area and Central Asia. It is represented by 24 species in the flora of Turkey. The fruit specimens of *Ferula halophila* Pesmen, an endemic species growing near Salt Lake in Central Anatolia, collected in June and July 2012. The hydrodistilled essential oils of the dried fruits of *F. halophila* were analyzed by GC and GC-MS systems, 27 and 24 compounds representing 92.1% and 79.8% of the essential oils were characterized, respectively. The main component of the essential oils was identified as β-phellandrene. The antibacterial and anticandidal effects of the essential oils were determined by using partly modified CLSI methods M7-A7 and M27-A2, respectively. The essential oils from two specimens showed weak to moderate inhibitory effects on the tested pathogenic bacteria (MIC, 125–2000 μg/mL) and *Candida* panels (MIC, 156–1250 μg/mL).

CHEMICAL COMPOSITION OF HYDRODISTILLED OIL OF *Centaurea cuneifolia* FROM TURKEY

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Essential oil composition of *Centaurea cuneifolia* Sm. flowers were investigated with GC, GC/MS analysis. Essential oil compositions were identified employing simultaneous GC, GC/MS analyses under same conditions (Innowax FSC Column, 60 m × 0.25 mm × 0.25 μm; 1 mL/min Helium; Split ratio 40:1; Temp. Prog. 60°C 10 min→220°C at 4°C/min→220°C 10 min→240°C at 1°C/min). Identification of the essential oil components were achieved by comparison of RRI to a series of homolog n-alkanes and as well as computer matching against in house MS databases (Wiley 8th Ed./NIST 05 Mass Spectra Library, Adams Essential Oil Mass Spectral Library, Pallisade 600K Complete Mass Spectra Library). Twenty-five compounds were identified representing 69.9% of the flower oil. Hexadecanoic acid 32.9%, tetradecanoic acid 14.4%, heptacosane 6.1% and nonacosane 4.3% were encountered as the major components of the oil. High proportion of the oil was composed of saturated fatty acids however oxygenated monoterpenes and oxgenated sesquiterpenes such as hexahydrofarnesyl acetone, spathulenol and caryophyllene oxide also exist as minor components ranging between 2.0–0.1%.

The authors would like to thank Dr. Gizem Bulut from the Faculty of Pharmacy of Marmara University for the identification of the plant.

EFFEKT OF RHIZOTORPHINE TREATING ON PRODUCTIVITY OF DIFFERENT CULTIVARS OF TWO SPECIES OF *Onobrychis* UNDER THE CONDITIONS OF THE MOUNTAIN DAGHESTAN

M. K. Kuramagomedov, F. A. Vagabova

Mountauin Botanical Garden Daghestan Science Center Academy of Sciences, Makhachkala, 367025, st. Gadgieva, 45, Russia

We studied the effect of rhizotorphine treating (strain 820) on productivity of different cultivars of *Onobrychis transcaucasica* Gross. (Almaatinskii-1, Kubanskii-1) and *Onobrychis arenaria* L. (Gibrid-2855, Tslinnii). Small-plot fields experiments were conducted in the territory of the Gunib Plateau at 1750 m above see level.

According to the obtained data rhizotorphine makes different effect on growth and productivity of different cultivars studied. The Almaatinskii-1 cultivar of *Onobrychis transcaucasica* and the Gibrid-2855 cultivar of *Onobrychis arenaria* L. proved to the most responsive to inoculation. In control the mean plant height in the second year of vegetation amounted 108 ± 2.9 cm for the Almaatinskii-1 and 93 ± 3.8 cm for the Gibrid-2855. In the experiment the corresponding mean plant height of the two cultivars increased up to 118 ± 1.7 and 127 ± 1.0 cm, respectively. These two cultivars were also characterized by maximal level or accumulation on dry plant mass.

Leaves area of the plants of the cultivars treated with rhizotorphine was 2–3 times as large as in control. Powerful leaf system of plants in the experiments promots an increase of net productivity of photosynthesis (PPPh). Increase of PPPh of the two cultivars up to 9.9 ± 1.3 and 10.5 ± 0.8 g/m^2 for days, as compared to respectively 6.6 ± 0.6 and 6.8 ± 1.3 g/m^2 for day in control, suggests that the leaves area of the plants was most optimal providing for a high level obtained by estimating specific surface density of the leaves.

The results of determining protein content in leaves of *Onobrychis* showed an increasing of the nitrogen accumulation on the background of inoculation. While in the control plants of the Almaatinskii-1 and Gibrid-2855 cultivars the protein content amounted 8.46 and 8.08%, respectively. In the plants grown in symbiosis with root nodule bacteria the protein content hightened up to 14.55 and 9.59%. The increase in protein content over the control following inoculation was in the two cultivars 3.1 and 1.17%, respectively.

Thus, the obtained results shows that the *Onobrychis* cultivars the Almaatinskii-1 and Gibrid-2855 exhibit an increase of productivity and a rise in its quality when treated with rhizotorphine.

EFFECTS OF SYNTHETIC ALLOBETULINOL ANALOGUE ON HUMORAL AND CELL IMMUNE RESPONSE

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The class of triterpenoids widely occurring in nature attracts increasingly more attention of the experts in the field of medical chemistry and pharmacology. Synthetic analogues of allobetulin have wide spectrum of biological activities including bactericidal, fungicidal, antiviral, cytotoxic, analgetic, anticancer, spermicidal, cardiovascular, antiallergic and etc.

The object of the study was the synthetic analogue 3-*O*-propionate of allobetulinol (further investigated substance, IS). The aim of the study was to evaluate the immunological effects of IS for the cell and humoral immune responses.

Male Balb/c mice were administered with IS in doses 0.1, 1, 10 and 50 mg/kg subcutaneously for 7 days. To evaluate the cellular immune response a hypersensitivity reaction (DTH) with DNCB was used. Hemagglutination reaction with sheep erythrocytes was used to study the antibody production. Functional activity of spleen *T*-lymphocytes was studied by analyzing the IL-4 и IFNγ cytokines production.

The results shown that IS decreased the DTH reaction in a dose-dependent manner. It was shown that in a dose 50 mg/kg there was a significant reduction of the paw edema in 2.5 times compared with control group. Antibody titer increasing was found in a dose dependent manner. Antibody concentration was 4–8 fold higher compared with control group in a dose 50 mg/kg. The IL-4 and IFNγ analysis in spleen cells after the KonA stimulation shown that IS regulated the production of cytokines changing the Th1/Th2 balance with the increasing of Th2 subset.

The synthetic analogue of allobetulinol had the significant effects on immune response. It was shown that IS administration in doses 0.1, 1, 10 and 50 mg/kg led to the Th1/Th2 balance changing, increasing the Th2 formation and antibody production. Because the humoral immunity have the pivotal role in immunological response to the bacterial and virus infections the investigated synthetic analogue of allobetulinol may be a perspective drug candidate.

ESSENTIAL OIL COMPOSITION OF *Centaurea kılaea* FROM TURKEY

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Essential oil composition of *Centaurea kilaea* Boiss. flowers and stems were investigated with GC, GC/MS analysis. Essential oil compositions were identified employing simultaneous GC, GC/MS analyses under same conditions (Innowax FSC Column, 60 m × 0.25 mm × 0.25 μm; 1 mL/min Helium; Split ratio 40:1; Temp. Prog. 60°C 10 min→220°C at 4°C/min→220°C 10 min→240°C at 1°C/min). Identification of the essential oil components were achieved by comparison of RRI to a series of homolog *n*-alkanes and as well as computer matching against in house MS databases (Wiley 8th Ed./NIST 05 Mass Spectra Library, Adams Essential Oil Mass Spectral Library, Pallisade 600K Complete Mass Spectra Library). Nineteen compounds were identified representing 59.5% of the flower oil. Hexadecanoic acid 26.2% and tetradecanoic acid 18.1% were encountered as the major components of the oil. High proportion of the oil was composed of saturated fatty acids however sesquiterpene alcohols such as β-eudesmol, isospathulenol and *T*-muurolol exist as the secondary components ranging between 3.3–1.5%. Twenty compounds were identified representing 77.6% of the stem oil. Hexadecanoic acid 55.5% was the main component of the oil. Similar to the flower oil high portion of the oil was composed of saturated fatty acids; however as secondary components the oil contains oxygenated sesquiterpenes β-eudesmol, spathulenol and caryophyllene oxide ranging between 3.2–1.9%.

The authors would like to thank Dr. Gizem Bulut from the Faculty of Pharmacy of Marmara University for the identification of the plant.

BIOLOGICAL ACTIVITY AND COMPOSITION OF THE ESSENTIAL OIL OF *Ferula rigidula*

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The genus *Ferula*, withmore than 180 species, is the largest genus of *Apiaceae* in Asia. *Ferula rigidula* DC. is distributed throughout the Central and Eastern Anatolia regions of Turkey, as well as in the adjacent areas of neighbouring countries. The hydrodistilled essential oil of the dried fruits of *Ferula rigidula* DC. was analysed by GC and GC-MS system simultaneously. Thirty one compounds representing 98.2% of the essential oil were characterized and the major componentswere identified as α-pinene and camphene (24% and 20%, respectively).The antibacterial and anticandidal effects of the essential oil was determined by using partly modified CLSI methods (M7-A7) and (CLSI M27-A2), respectively. The essential oil of the fruitsshowed weak to moderate inhibitory effects on tested pathogenic bacteria (MIC, 62.5 to 2000 μg/mL) and *Candida* species (MIC, 125 to 1000 μg/mL).

OXIDIZED CELLULOSE AS A BASIS FOR THE CREATION OF NEW LOCAL HEMOSTATIC AGENTS

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Available natural biopolymers such as cellulose, starch and chitin are very promising starting products for creation of new biocompatible and biodegradable materials for medicine.

Ability to stop the bleeding occurred during operation and traumatic injuries of organs is one of the most important complication of modern surgery. Adequate hemostasis during the surgery and in the postoperative period leads to improvement of operation results, reduces the risk of surgical complications and transfusion equipment consumption. Special attention is paid to the local hemostatic agents that operate precisely and can be used in cases where other approaches are ineffective. On the moment there is wide variety of drugs with different chemical structure and action, as well as composite local hemostatic products. However, existing materials aren′t able to provide sufficient hemostasis during open surgery such as cardiovascular surgery, abdominal surgery etc. That is why search and creation of new effective local hemostatics providing adequate hemostasis are still relevant tasks.

Vegetable origin of cellulose is an advantage during creation of hemostatic agents. One of the most examined hemostatic agents derived from cellulose is oxidized cellulose (OC). Ability to be dissolved in tissues of a living organism is an important feature of OC. Moreover, OC is a natural compound-leader for creation of wide action spectrum hybrid materials.

The main method of OC production for medical purposes as local hemostatics is oxidation of cellulose by nitrogen oxide (IV). The quality and medical properties of OC depend on the oxidation conditions. The methods of OC creation, physico-chemical, hemostatic and other biological properties of the materials created on the basis of OC are presented in this report. The examples of hemostatics based on OC applied in various spheres of surgery are presented.

STRUCTURE OF MAJDINE AND ISOMAJDINE

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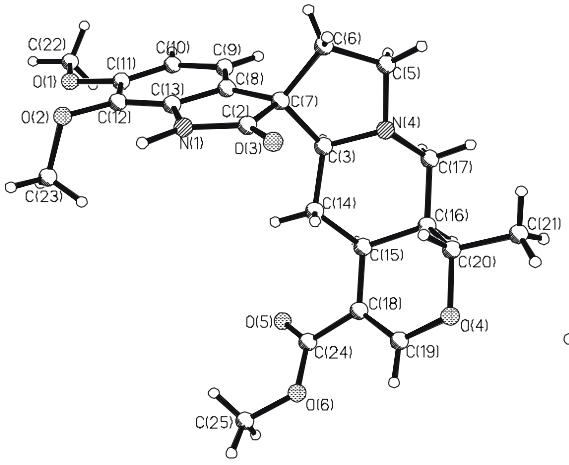
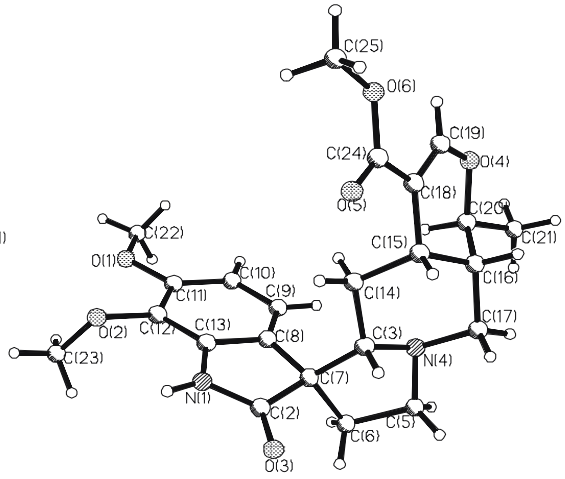
In order to clarify the absolute configuration of alkaloids majdine and isomajdine [$C_{23}H_{28}N_4O_6$] XRD studies have been performed of these alkaloids isolated from plants *V. major* and *V. herbaseae*, respectively [1, 2]. The structures of alkaloid were determined by NMR spectroscopy [3]. In this paper, X-ray diffraction confirmed the absolute configuration of the selected alkaloids, the reliability of establishing the absolute configuration (Fleck parameters for majdine is 0.2 (4) and for isomajdine is –0.2 (3)).

X-ray data confirm that alkaloids differ according to spirocenters configuration of five asymmetric centers, hence are diastereomers. Spirocenter – C7 atom of the molecule accepts 7*R* and 7*S*-configuration in case of majdine and isomajdine, respectively. In the molecules sequentially condensed three heterocyclic: Trans, *cis*-jointed, and linked with the indole ring spirocenter C7.



Majdine (3*S*,7*R*,15*S*,16*S*,20*S*)



Isomajdine (3*S*,7*S*,15*S*,16*S*,20*S*)

The core of the indole alkaloids has a close structure: the torsion angle of C13-C12-O2-C23 bonds are –90.1 (9)° and –106.6 (4)°, respectively. This indicates, that the nitrogen atom N1 is not involved in the formation of intramolecular hydrogen bond. N1 nitrogen atom in the crystal structures involved to the intermolecular interactions. In majdine crystal intermolecular hydrogen bond-type N1-H ... O1, N1′-H ... O2 is observed, which links the molecule along the axis *a*, and in isomajdine type N1-H ... O5 = C24 observed, which links the molecule along the axis *b*.

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ANTI-INFLAMMATORY EFFECT OF A CINNAMON FOR MULATION AGAINt SCARRAGEENAN-INDUCED PAW EDEMA IN RATS

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Arthritisis a form of joint disorder that involves inflammation of one or more joints. The major complaint by individuals who have arthritis is joint pain. The pain from arthritis is due to inflammation that occurs around the joint. Severe side effects of steroidal and non-steroidalanti-inflammatory drugs used for joint pain,such as gasterointestinal, cardiovascular, liver, rash, fever which all dependant on dose and duration, evoked us to searchfor new anti-inflammatory agents from natural botanicalsources which may have minimal drawbacks. A Cinnamon bearing formula consists of several patented herbs and oils used in folk medicine as anti-inflammatory and analgesic agents. The formulation has shown promising effects on the non-official market. Current study aims on formulation, fabrication and anti-inflammatory evaluation of this cream.

Physicochemical characteristics and stability of the formulation were assayed. In anti-inflammatory assay, 50 male Wistar rats weighting between 200–240 g were used which divided into five groups of 10. Carrageenan as a paw edema inductive was used. Paw volume increase was evaluated in positive group (piroxicam), negative group and treatment just after, 0.5, 1 and 2 hours after carrageenan administration by tismograph instrument. In treatment groups, rats were received formulation cream just after, 0.5, 1 and 2 h after carrageenan administration. Statistics analyses were performed using Variance, ANOVA and t-test. Formulation showed promising anti-inflammatory effects. Skin toxicity test showed no toxicity for the product.

NEW AMINOMETHYL DERIVATIVES OF NATURAL FLAVONOID DIHYDROQUERCETIN

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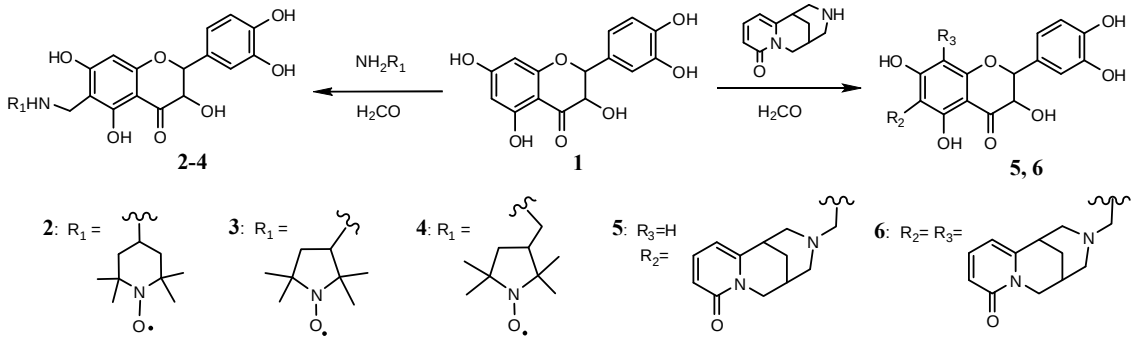
Flavonoids represent a large group of bioactive compounds. Chemical modification of flavonoids leading to new pharmacologically active compounds creation is a relevant task for both organic and medicinal chemistry. It is known that the introduction of modifying fragments in the molecules of bioactive substances may lead to creation of new and strengthening of existing biological properties of the parent compound.

Natural flavonoid dihydroquercetin (DQv), isolated from *Larix Sibirica* larch, possesses pharmacological properties of broad-spectrum and low toxicity that allow including it into a group of compounds–leaders for the synthesis of new hybrid multifunctional pharmacologically active compounds. Literature describes methods of receiving aminomethyl derivatives of DQv with both primary and secondary amines, however, no examples of modifying it with nitroxides or alkadoids were found. Nitroxyl radicals are spin-labels for biomedical research by EPR and MRT methods; alkaloid cytisine shows neuropharmacologic, analeptic, gipolipidemic and anti-inflammatory activities.

In this paper as a result of the Mannich reaction of DQv **1** with nitroxyl radicals in presence of formaldehyde the spin-labeled derivatives **2**–**4** were obtained, reaction with cytisine resulted in mono- and disubstituted derivatives **5** and **6.**



The structures of the compounds **2**–**4** were established by UV-, IR-spectroscopy and mass spectrometry methods. In order to confirm the structures of the compounds **2**–**4** they were reduced to their corresponding hydroxylamines, the structure of which was established by ^{1}H and ^{13}C NMR methods. The structures of compounds **5** and **6** were established by UV, IR, ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry methods.

Thus, aminomethyl derivatives of DQv with nitroxides and alkaloid cytisine were obtained for the first time. Synthesized compounds are promising bioactive hybrid polyfunctional compounds.

MORPHOLOGICAL, CHEMICAL AND INDUMENTUM CHARACTERISTICS OF *Rhododendron ponticum* L. subsp. *ponticum*

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Morethan 850 species of *Rhododendron* are distributed in the North Hemisphere. *Rhododendron* distributed in North Easternand West Anatolia is represented by 5 species one being endemik and altogether12 taxaand 4 hybrid taxa.

Leaves and flowers of *Rhododendron* (especially *R. luteum* Sweet and *R. ponticum* L.) contain toxic compounds (and romedotoxin). Honey from the flowers of *Rhododendron* is locally known as "deli bal, aci bal, tutar bal". It has antihypertension activity. And when consumed it has toxic effects. *Rhododendron* species are also used as decorative plants.

This report concerns morphological, chemical and indumentum characteristics of *Rhododendron ponticum* L. subsp. *ponticum* (*Ericaceae*) collected from Bartın Province. A detailed description of the species has been prepared and compared with that published in the Flora of Turkey of Davis in a tabular form. The taxonomic and morphological characteristics of the plant material have been described and illustrated by drawings. Indumentum characteristics were also investigated.

*R. ponticum*is an evergreenplant, growingupto 10 m, in North and Eastern Anatolian mountains. This plant known as "Mor cicekli ormangulu, Alp gulu, Komar, Karaagu, Kara Kumar, Kumar". Leaves elliptic-obovate, glabrous-glandularhairs on surfaces. Flowers are pink-purple. Flowers are usually with 5 fragments. Flowering period, usually in summer months.

Head space volatiles of fresh flowers of *Rhododendron ponticum* and hexane extract were analyzed by gas chromatography/mass spectrometry. The volatiles were trapped by SPME in a dynamic headspace set up. *Rhododendron* flowers blue –Polydimethyl siloxane/Divinylbenzene (PDMS/DVB) fibre was used.

Volatiles of *Rhododendron ponticum*were trapped by blue SPME fibreover a period of 1.5 hours. Main components were identified as α-pinene (44.5%), β-pinene (10.8%), linalool (4%) and limonene (3.3%).

Volatiles of the hexane extract of *Rhododendron ponticum*were trapped on an HS-SPME (Blue fibre). Main components were identified as linalool (19.6%), phenylethyl alcohol (19.1%), myrtenol (10.1%). citronellol (9.4%) and phenylacetaldehyde (7.8%).

This is the first report on the headspace volatiles of this plant.

SYNTHESIS OF ORTO-CHLORBEZOYLCHLORIDE DERIVATIVES OF 20-HYDROXYECDYSONE

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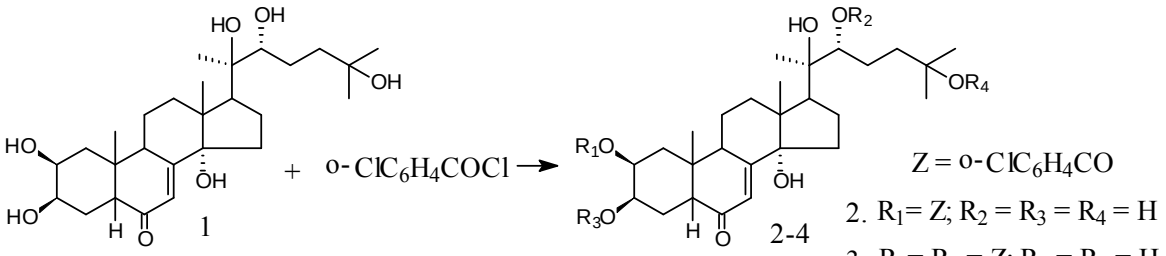
Phytoecdysteroids are natural substances, that enter the body with plant food and can control the vital functions of the body on the integral level, tie into one whole the functioning of nervous, sensory, endocrine, cardiovascular and digestive system, metabolism and energy, immunity and reproduction.

One of the distinguishing features of the molecular structure of the ecdysteroids is the presence of a large number of OH-groups, which differ greatly in their reactivity. Consequently ecdysteroids are extremely suitable for finding new biologically active substances, which can be obtained by a variety of chemical transformations of the initial compounds.

It is widely spread in plants and is a useful raw material for producing of new bioactive derivatives.

The synthesis of ortho-chlorbenzoyl of 20-hydroxyecdysone is undertaken by us during the work. One of the major ecdysteroids is 20-hydroxyecdysone. The acylation reaction of 20-hydroxyecdysone was carried out under the influence of orto-chlorbezoylchloride in pyridine at a temperature of 45–50°C during 2–2.5 hours.

It is established, that in this condition a mixture of the four ortho-chlorbenzoil derivatives is formed. This mixture was successfully divided into individual components by column chromatography. Thus, new derivatives of 2-*O*-(*o*-chlorobenzoyl)-20-hydroxyecdysone (**2**), 2,3-di-*O*-(*o*-chlorobenzoyl)-20-hydroxyecdysone (**3**), 2,3,22-tri-*O*-(*o*-chlorobenzoyl)-20-hydroxyecdysone (**4**) were obtained. Their structures are identified by ^{1}H, ^{13}C, NMR spectral analysis and experiment Dept, Hetcor.



ACYL DERIVATIVES OF PYRROLIZIDINE ALKALOIDS LINDELOFINE AND LINDELOFINE *N*-OXIDE

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Pyrrolizidine alkaloid lindelofine and their derivatives have a weak *m*-cholynolytic and gangliobloking actions.

We obtained the aliphatic and aromatic acyl derivatives of alkaloids lindelofine and lindelofine *N*-oxide in order to study their biological activity.

To confirm the structure of lindelofine *N*-oxide and determine the stereochemistry of the *N*-oxide group X-ray diffraction analysis used (Fig. 1)

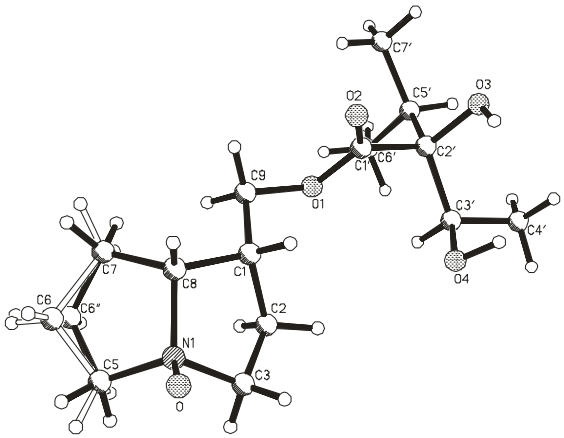

Fig. 1. Spatial structure of the lindelofine *N*-oxide.

The results shown, that the *N*-oxide bond in the lindelofine *N*-oxide is β-oriented and has *R*-configuration.

We have studied the acylation of lindelofine and lindelofine *N*-oxide by acetyc and propionyc anhydrides, as well as by benzoyl chloride in different conditions. The structure of the obtained products was determined by IR -, NMR spectra and X-ray diffraction analysis.

DIHYDROFURANOCOUMARINS FROM *Ferulago macrocarpa*

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Ferulago macrocarpa is a plant growing wild in Middle East such as Western Iran and is used as food seasoning. It has previously shown larvicidal effects. There is no report on phytochemical investigation of the plant, so we decide to isolate some of its constituents.

Plant material was collected from Saleh Abad, Ilam, Iran, in 800 meters above sea level. Fruits were separated carefully and shadow dried. 500 g of fruits were extracted with acetone (×3) at room temperature, and the extract was vacuum dried. It was then suspended in MeOH and kept chilled to separate the insoluble fatty mass. The solution part was fractionated using vacuum liquid chromatography (Silica, Heptane–EtOAc) to render several fractions in which were further purified using normal phase open column chromatographies and preparative HPLC separations.

Finally, several coumarins including dihydrofuranocoumarins like prantchimgin were purified and structures were elucidated using NMR and mass spectroscopy. Anti-inflammatory effects including 5-lipooxigenase activity have been reported from prantschimgin.

SYNTHESIS OF 1-ARYL-6,7-METHYLENEDIOXY-1,2,3,4-TETRAHYDROISOQUINOLINE

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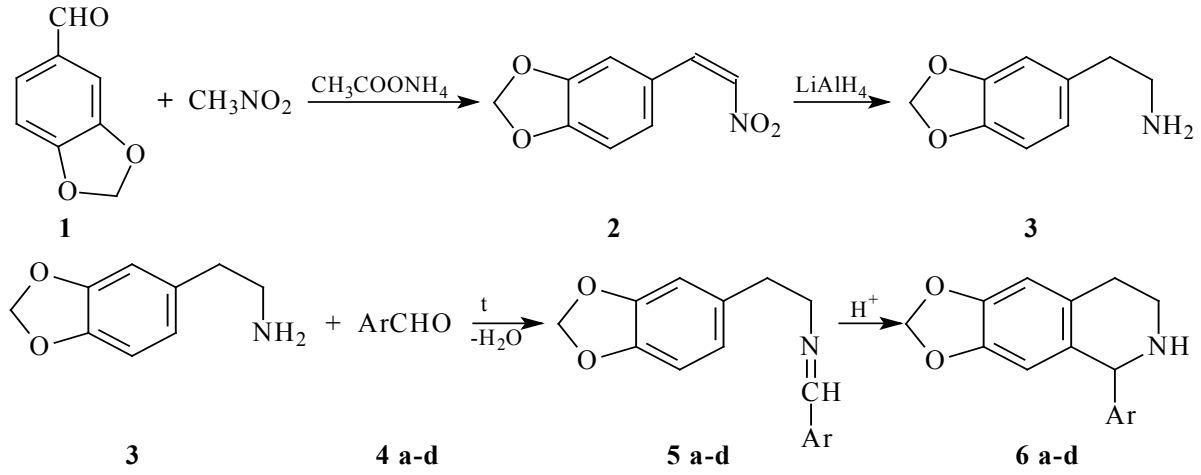
Nitrostyrene **2** was obtained by the condensation of 3,4-metilendioxybenzaldehyde (**1**) with nitromethane in the presence of ammonium acetate. Its $LiAlH_4$ reduction in absolute ether solution provides homopiperanilamine (**3**) [1].

The target 1-aryl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinolines were prepared by Pictet–Spengler reaction based on homopiperanilamine (**3**) and the appropriate aldehyde **4a–d**. Imines **5a–d** were cyclized in acidic medium to obtain tetrahydroisoquinolines **6a–d.**



The structure of obtained compounds was proved by ^1H NMR spectroscopy.

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STUDYING OF THE MECHANISM OF ACTION OF PREPARATION К-48 RECEIVED ON A BASIS COLCHICINES

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The clinical oncology has located big number of effective preparations. However their expressed overall toxic the effect, quickly developing resistance of an organism to them, and also a variety of forms of oncological diseases dictates necessity of expansion of an arsenal of operating preparations. In NSCO of MH of RUz the big group of new substances (15) on a basis tropolone alkaloids colchicine and colchicine with the activity exceeding activity of known applied antineoplastic preparations that is shown at comparison of their action in experiment on 3 штаммах tumours with world known preparations of the similar mechanism of action tacsol and etopozide, and also with effect of preparations of other mechanism of action widely applied in oncology is developed: ciklophocphane, 5-ftoruratsilom and to its new derivatives capecitabine (kselods).

One of the most interesting preparations of this number is К-48 for which have been conducted research of its toxic properties (LD_{50} 1440 mg/kg) and antineoplastic activity as in NCI *in vitro*, and also in vivo on 8 tumor strains.

It is revealed it immunomodulation action after the spent treatment. All it has shown perspectivity of this substance for the further clinical use.

Studying of its mechanism of action was the purpose of the present research, were considered: mitotic activity, alkylating action (influence on synthesis of DNA and RNA tumours, on interrnucleoconic degradation and DNA fragmentation), influence on topoizomeraze I and II, influence on MDR, on mutagenicity, SFUs, immunity.

К-48 Possesses mitotic and alkylating activity, promote interrnucleoconic to degradation and a fragmentation of DNA by means of inhibition topoizomeraze I and II and possess high degree of ability of overcoming MDR by means of updating of activity of medicinal conveyor Pdr5p above, than etopozid.

К-48 causes 40–60 units SFUs, does not possess mutagenecity, does not suppress immunity at different ways and application doses, In a dose of 1 mg/kg when К-48 induces a move quantity SFUs, are shown its move immunomodulation properties, it is known that in this dose the preparation possesses and growthinhibitory activity which, can be more likely caused its ability to immunomodulation, than alkylating or mitotic activity.

It is necessary to notice that К-48 is owing to the structural features (because of introduction alkylating fragments) more expressed radiomimetic, than colchicine, and in greater to a measure strengthen emission SFUs that, possibly, causes both immune properties, and absence mutagenicity, and overcomings MDR. It is visible that at stimulation SFUs till 40–60 unit at К-48 there are properties, not characteristic for cytostatic – absence mutagenicity and occurrence immunomodulatory properties. It was found out that К-48 twice or more reduces level of the chromosomal aberrations, peculiar tumours for carriers. It is one more aspect of application of substance with such properties as decrease in level of chromosomal aberrations, on genetic researches, reduces risk of occurrence or tumour relapse.

AMIDOMETHYL CYTIZINE AND ANABAZINE CONTAINING OXA- AND THIADIAZOL FRAGMENTS

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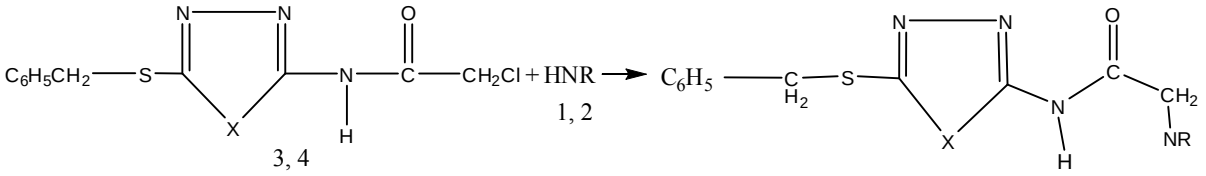
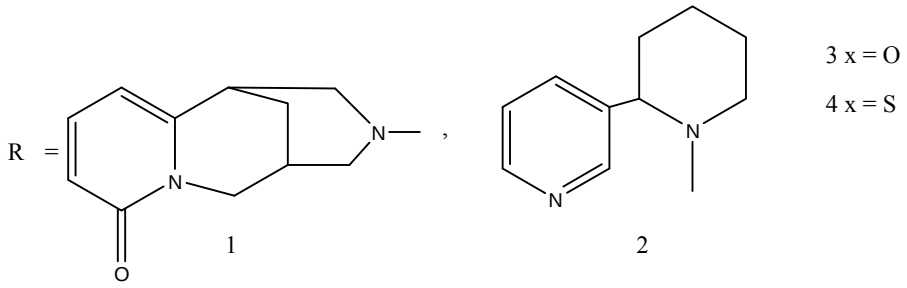
The wide spectrum of biological activity of alkaloids cytizine (**1**), anabazine (**2**) and nitrogen containing heterocycles – 1,3,4-oxa(thia)diazoles (**3**, **4**) made them interesting to obtaining new compounds with more effective properties [1–4]. In this purpose we have studied amidoalkylation reaction 1,2 with 2-benzylthio-5-chloroacetylamino-1,3,4-oxa(thia)diazoles (**3**, **4**). Reaction carried out by refluxing mixture of reagents in organic solvents with various ratios of them and dehydrohalogeneted agent:





Products of reactions obtained in sufficient quiantities. Their structures confirmed by IR- and ^{1}H NMR spectroscopy.

Those, the synthesis of new amidoalkylderivatives of cytizine and anabazine with oxa- and thiadiazol fragments realized.

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF 5-ARYL-1,3,4-OXADIAZOLYNE-2-THIONE SALTS

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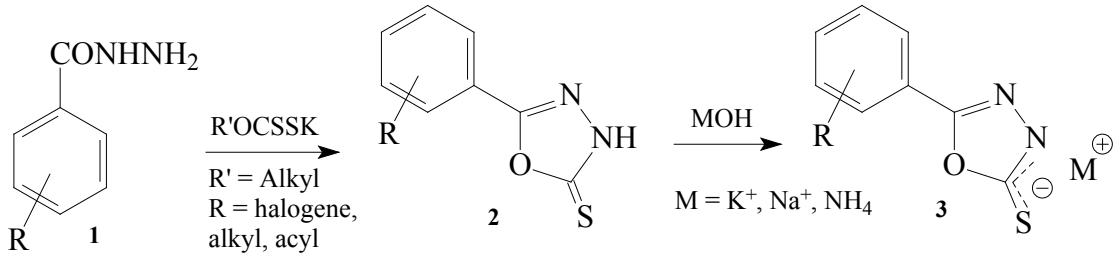
Due to high biological activity and wide spectrum of effects of 5-aryl-1,3,4-oxadiazolyne-2-thiones attracted a great interest [1, 2]. We have studied synthesis of salts of 5-aryl-1,3,4-oxadiazolyne-2-thiones and investigated their pesticide activity, because such data are not presented in the state of the art.

Synthesis of 5-aryl-1,3,4-oxadiazolyne-2-thiones (**2**) have been done by interaction of carbon acids hydrazides (**1**) with sodium alkylxanthogenates, which are more available and less badly, than CS_2 used in such reactions. Usage of equimolar quantity (**2**) and the base provides the water soluble salts of 5-aryl-1,3,4-oxadiazolyne-2-thiones:



It was shown, that biological activities of obtained salts are depended from nature of substituent in aromatic cycle and positive ion. Sodium salts were more effective. They displayed the potential herbicide activity.

Structures of 5-aryl-1,3,4-oxadiazolyne-2-thiones confirmed by UV- and ^{1}H NMR spectrums.

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ISOLATION OF POLYMERIC PROANTHOCYANIDINS SUM FROM THE ROOTS OF *Polygonum coriarium*

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Currently the treatment of various diseases mostly used drugs derived from plant material. The main advantage of these drugs is an affinity for the human body and the virtual absence of side effects. Therefore, the creation of domestic high effective drugs based on plant flora of Uzbekistan is an actual.

Po1ygonum coriarium is perennial plant widespread in the Central Asia. In folk medicine herbal teas and tinctures from the roots of this plant are used in acute, chronic diarrhea and other intestinal inflammatory processes [1].

Pharmacological research of polymeric proanthocyanidins sum extracted from the roots of the plant have shown that they possess antihypoxic action at a relatively low toxicity (7000 mg/kg) [2], what makes the isolated compounds promising for the creation of a new original antihypoxic drug.

The aim of this study was to investigate the process of extraction the amount of polymeric proanthocyanidins from the roots of *Po1ygonum coriarium.*

Extraction method includes a method of fractional maceration. We studied the production process parameters such as extraction efficiency, temperature control, process of extraction, extraction time, the ratio of raw material/extractant, multiple extraction. All parameters have been studied at all levels of extraction.

During experiments it were established the basic parameters of the process of rational extraction of polymeric proanthocyanidins. It was founded, that the four time extraction of material with degree of milling 1.0–2.5 cm by 40% ethyl alcohol at a total liquid ratio 1:15 at room temperature for 6–8 hours can remove 84.6% of the polymeric proanthocyanidins from their total content in the feedstock.

The results were used in an optimal pattern of production of the drug "Katacine".

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INFLUENCE OF UCHKUN PREPARATION ON GREEN PIGMENT CONTENT IN FOUR TYPES OF WHEAT

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It is well known, that intensively growing and developments, biomass increasing and yielding ability of plants as autotrophy organisms are basically depends from intensiveness of photosynthesis process. So, regulating of photosynthesis apparatus activity by biologically active substances in plants has great theoretical and applied interest. It opens ability of effective regulation of yielding.

In this view the special interest is attracted to study the influence of plant growth biostimulator Uchkun created in the Institute of the Chemistry of Plant Substances AS RUz, on content of chlorophylls “a” and “b”, biomass increasing and yielding ability of wheat. Trials were made on Friendship, Chillaki, Tanya and Vostorg sorts on experimental field of Gulistan State University. The preparation was applied by two ways: seeds wetting and spraying of growing plants.

Application of Uchkun in both ways led to essential magnification of green pigments up to 33–53% depending from the wheat sort. Maximal improving of quantity of chlorophylls “a” and “b” content are observed in beginning of shrub formation from initial 1.13 mg/g (100%) up to 1.73 mg/g (153%). Further their contents decreased due to destruction or ageing.

It is known that increasing of green pigments leads improving activity of photosynthetic apparatus. Hence, it leads to improving of evolution of plants.

It was shown positive influence preparation of Uchkun to photosynthetic apparatus of wheat, improving of biomass and yielding ability.

TOXICITY OF PEGANUM HARMALA L. QUINAZOLINE ALCALOIDS AND THEIR SYNTHETIC ANALOGUES: QSAR STUDY FOR SEARCHING AN ACCEPTABLE MODEL

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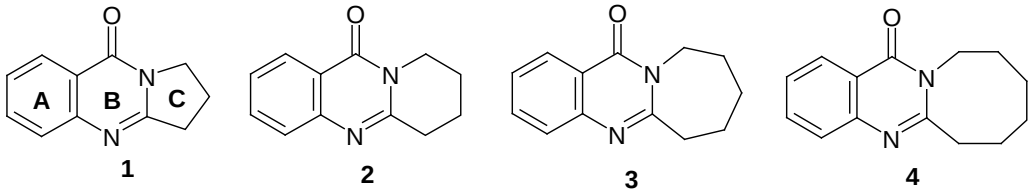
It is known, that *Peganum harmala* L. is used in national medicine for a long time as an emmenagogue and an abortification agent in the Middle East and North Africa [1]. More than 12 quinazoline alkaloids – deoxypeganine (2,3-trimethylen-3,4-dihydroquinazoline, **1**) and others, possessing anticholinesterase activity [3] have been isolated from the plant.

According to the pharmacological data of the deoxypeganine and its derivatives [2], the rigid tricyclic structure is important in appearance of high anticholinesterase activity. In increasing of the "C" cycle size (**1**–**4**) the muscle relaxant effect dominated than anticholinesterase activity. Similar changes have been found also in chemical and spectral (IR – UV/Vis) behavior of these compounds. Definition of especially influencing parameters gives possibility to find the tendency of pharmacological, chemical and also spectral changes of the compounds.



In this connection, we carry out QSAR analysis for 42 synthetic and natural analogues of deoxypeganine by dividing into training and test sets. Variable selection procedure by DRAGON [3] descriptors and quantum-chemical parameters was made by GA MLRA approach using Build Qsar program [4].

As a result of the investigations the correlation diagram between correlation coefficients (r^2) and number of descriptors (from 1 to 6) for training and test sets was drawn. On the basis of the diagram an acceptable model for toxicity prediction of deoxypeganine and its analogues is selected.

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ISOLATION AND CHARACTERIZATION OF ANTIMICROBIAL PROPERTIES OF CYCLOTIDES FROM *Capsicum anuum*

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Cyclotides are a plant-derived family of small proteins characterized by their head-to-tail cyclic backbone and a cystine knot arrangement of three conserved disulfide bonds. They were first discovered in plants from *Rubiaceae* and *Violaceae* families, but have since been reported in a range of other plants from the *Cucurbitaceae* and *Fabaceae* families and it has been predicted that they are widely distributed within the plant kingdom. Cyclotides are notable for their exceptional stability and their diverse range of bioactivities, as well as for their expression in a wide range of plant tissues, including leaves, stems, flowers, dormant seeds and roots. There have been a number of recent reviews on the discovery, structures, and applications of cyclotides, to which the reader is referred for more background but here the focus on their pesticidal and/or toxic activities.

In this work we isolated and characterized peptide fractions from seeds of *Capsicum anuum* (*Solanaceae*). Seeds were grinded using a mortar and pestle and extracted with chloroform–methanol (1:1 v/v) overnight. The mixture was transferred to a separation flask and the layers separated after the addition of water. the aqueous layer was ollectrd and concentrated on a rotary evaporator. Load the concentrated aqueous layer onto a C_{18} column and wash with increasing concentrations (20%, 40%, 60% and 80%) of solvent A (acetonitrile–water–trichloracetic acid) to elute the peptides and remove any impurities. Concentrate the solvent A fraction on a rotary evaporator and lyophilize for MS and purification.

Fractions were analyzed by Accurate-Mass Q-TOF LC/MS to test for the presence of cyclotides. The fraction, eluted 40% solvent A, showed a wide diversity of peptides with masses in the range 1351-4727 Da, typically the range of masses expected for cyclotides and fraction, eluted 60%, showed peptide with mass 903 Da.

Fractions were tested against a range of human pathogenic bacteria using the micro-dilution method. The most potent example was fraction, eluted 40% against a Gram-positive *Staphylococcus aureus* and a Gram-negative *Escherichia coli* and fraction, eluted 60% against *Escherichia coli* at a concentration of 25 mkg/mL.

Protein fractions showing antimicrobial activity were tested for cytotoxic activity in HeLa (Human cervical cancer cell) line. Cultures of HeLa cells were conducted in the presence of three protein concentrations. Viability of cell cultures was appraised using XTT colorimetric test. The most pronounced effect was obtained with the highest concentration of the fractions, eluted by 40% (100 μg/mL), where 54 ± 3% mitochondrial activity of HeLa cells were inhibited.

PHARMACOKINETICS OF *N*-GALLOIDALKYLAMINES IN NORM STATE AND PATHOLOGY

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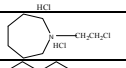
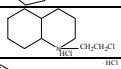
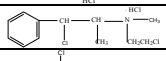
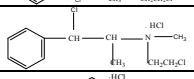
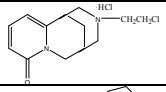
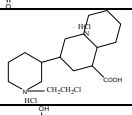
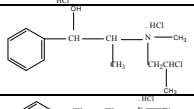
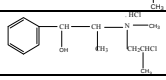
To find out the influence of modifying factors to biokinetic cellular processes it has been researched biotransformation and pharmacokinetic parameters of "direct action" alkylators – *N*-galloidalkylamine derivatives of heterocyclic compounds and some alkaloids.

TABLE. **Anticancer activity of Heterocyclic *N*-Chlorialkylamines and Alkaloids**

№n/n	Compound	LD_{50} mg/kg	Dose mg/kg	Growth inhibition of tumors, %			
				АРЭ	S-180	La	K.G
I		50	20	60	65	115	–
II		37	20	70	90	110	–
III		80	20	50	60	105	–
IV		18	10	55	70	120	–
V		25	10	90	85	135	–
VI		83	20	20	45	–	–
VII		93	20	–	40	–	–
VIII		150	40	50	53	–	–
IX		200	40	50	52	–	–

Research shows that urinary excretion kinetics of compounds **1–5** and changes of metabolites content in urine, increased concentration of lipophilic products of metabolism at timorous animals persists in all cases in comparison with intact animals.

Anticancer activity of *N*-(B-chloroethane)-derivatives of nitrogen-containing compounds and alkaloids doesn't correlate with toxicity of applicable preparation, i.e. data comparison shows selective interaction of compounds with dividing cell of tumor.

PHOSPHOLIPIDS IN A HUMAN SKIN: ISOLATION AND CHARACTERIZATION

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Phospholipids are amphiphylic lipid molecules comprising structural basis of biomembranes and playing a significant role in life-sustaining activity of cells and an organism as a whole. Normal functioning of organs and tissues is performed upon integrity of membrane phospholipids. Any disturbances of content and composition of phospholipids result in shifts in functional activity of cells and trigger pathological processes. Despite sufficient number of works devoted to study on phospholipids of various tissues in organism, the phospholipids of the human beings the skin have been explored insufficiently. That is why, the work was initiated to isolate, study fraction composition and perform quantitative assessment of human skin phospholipids. The study was performed on biopsy material of healthy subject skin. Extraction of phospholipids from the skin as well as their isolation and purification were performed by means of chloroform- methanol mixture in compliance with method by Folch J. et al. (1957) in modification by Kaets (1975). Quantitative assessment of the isolated phospholipids was performed by content of phosphorous in them. In healthy subject skin the total phospholipids comprise 1324.4 ± 57.9 μg of lipid phosphorous per 1 g of dry tissue undergoing significant changes upon skin diseases. For example, in vitiligous patients mean phospholipid content is 1039.5 μg P/g of dry tissue. Fraction composition of phospholipids was measured by thin layer chromatography on silica gel. On the chromatograms we founded and identified 8 fractions, among which phosphatidylcholine comprising 37.61% of total phospholipids (498.1 ± 21.2 μg P/g of tissue) is the most significant. Cardiolipin is the least fraction with the content of 29.3 ± 1.3 μg P/g of tissue comprising 2.21% of total phospholipids. Neutral phospholipid fractions, such as, phosphatidylcholine, phosphatidylethanolamine and sphingomyeline, comprise 81.22% of total phospholipids, while acidic fractions, such as, lisophosphatidylcholine, phosphatidylserine, phosphatidylinositol, cardiolipin and phosphatidic acid comprise 18.78%. Mean phospholipid acidic-to-neutral fractions ratio in the healthy subjects′ skin is 0.23. It should be noted that fraction composition of skin phospholipids does not differ from those of other organs and tissues of a human being. However, there are significant differences in quantities and ratios of some skin phospholipid fractions and those of other organs.

THE DEVELOPMENT OF NTD AND OF TECHNOLOGY FOR OBTAINING THE MEDICINAL REMEDIES ON THE BASE OF GLYCYRRHIZIC ACID

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Glycyrrhizic acid (GA) was obtained from licorice root, and its derivatives show the high antiinflammatory, antiulcer, antiviral, antitumour and other activities. In this connection, the organization of production of domestic medicinal preparation on GA base, showing the above said activities, is actually.

The possibility of the creation of such medicinal remedies has brought us to need of the development normative-technical documentation (NTD) and organization of medicinal remedies production on the base of glycyrrhizic acid. Authors were worked out high effective, suitable with industrial standpoint technology of obtaining GA substance (OPR), with contents of main acting material not less 85% from thick extract of licorice root. NTD on glycyrrhizic acid was registered (FS 42 Uz-0979-2012, registration certificate – 12/362/14).

In order to create high effective antiulcer remedy on the base of GA GA threesodium salt was synthesized. Authors worked out the technology of obtaining of GA threesodium salt substance – "Glycythrinat" (OPR), possessing with high antiulcer activity, with contents of main acting material not less 97%, as well as the necessary NTD (FS 42 Uz-1104-2012, registration certificate 07/384/1).

At present on the base of glycyrrhizic acid the authors are working under the technology of antiviral preparation "Glycytogen" obtaining. The optimal composition of the preparation with contents of acting material – glycyrrhizic acid 0.1% is selected. Antiviral preparation "Glycytogen" is also the efficient immunomodulating remedy.

GAS CHROMATOGRAPHIC ANALYSIS OF PCB IN SOIL SAMPLES AROUND CHIRCHIK TRANSFORMER PLANT

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PCBs are a group of chlorinated organic compounds with the general title "persistent organic pollutants" (POPs). Republic of Uzbekistan was carried on State List of Persistent Organic Pollutants (POPs). Our aim is the study of PCBs pollutants around Chirchik transformer plant with polychlorinated biphenyl.

Twenty samples for PCBs pollution in the central Region of Samarkand and Tashkent Region were investigated. Soil samples were collected around of electricity supply of the Samarkand region and Chirchik Transformer plant of the Tashkent region. The soil samples were extracted with chloroform mixture (1:1 v/v) for 4 hours. The final extract of 2.0 mL was analyzed for PCBs using a gas chromatograph equipped with 10 mCi 63Ni electron capture detector GC-ECD model 86/30. The total runtime was 10.00 min. The retention times for the PCBs standards C = 1 mg/L and C = 10 mg/L are provided in the Table 1. The identification of PCBs congeners in the sample was carried out by comparing the retention times of the PCBs congeners in sample to that of the PCB standards. The concentrations of the individual PCBs congeners in mg/kg were calculated on dry weight basis, and the total PCBs concentration (ΣPCB) calculated by summing up the concentrations of individual PCB congeners.

TABLE 1. **PCB Empirical Formulas, Molecular Weight, and Number of Corresponding Isomers**

PCB	Retention time for the PCB standard C = 1 mg/L, min	Retention time for the PCB standard C = 10 mg/L, min
2,4,4′-Trichlorobiphenyl	3.683	3.68
2,2′5,5′-Tetrachlorobiphenyl	3.963	3.96
2,2′3,4,4′5,5′-Heptachlorobiphenyl	4.697	4.7
2,2,3′,4′5,5′-Pentachlorobiphenyl	5.237	5.24
2,3′4,4′5-Pentachlorobiphenyl	5.427	5.43
2,2′4,4′5,5′-Hexachlorobiphenyl	5.67	5.68
2,2′3,4,4′,5′-Hexachlorobiphenyl	6.290	6.25

The variations of the microelements in soil around Chirchik Transformer plant were analyzed by the method of atomic absorption on spectrometer “Saturn”. The Saturn AAS was used for the metal analysis. The mean concentration (in mg/kg) of the metals were Ca (416 ± 19.1) > Na (222 ± 13.6) > Cu (100 ± 3.9) > Ni (87 ± 5.1) > Pb (57.1 ± 2.9) > Zn (40.0 ± 2.5) > Co (29.0 ± 1.9) > Cd (21.3 ± 1.5) > Fe (18.0 ± 1.3) > Mn (10.0 ± 1.2) > Cl^- (0.32 ± 0.02). The variations in the levels of the microelements were in the order Ca > Na > Cu > Ni > Pb > Zn > Co > Cd > Fe> Mn > Cl^-.

STRUCTURE OF CYCLOLEHMANOSIDE A FROM *Astragalus lehmannianus*

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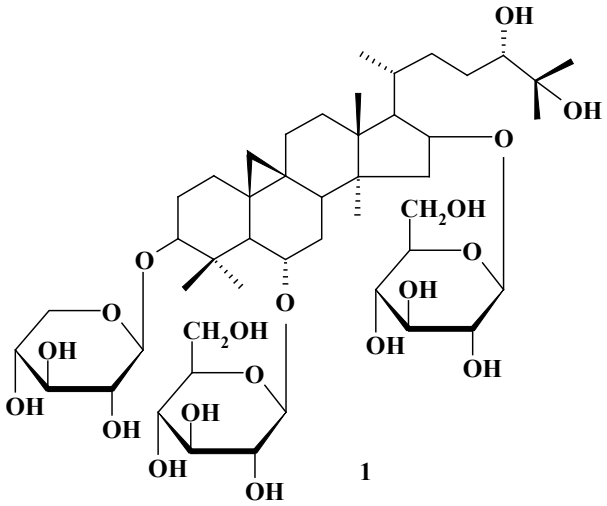
34 species of *Astragalus* plants grows in Karakalpakstan by the literature data.

All species of *Astragalus* plants are important cycloartane containing plants and sources for cycloartane triterpenoides isolation. Therefore we have investigated cycloartanes of *Astragalus lehmannianus* Bunge.

By column chromatography method we have isolated from arial part of *Astragalus lehmannianus* the new triterpen glycoside, cyclolehmanoside A (**1**), which have the structure 3-*O*-β-*D*-xylopiranoside, 6,16-di-*O*-β-*D*-glucopiranoside-24*S*-cycloartane-3β,6α,16β,24,25-pentaol.

The ^{1}H NMR spectrum of the novel glycoside **1** has at δ 0.35 and 0.58 (each 1H, d, J = 4.2 Hz) signals of cyclopropane ring protons and signals of protons of the seven methyl groups at δ 0.99–1.29. These data allow us to make conclusion that the glycoside is a cycloartane line triterpenoid.

Acidic hydrolysis of cyclolehmanoside A gives aglicon identified with cyclocanthogenin. Carbohydrate part of glycoside was determined by TLC as *D*-xylopyranoside and *D*-glucopyranoside.



1

A NEW FLAVONE GLYCOSIDE FROM AREAL PART OF *Alhagi pseudalhagi*

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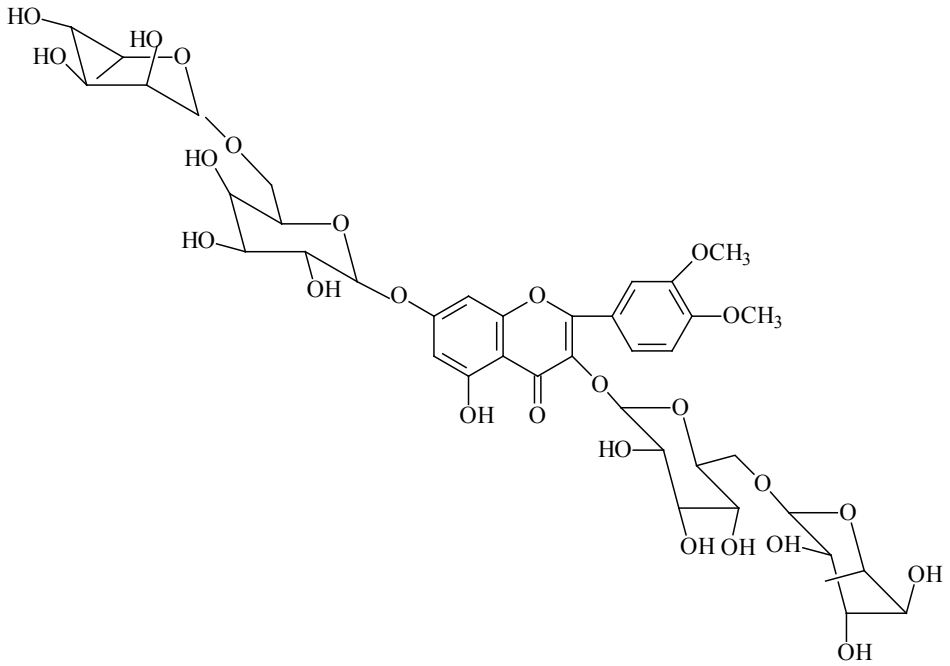
Alhagi pseudalhagi (Bieb.)-Fisch is a perennial herb (*Fabaceae* family) widely distributed in the world.

Earlier from *Alhagi pseudalhagi* we have isolated flavonoids, catechins, di- and oligomer proantocyanidins.

In continuation of our studies of the chemical composition of *Alhagi pseudalhagi*, the aerial part of the plant was collected in flowering time in the Tashkent region of the Uzbekistan. From this plant we isolated a new flavone glycoside named by us alhaozide (**1**), which has the composition $C_{41}H_{54}O_{25}$, mp 194–196°C (methanol).

Structure of alhaozide had been established on the basis of its physical and chemical properties and the analysis of IR, UV, ^{1}H, ^{13}C NMR, DEPT spectral data.

Thus, for alhaozide we proposed the structure quercetin-3′,4′-dimethoxy-3-*O*-α-*L*-rhamnopyranosyl-(1→6)-β-*D*-glucopyranoside-7-*O*-α-*L*-rhamnopyranosyl-(1→6)-β-*D*-galactopyranoside.



COMPOUNDS OF *Mausolea eriocarpa*

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Mausolea eriocarpa (Fam. *Asteraceae*) is a semi-shrub plant of 25–55 cm height with thick woody roots and covered by grey bark high wooded stems. It grows in arid zones of Uzbekistan (Bukhara, Surkhandarya, Chorezm, Kashkadarya regions, and Karakalpakstan).

Secondary metabolites of *Mausolea eriocarpa* plant aren′t studied yet. Only one fact known, that aerial parts of plant contains carotinoids. In connection with these findings we have studied compound composition of hexane and benzene extracts of aerial parts of *Mausolea eriocarpa,* gathered in stage of buds forming and bloom begin in South-Eastern Kyzylkum and South subhill plane Kuldzhuktau of Bukhara region by method of chromato-mass-spectral analysis. In hexane extract identified following compounds (compounds name, R_t in min; % of area): xylene (4.62; 24.70), nonane (4.72; 1.16), 1,2,3-trimethylbenzene (7.12; 1.83), dodecane (13.69; 1.18), 4,4,7A-trimethyl-5,6,7,7A-tetrahydro-1-benzofuran-2(4*H*)-one (24.29; 3.39), 1-butyl-2-(2-ethylhexyl)phthalate (38.09; 32.03).

In benzene extract identified: octane (3.10; 2.56), butyl acetate (3.31; 7.70), ethylcyclohexane (3.61; 3.09), 4-hydroxy-4-methyl-2-pentanone (3.75; 2.45), propylcyclohexane (5.47; 0.91), 1,2,3-trimethylbenzene (7.15; 0.89), decane (7.30; 1.39), 4,4,7A-trimethyl-5,6,7,7A-tetrahydro-1-benzofuran-2(4*H*)-one (24.29; 1.49), (–)-*trans* pinane (33.86; 11.59), isobutylpropylphthalate (38.14; 26.66).

It needs to note, that the above-mentioned compounds were identified in aerial parts of this plant for the first time.

PREBIOTIC ACTIVITY OF SOME PECTIN SUBSTANCES OF THE HIGHEST PLANTS

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The pectin substances have adsorption, antioxidant, anti-inflammatory, antitumor, hypocholesterinemic and hypolipidemic activity, as well as withdraw the heavy and radioactive metals from the body. We studied pectin substances isolated from the elevated part of plant *Ferula kuhistanica* (PS-F) from Uzbekistan and from waste products of mandarin crust (PS-C) with regard to prebiotic activity. The pectin substances were extracted by mixture of oxalic acid and ammonium oxalate in ratio 1:1 with output 8.6 and 14%, respectively. PS-F and PS-C consist of uronic acid and neutral monosaccharides: galactose, glucose, arabinose, xilose and ramnose related to the highly esterified pectins (λ – 72–90%).

The purpose of this research was to study effect of PS-F and PS-C on the growth of the associated culture from bifidobacteria and various monostrains of lacto bacilli.

The objects of study: cultures-associations from *Bifidobacterium longum* 17x and *Propionibacterium avidum* 1, *Lactobacillus bulgaricus* 906, *L. plantarum* 8-RAZ, *L.casei* 171 and *L. rhamnosus* 925 ak.

The studied substance was brought into the sterile MRS-broth achieving concentration 0.25% in the medium. 0.5 mL of studied cultures inoculum was brought on the 9.5 mL of medium in the test tube. All cultures were growing in the thermostat at 38 ± 1°C, except *Bacillus bulgaricus* – 43°C, during 24 hours in the atmosphere of nitrogen.

The effect of PS-F and PS-C on the quantity and morphology of microorganism viable cells was studied in 1 mL of culture liquid Log_{10} KOE/mL.

It was established, that the studied substances contributed to restoration of morphology of the lactobacilli from coccoforms into bacilliforms, as well as in concentration 0.25% they affected on the quantity of the viable cells.

The most stimulating effect was noted in the lactobacilli located on the plant objects, differed by the wide spectrum of the carbohydrate fermentation. There was noted increasing of growth in cultures of *L. plantarum* 8 RAZ, *L. rhamnosus* 925 ak and *L. casei* 171 for 45.8–48.7%. The percent of viable cell stimulation in *Bulgarian bacilli* on the dairies was determined about 36%. With regard to Bulgarian bacilli the restoration of bacilliform cells is the important moment. The viability of the bifidobacteria was increased for 37%. In relation to morphology, *L. plantarum* 8 RAZ culture preserves the form of cells – barrel-shaped short bacilli and *L. casei* 171 culture – small short bacilli in short and long chains.

From the data obtained it may be concluded, that the studied pectin substances provide stimulating effect on the local strains of lactobacilli and bifidobacteria. Variation in the percentage of growth increasing is associated with kind, sort, origin and strain of the culture.

CHEMICAL AND BIOLOGICAL STUDY OF *Flueggea virosa* NATIVE TO SAUDI ARABIA

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Flueggea virosa Roxb. ex Wild (*Phyllanthaceae*), also known as Chinese waterberry, is a shrub up to 4 m high growing in wild tropical Africa, Middle East, tropical Asia, Japan, Australia and Polynesia and can also be grown domestically. The plant has been used for the treatment of fever, malaria, sexual dysfunction, pain, diabetes, epilepsy, snakebites, venereal diseases, rheumatism, antiarrhythmic, contraception, rashes, diarrhea, pneumonia, cough, hepatitis and HIV-related illness. A total of fourteen compounds were isolated from the ethanolic extract of the aerial parts of *Flueggea virosa* growing in Saudi Arabia, including the cardiac antiarrhythmia constituent bergenin as the major constituent. In addition, four alkaloids namely *ent*-phyllanthidine, securinine, securinol, viroallosecurinine, two cyanogenetic glucosides menisdaurin and amiroside, four phenolic constituents rutin, gallocatechin (as a mixture), *epi*-gallocatechin, and 2,2′,5,5′-tetrahydroxybiphenyl, two ethyl monosaccharides (ethyl-α-*D*-manopyranoside and ethyl-α-*D*-glucopyranoside) and the triterpene precursor squalene. The cyanogenetic glucosides, menisdaurin and amiroside were isolated for the first time from the genus *Flueggea*, as well as from the plant family *Euphorbiaceae*. The isolation, structure elucidation and biological significance of these compounds will be discussed in this presentation.

NOVEL CYCLOARTANE GLYCOSIDE FROM *Astragalus mucidus*

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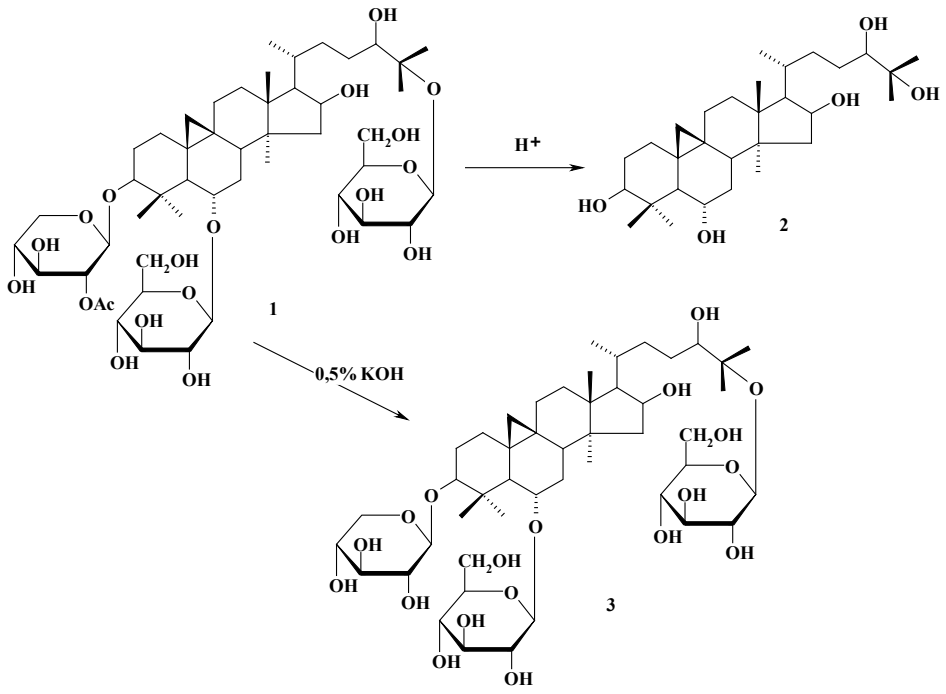
The novel cycloartane glycoside, 3-*O*-β-*D*-(2-OAc)-xylopyranoside, 6,25-di-*O*-β-*D*-glucopyranoside-24*R*-cycloartane-3β,6α,16β,24,25-pentaol named as cycloascidoside B (**1**) was isolated from above the ground part of *Astragalus mucidus* Bunge. The structure of the glycoside was established by ^{1}H and ^{13}C NMR spectroscopy and chemical methods.

The ^{1}H and ^{13}C NMR spectrum of the compound **1** showed singlet signals at δ 2.03 due to three protons and signals of carbon atoms at δ 21.19 and δ 170.07 indicating about presence of one acetyl group in the molecule.

Alkaline hydrolysis of cycloascidoside B (**1**) gives glycoside **3**, identified with cycloascidoside E (**3**).

Acidic hydrolysis of the glycoside **1** gives aglycone **2**, identified with cycloasgenine C. Anomeric protons of sugar moieties of the novel glycoside **1** were observed in ^{1}H NMR spectrum at δ 4.71 (H-1 of β-*D*-xylopyranose), δ 4.81 (H-1 of β-*D*-glycopyranose) and δ 5.08 (H-1 of β-*D*-glycopyranose) (d, ^{3}J = 7.5, ^{3}J = 7.5 and ^{3}J = 7.5 Hz appropriately).



Thus, above mentioned experimental data allowed us to conclude, that the novel cycloartane glycoside, cycloascidoside B has the structure 3-*O*-β-*D*-(2-OAc)-xylopyranoside, 6,25-di-*O*-β-*D*-glycopiranoside-24*R*-cycloartane-3β,6α,16β,24,25-pentaol.

THE ACTUAL ASPECTS OF STANDARDIZATION OF SOME PHARMACOPOEIAL PLANTS CONTAINING FLAVONOIDS

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The flavonoids are the biologically active compounds of the medicinal plants, which using as hepatoprotective, antioxidative, spasmolytic, anti-inflammatory and neurotropic preparations. In the course of our investigations there were studied the possibilities of the using of the flavonoids for purpose of the standardization of *Helichrysum arenarium* (L.) Moench., *Tanacetum vulgare* L. flowers, *Agrimonia eupatoria* L. herbs, *Ginkgo biloba* L. leaves, *Tilia cordata* Mill., *Crataegus sanguinea* Pall. flowers and fruits, *Artemisia dracunculus* L. herbs, *Matricaria chamomilla* L. flowers, *Achillea millefolium* L., *Polygonum persicaria* L. herbs, *Polygonum hydropiper* L. herbs.

In the course our investigations there were isolated for the first time from the investigated plants the predominant flavonoids pinostrobin (*Polygonum hydropiper*), polygochalcone (*Polygonum hydropiper*), persicochalcone (*Polygonum persicaria*), tilianin (*Tanacetum vulgare*), estragonoside and tarkhunoside (*Artemisia dracunculus*), which have diagnostic significance. The structural elucidation of the isolated diagnostic flavonoids was carried out by means of the UV, ^{1}H NMR spectroscopy, mass spectrometry and several chemical transformations. There was established that polygochalcone, persicochalcone, estragonoside and tarkhunoside are new natural compounds, which have the structures of 2′,6′-dihydroxy-4′,5′-dimethoxychalcone, 6′-hydroxy-2′,4′-dimethoxychalcone, 7-*O*-β-glucopyranoside of pinocembrin, and 8-*O*-α-*L*-rhamnopyranoside of annagenin respectively.

On the results of chemical investigations the methods of identification of herbal materials and preparations of above mentioned plants were developed with the using of spectrophotometry, thin layer chromatography (TLC) and high performance liquid chromatography (HPLC). On the basis of the present findings we have been motivated the use for purpose of the standardization of pinostrobin (*Polygonum hydropiper* L. herbs), isoquercitrin (*Polygonum persicaria* L. herbs), isosalipurposide (*Helichrysum arenarium* flowers), cynaroside (*Tanacetum vulgare* flowers, *Agrimonia eupatoria* herbs), hyperoside (*Crataegus sanguinea* flowers and fruits, *Tilia cordata* flowers), rutin (*Artemisia dracunculus* herbs, *Ginkgo biloba* leaves) as standard samples. The methodics of the quantitative estimation of the flavonoid contents in the corresponding herbal materials and phytopharmaceuticals of above mentioned plants were carried out by means of the UV-spectroscopy and HPLC-analysis.

There were substantiated the pathways to the standardization of *Ginkgo biloba* L. leaves and their phytopharmaceuticals, which are caused in the combined using of spectrophotometry, TLC and high HPLC. It was shown, that the predominant flavonoid for of *Ginkgo biloba* leaves is ginkgetin, which has diagnostic significance.

FLAVONOL GLYCOSIDES FROM THE FLOWERS OF *Apocynum lancefolium*

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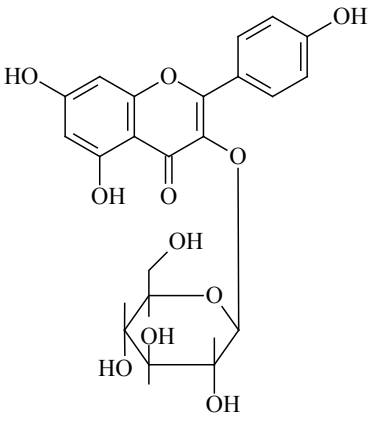
The plant *Apocynum lancefoluim* (*Apocyaceae*) is broadly distributed in Central Asia, Iran, and China.

Flowers of *A. lancefolium* long been used in folk and modern Chinese medicine as a medicinal tea. The plant extract increases blood pressure and exhibits hepatoprotective, hypolipidemic, hepatotropic, anti-oxidant, and antiviral properties.

We investigated flowers of *A. lancefolium* collected in Xinjiang Autonomous Region of the PRC. Ground air-dried raw material was extracted exhaustively with EtOH (70%) at room temperature. The *n*-BuOH extract was chromatographed over a column of silica gel with elution by $CHCl_3$–MeOH (97:3, 95:5, 90:10, 85:15). Three compounds, **1–3**, were isolated.

A comparison of spectral data (UV, IR, PMR, ^{13}C NMR) with the literature and direct comparison with authentic samples identified the isolated compounds as kaempferol-3-*O*-*D*-glucopyranoside (**1**), quercetin-3-*O*-*D*-glucopyranoside (**2**) and quercetin3-*O*-*D*-rhamnoside-glucopyranoside (**3**).

The listed compounds were isolated for the first time from *A. lancefolium*



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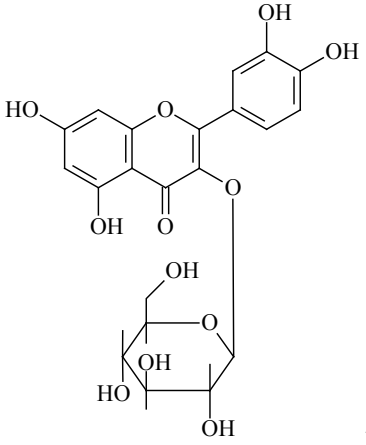

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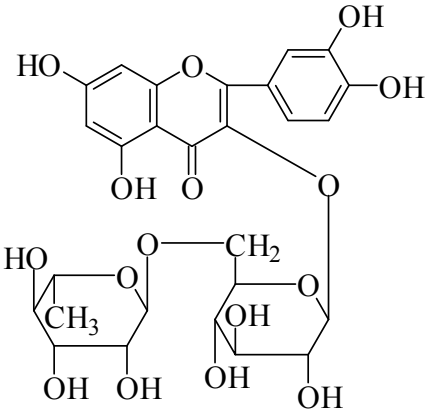

3

ANTIPROLIFERATIVE EFFECTS OF ISOFLAVONES EXTRACTED FROM CHICKPEA SPROUTS THROUGH APOPTOSIS ON HUMAN BREAST CANCER CELLS

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Breast cancer is one of the most common malignancies affecting western women, whereas Asian women, who consume isoflavone-rich diets frequently, have a relatively low incidence. Isoflavone has been proposed as the agent responsible for lowering the rate of breast cancer in Asian women. Chickpea is a traditional Uighur herb, has been found to have considerable quantities of isoflavones in its sprouts. In Zhao′s recent study, eight isoflavone components, including biochanin A, formononetin, genistein, calycosin, biochanin A-7-*O*-β-*D*-glucoside, trifolirhizin, ononin, and sissotrin, were isolated from sprouted *Cicer arietinum* L. seeds using reverse chromatography separation. However, there have been no specific reports of the antiproliferative effects of ICS on human breast cancer cells and the precise molecular mechanism of the ICS-induced apoptosis is unclear.

In this work, which incorporated several *in vitro* bioassays methods, we systematically investigated the effects of ICS on breast cancer cells viability, and explored its underlying mechanism in the human breast cancer cells SKBr3 and MCF-7. MTT assay showed that ICS at the concentration ranges (10–60 mg/L) significantly inhibited the proliferation of both cell lines in time- and dose-dependent manners. Flow cytometric analysis showed that ICS led to the significant accumulation of small DNA fragments which are often found to be apoptotic cells, in the sub-G1 phase of SKBr3 and MCF-7 cell lines. Wright-Giemsa staining and Annexin V-FITC staining showed that exposion to the ICS, cytoclasis and apoptosis bodies could be found under light microscopy and fluorescent microscopy. Furthermore, the quantitative Annexin V-FITC assay showed that the number of apoptotic cells significantly increased in a dose-dependent manner of ICS. Then semi-quantitative RT-PCR analysis showed that ICS caused an increase of the gene bax expression, as well as a decrease the gene bcl-2 expression.

Our current study is the first to demonstrate that ICS significantly inhibits the growth of SKBr3 and MCF-7 breast cancer cells, regulates the expression of apoptosis-related genes and proteins, and induces apoptosis via the mitochondrial-dependent pathway. These results suggest that ICS may be a potentially effective chemopreventive or therapeutic agent against breast cancer.

Acknowledgment. This work was supported by the Projects of National Natural Science Foundation of China (Grant No. U1203203).

ISOLATION OF FLAVONOIDS FROM *Apocynum venetum* L.

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Apocynum venetum L. belongs to the perennial herb of *Apocynaceae*, which leaves are commonly used to make tea in China. Moreover, its leaves have been used in Chinese medicine for treatment of hypertensive, hepatoprotective and anxiety and depress [1–3], and the main active ingredients are flavonoids. In our study, six compounds are isolated from the leaves of *Apocynum venetum* L. The dry raw material was refluxed with EtOH, worked up successively with petroleum ether, EtOAc, and *n*-BuOH. Six compounds were isolated from the EtOAc extract, and identified by spectral data (^{1}H, ^{13}C NMR), the compounds are as follows, isoquercetin (**1**), rutin (**2**), scopoletin (**3**), astragalin (**4**), kaempferol (**5**), quercetin (**6**). The compounds (**1**, **2**, **4**, **5**, 6) are flavonoids, however, scopoletin (**3**) is coumarins.

Ackowledgment. Thanks for financial support of the High Tech Research and Development Program of Xinjiang (Grand No. 201315108) and XTIPC Postdoctoral Foundation (Y25P941401).

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GC-MS ANALYSIS OF PHYTOCOMPONENTS THE FLOWERS OF *Apocynum lancefolium*

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The presence of diverse secondary metabolites has been reported from species of the genus *Aposynum*. However, there has been not much information available on phytochemical components of *Apocynum lancefolium.* This investigation was carried out to determine the possible chemical components from *A. lancefolium* (*Apocyaceae*) collected in Xinjiang Autonomous Region of the PRC by GC-MS.

We extracted the flowers of *A. lancefolium* with benzine and investigated by GC-MS. In benzine extract identified following compounds (compounds name, R_t min., % of area): phenol, 2,2′-methylenebis[6-(1,1-dimethylethyl)-4-methyl (22.34; 3.14), 1,2-benzenedicarboxylic acid, diisooctyl ester (23.49; 4.63), behenic alcohol (30.73; 26.24), 1-heptacosanol (32.92; 28.73), lupeol (34.34; 31.44).

After benzine extract, *A. lancefolium* was extracted exhaustively with EtOH (70%), the solvent was vacuum distilled. The dry solid was worked up successively with hexane, $CHCl_3$, EtOAc and *n*-BuOH.

The hexane fraction investigated by GC-MS too. In hexane fraction identified following compounds (compounds name, R_t min., % of area): dimethyl phthalate (12.61; 1.30), ethanone, 1-(4-hydroxy-3-methoxyphenyl) (13.03; 2.70); *n*-hexadecanoic acid (18.15; 74.70), phthalic acid, butyl tridecyl ester (18.23; 12.00), phenol, 2,2′-methylenebis[6-(1,1-dimethylethyl)-4-methyl (22.33; 2.00), 1,2-benzenedicarboxylic acid, diisooctyl ester (23.48; 2.00).

From the results, it is evident that *A. lancifolium* contains various bioactive compounds and these compounds were identified for the first time from the flowers of *A. lancifolium*.

Acknowledgment. This work was supported by the Projects of International Cooperation and Exchanges of the National Natural Science Foundation of China (Grant No. 31110103908), the Projects of International Science & Techology Cooperation of the Xinjiang Uygur Autonomous Region (Grant No. 20126023), and the Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

CHEMICAL COMPONENTSTHE FLOWERS OF *Apocynum venetum*

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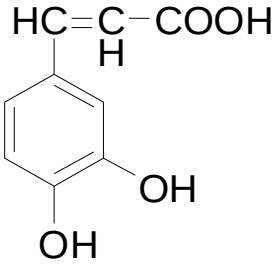
In continuation of research on chemical components the flowers of *Apocynum venetum* (*Apocyaceae*) [1] collected in Xinjiang Autonomous Region of the PRC, which widely used in folk and modern Chinese medicine as a medicinal tea. We isolated two compounds from neutral fraction.

$C_9H_8O_4$, mp 222–224°C (**1**), $C_9H_6O_4$, mp 268–270°C (**2**).

A comparison of spectral data (UV, IR, PMR, ^{13}C NMR, HSQC, HMBC) with the literature identified the isolated compounds as caffeic acid (**1**), and esculetin (**2)**.



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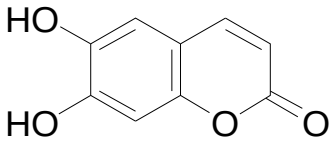

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The caffeic acid and esculetin were isolated for the first time from genus *Apocynum.*

Acknowledgment. Thanks for Academy of Sciences “Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences”.

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ALKALOIDS OF *Fritillaria pallidiflora*

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Fritillaria pallidiflora Schrenk belongs to the *Fritillaria* genus of *Liliaceae* family, which is mainly distributed in Xinjiang Province of China. The important alkaloids are the steroidal alkaloids. The bulbs of *F. pallidiflora* have been used to as antitussive, antiasthmatic and expectorant medicine for more than two thousands of years in antitr anditional Chinese medicine. This paper describes the isolation and structure of two alkaloids that were first found in the plant, verticinnone-3-*D*-glucoside (**1**) and daucos erol (**2**) together with two known steroidal alkaloids, imperialine (**3**) and imperialine-3-*D*-glucoside (**4**).

Acknowledgment. Thanks for financial support by the National Natural Science Funds of China (No. 31110103908) and Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

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FLAVONOIDS OF *Hippophae rhamnoides* L. subsp. *turkestanica* FRUITS

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As a subspecies of sea buckthorn, *H. rhamnoides* L. subsp. *turkestanica* is a deciduous shrub and grown widely throughout many regions of central Asian (Xinjiang of China, northwest of Indian, Pakistan, Uzbekistan, etc.) [1]. The fruit of *H. rhamnoides* L. subsp. *turkestanica* has been used as traditional therapies for reliving cough, aiding digestion and treating wounds over centuries [2]. From the methanol fraction of *H. rhamnoides* L. subsp. *turkestanica* fruit, we have isolated eleven flavonoids. Their structures were elucidated as isorhamnetin (**1**), kaempferol (**2**), isorhamnetin-3-*O*-rutinoside (**3**), rutin (**4**), isorhamnetin-3-*O*-β-*D*-glucopyranoside (**5**), quercetin-3-*O*-β-*D*-glucopyranoside (**6**), quercetin-7-*O*-β-*D*-glucopyranoside (**7**), isorhamnetin-3-*O*-β-*D*-glucopyranoide-7-*O*-α-*L*-rhamnoside (**8**), Isorhamnetin-3-*O*-β-*D*-sophoroside-7-*O*-α-*L*-rhamnoside (**9**), quercetin-3-*O*-β-*D*-sophoroside-7-*O*-α-*L*-rhamnoside (**10**), quercetin-3-O-α-*L*-rhamnoside-(1→2)-[α-*L*-rhamnoside-(1→6)]-β-*D*-glucopyranoide (**11**). Compounds **6**–**11** were firstly isolated from this plant.

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RESEARCH ON ALLELIC CHARACTERS OF *CAO* GENE WITH *CBN1* MUTANT GENE AND ONLY KEY GENE CHARACTERS OF *CAO* GENE IN CHLOROPHYLL b SYNTHESIS PATHWAYS

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Currently, in the field of genetic control of photosynthetic pigment biosynthesis, it is still uncertain that whether the *Chlamydomonas reinhardtii cbn1* (chlorophyll b and neoxanthin deficiency) mutant gene and *cao* (chlorophyllide a oxygenase) mutant gene are allelic genes, where are their molecular mapping and is there other pathway to synthesize or regulate chlorophyll b.Thereby it needs to be further investigate.This paper reports on the research work in this regard.

Plasmid Psp109-E8 with *CAO* was transformed into *Chlamydomonas cbnl-48 mt+* mutant strain by electroporation, recovery expression of chlorophyll b was detected, which verified primarily that *cbn1* and *cao* without the ability of chlorophyll b synthesis both possess allelic characters; Mutant strains, 1641-1b (*cbn1-43 mt+*) and CC-1354 (*cbn1-48 mt+*), were taken to mate with segregants of mutant strain CBS5-c1 (*cao5 mt-*) and CBS5-c5(*cao5 mt-*), 1842 meiotoc segregants were obtained by random cell mating but no wild type segregants was found .This proved the closely linkage between mutant gene *cbn1* and *cao*. And among the 50 segregants obtained by cell mating tetrad analysis no wild type segregants was detected, which further verified the allelic characters of mutant gene; Design two probes according to *CAO* sequence, and carry out DNA dot blot with 21 BAC clones between the two molecular markers, GBP1 and RB47, on *Chalamydomonas* linkage group I. The experimental result showed that two probes possess the homology region with 21th BAC clones (BAC number: 33e2). This result proved that *CAO* exactly locates at cbn1 loci. Data obtained in experiments for progeny random analysis prove the closely linkage between the mutant genes, *cbn1* and *cao*. Experimental results of genetic tranformation prove that mutant genes, *cbn1* and *cao* possess allelic character. Experimental results of DNA dot blot analysis proved that the genetic loci of *CAO* is near cbn1 and in the fragment region of 33e2 BAC clone which is between the two molecular markers, GBP1 and RB47.

Roundness xenon lamp with 500w was used in this experiment. Glaucous light wave of 475, which can be filtered by GBI2 cyanine impeditive filter and JB450 yellow impeditive filter, was used in respect that lamp-house of 475nm is absorbed only by chlorophyll b. Experiment results revealed that, among the *Chlamydomonas reinhardtii* which are photosynthetic cultivated in L_2 min solid medium, only wild type strain CC-124 and CC-125 were grown tardily while inserted deficient mutants CBS3 (*cao3*) and CBS1 (*cao1*) were not grown. It can be easily seen that there is not anyother pathway which can resume the ability of chlorophyll b biosynthesis while *CAO* gene is inserted deficient mutant. Experiment results mentioned above further proved the viewpoint that all the mutant genes that lost chlorophyll b biosynthesis ability of *Chlamydomonas reinhardtii* are allelic genes, and *CAO* (*CBN1*) gene is the only main control gene.

Acknowledgment. We thank professor Ayumi Tanaka for providing some mutants and plasmid to us for this research. We also are grateful to Dr. E.Harris for her supporting and for her suggestion.

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FATTY OIL ANALYSIS OF SWEET POMEGRANATE AND SOUR POMEGRANATE BY SUPERCRITICAL CO_2 EXTRACTION AND GC-MS

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Pomegranate seeds are the seed nucleus of *Punica granatum* L., pomegranate seed nucleus contain about 50 % oil, in which punicic acid have a high content. Pomegranate seeds are believed to have antioxidant activity and against human breast cancer, which can be used to prevent and treat heart diseases that result from breast cancer and arteriosclerosis and delay the decrepitude of human body [1–4]. Pomegranate is widely planted in Kashgar (sour megranate) and Khotan (sweet megranate) of Xinjiang, The research about pomegranate seeds oil will provide a basis for further development and utilization Xinjiang pomegranate resources.

In this study, supercritical CO_2 extraction was applied to extract seed oil with sour megranate seeds and sweet megranate seeds as raw material. The fatty acid compositions of the two megranate seeds oil were determined and compared by gas chromatography-mass spectrometry (GC-MS). The results showed that the sour megranate seeds oil contained 12 fatty acids, among them, punicic acid (50.95%), linolenic acid (27.09%) and linoleic acid (7.71%) were the most abundant unsaturated fatty acids. There are 8 kinds of fatty acids in sweet megranate seeds oil and punicic acid is the main component which covers 72.86% of total, the other unsaturated fatty acids are linoleic acid (10.51%), oleic acid (7.94%) and linolenic acid (1.99). Punicic acid and linolenic acid are main active compounds in Pomegranate seeds, there are major difference in punicic acid and linolenic acid of the two Pomegranate seeds oil, so great attention should be paid to the activity in pomegranate seed oil from the different origin.

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SESQUITERPENES FROM *Vernonia anthelmintica*

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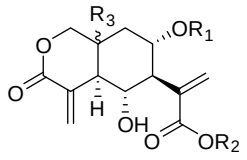
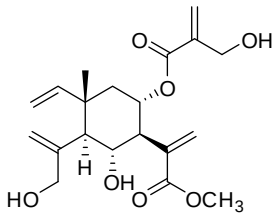
Vernonia anthelmintica (L.) Willd., distributes in India, Pakistan and South Xinjiang of China. *V. anthelmintica* seed, the major component of many anti-vitiligo pharmacons, was traditional herb medicine used for treatment of vitiligo by Uyghur physicians for thousands of years. *V. anthelmintica* belonging to Asteraceae have been shown to produce various types of sesquiterpene lactones, such as eudesmanolides [1], germacranolides [2], guaianolides [3], and elemanolides [4].

In the previous study of our team, two novel elemanolide dimers, vernodalidimera A and B [5] were isolated from *V. anthelmintica.* As a follow-up study, four sesquiterpenes lasiopulide [6] (**1**), vernodalinol [7] (**2**), epivernodalol [6] (**3**), and elemacarmanin [8] (**4**) were isolated and purified by silica gel, ODS, sephadex LH-20 column chromatographied, preparative HPLC and recrystallization from the seed of *V. anthelmintica*. Their structures were elucidated by 1D and 2D NMR data. Compounds **1**, **2**, and **3** were isolated from this plant for the first time, and **4** was isolated from genus *Vernonia* for the first time.



	R_1	R_2	R_3
1	H	CH_3	β-CH=CH_2
2	CO(C=CH_2)CH_2OH	H	α-CH=CH_2
3	CO(C=CH_2)CH_2OH	CH_3	β-CH=CH_2



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STUDY ON THE ANTHRAQUINONE CONSTITUENTS FROM *Eremurus anisopterus*

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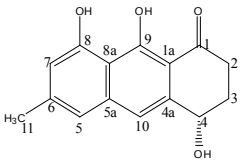
The genus *Eremurus* (*Liliaceae*), comprising nearly 50 species, is mainly restricted to central and western Asia, and four species are known to occur in the People's Republic of China. *Eremurus anisopterus* (Kar. et Kir.) Regel has a wide distribution in the western part of China, and it has been used in Chinese folk medicine for the treatment of rheumatism and physical weakness. In the course of our studies, three anthraquinones: chrysophanol [1] (**1**), chrysophanol 8-methyl ether [2] (**2**), aloesaponol [3] (**3**) were isolated from the whole plants. Their structures were elucidated by MS, 1D and 2D NMR techniques. All of the two compounds were isolated for the first time from *Eremurus anisopterus* (Kar. et Kir.) Regel.



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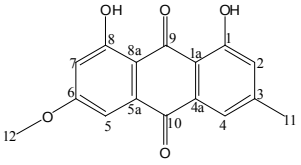

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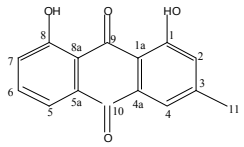

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PREPARATIVE SEPARATION OF ALKALOIDS FROM KURSI CAPER USING pH-ZONE-REFINING COUNTER-CURRENT CHROMATOGRAPHY

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Kursi Caper, a herbal formulation of Uyghur traditional medicine, is used by local people in the Xinjiang Uyghur Autonomous region of China for the treatment of rheumatism, arthritis, and gout. Total alkaloid is the active ingredient of Kursi Caper. However, methods currently used to separate alkaloids are time-consuming and have low recovery.

In the present study, we used pH-zone-refining counter-current chromatography to separate major alkaloids from a crude extract of Kursi Caper. The two-phase solvent system was methyl tertbutyl ether (MtBE)–acetonitrile–water (3:3:2, *v*/*v*). Triethylamine (10 mM) was added to the upper organic stationary phase as a retainer. Hydrochloricacid (5 mM) was added to the lower aqueous phase as an eluter.

From 1.0 g of crude extract, we obtained 304 mg harmine, 41 mg harmaline and 197 mg γ-harmine, respectively.

Structure of alkaloids have been established on the basis of it is physical and chemical properties and the analysis of it is spectral data UV, ^{1}H, ^{13}C NMR, DEPT, COSY, HMBC, NOESY.

These results demonstrated that pH-zone-refining counter-current chromatography is an effective method to separate and purify major alkaloids from Kursi Caper.

Ackowledgment. This work was supported by the Projects of International Cooperation and Exchanges of the National Natural Science Foundation of China (Grant No. 31110103908), the Projects of International Science & Techology Cooperation of the Xinjiang Uygur Autonomous Region (Grant No. 20126023).

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SYNTHESIS AND ANTICANCER ACTIVITY OF MONOCYCLIC β-LACTAMS AND 4-THIAZOLIDINONES DERIVATIVES CONTAINING ACRIDINYL

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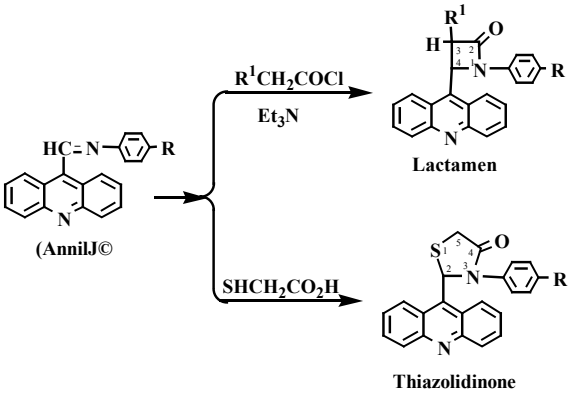
The monocylic β-lactams derivatives were synthesized through [2+2] cycloaddition reaction of the *N*-(*p*-substitutedaryl)-*C*-(9-acridinyl)formaldimines Schiff base with chloroacetyl chloride and benzyloxyacetyl chlorides ketenes in presence of triethylamine to yield 1-aryl-3-substituted-4-(9-acridinyl)azetidin-2-one derivatives **I**–**VI**, respectively. 4-Thiazolidinones derivatives were synthesized through cyclocondensation reaction of the *N*-(*p*-substitutedaryl)-*C*-(9-acridinyl)-formaldimines Schiff base with mercaptoacetic acid to yield 2-(9-acridinyl)-3-aryl-1,3-thiazolidin-4-one derivatives **VII–IX**, respectively. All the compounds were identified by UV, ^{1}H NMR, IR spectra and elemental analysis. The preliminary bioassay on the compounds showed that some compounds possess in *vitro* anticancer activity and the leukocyte common antigen activity to a different extent. The compound **IV** showed Leucocythemia activities against Human HL-60 inhibitory activity of 79.4%, at the test concentration of 10 μmol/L.

The compounds **V**, **VI** and **IX** showed Cdc25B phosphatase inhibitory activity of 80.64%, 99.75% and 99.34%, respectively at the test concentration of 20 μg/mL. The compounds **VI** and **IX** showed an inhibitory activity of 86.12% and 91.03% on CD45 protein tyrosine phosphatase A, respectively, at the test concentration of 20 μmol/mL. The rest of the compounds have growth inhibition rate (IC_{50} value) less than 50% to the Cdc25B (or Cdc25A) enzyme, the CD45 protein tyrosine phosphatase A and HL-60 cell line On this basis of these result, a preliminary discussion of the structure-activity relationship of these compounds were proposed.



Lactamen	R	R^1
ўс	$N(CH_3)_2$	Cl
ўт	$N(CH_3)_2$	OBn
ўу	$N(C_2H_5)_2$	Cl
ўф	$N(C_2H_5)_2$	OBn
ўх	OH	Cl
ўц	OH	OBn

Thiazolidinone	R
ўч	$N(CH_3)_2$
ўш	$N(C_2H_5)_2$
ўщ	OH

Scheme 1

This work was supported by the China National Natural Science Foundation (Grant No. 21062019) and Natural Science Foundation of Xinjiang Uyghur Autonomous Region (Grant No. 200421126)

STUDY ON THE DITERPENOID ALKALOIDS CONSTITUENTS FROM *Delphinium tianshanicum*

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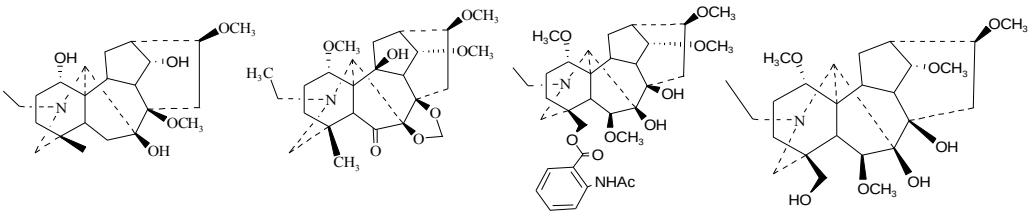
Diterpenoid alkaloids are a large group of natural compounds with diverse structural types and biological activities. Plants of the genus *Delphinium* are the main source of diterpenoid alkaloids and include more then 300 species in the world. Among them, more than 130 species grow in China and about 27 species grow in Xinjiang. These plants are widely used in folk medicine as an anesthetic, analgesic, anti-inflammatory, a sedative and to treat rheumatism and toothache [1].

We have investigated the alkaloids composition of *Delphinium tianshanicum* W.T.Wang (*Ranunculaceae*) growing in Tien Shan mountain of Xinjiang Province of China [2]. In the course of our studies, four norditerpenoid alkaloids: dehydroeldelidine (**1**), ajacine (**2**), lycoctonine (**3**), blacknidine (**4**), were isolated from the aerial parts of *Delphinium tianshanicum* W.T.Wang. MS, 1D and 2D NMR techniques elucidated their structures. All of the four compounds were isolated for the first time from the *Delphinium tianshanicum* W.T.Wang.



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STUDY ON CHEMICAL CONSTITUENTS AND EXTRACTION TECHNIQUE OF *Salix caprea* OF XINJIANG

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Salix caprea of Xinjaing is widely distributed in the Xinjiang Uygur Autonomous region of China. This medicinal herb has physiological activities such as anti-free radical, antioxidant, antivirus, anti-tumor, and invigoration of eyes, abirritation. Response Surface Method (RSM) was applied to optimize the extracting condition for total flavonoids from Salix caprea by supersonic wave. The optimum processes for supersonic extraction were 63.88% ethanol, 21.45 min supersonic time, 1:35.94 mass-liquid ratios. And we had studied on its chemical compounds of Salix caprea.

Salix caprea flowers was extracted with alcohol (70%), and distributed by petroleum ether, ether acetate, *n*-buthanol, respectively.

Isolated and purified via silica gel column chromatography, Sephadex LH-20, HPLC. Then, 12 compounds were isolated and 9 compounds were identified as: β-sitosterol, (+)-catechin, quercetin, kaempferol-3-*O*-β-*D*-glucoside, apigenin-7-*O*-β-*D*-glucoside,3′-methoxyl-kaempferol-7-*O*-β-*D*-glucoside, luteolin-7-*O*-β-*D*-glucoside (isorhamnetin-3-*O*-α-*L*-rhamnosyl-(1→6)-β-*D*-glucoside), rutin.

FOOD ADDITIVES AND SAFETY OF PRODUCTION OF PLANT ORIGIN

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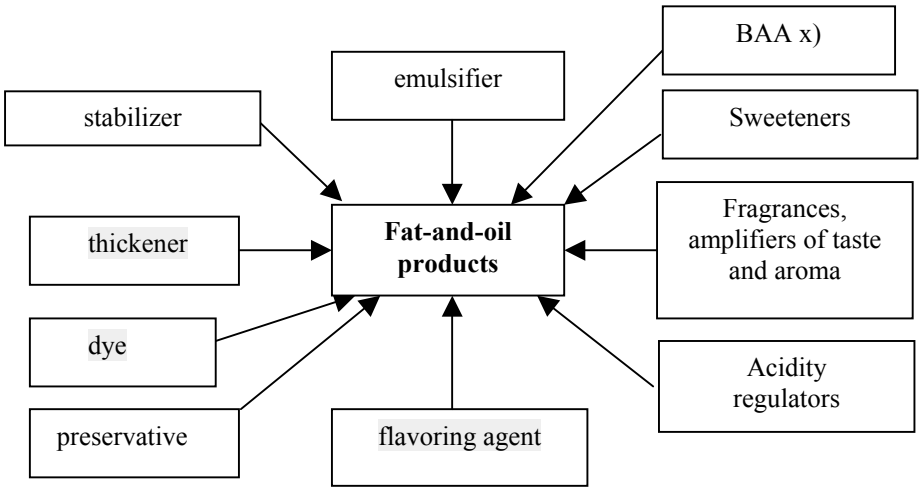
For production of the flavored refined salad oil the cotton oil, food and biologically active components are used as the main raw materials. In researches cotton oil with various physical and chemical indicators and fatty acid structure is used. Food additives and biologically active agents used for production of fat-and-oil products, it is possible to present in the following scheme:



Addition of new types of fragrances and enrichment of vegetable oils by vitamins was made under production conditions in technology of deodorization, fractionation and crystallization of vegetable oil.

Type of fragrance	Type of oil, quantity of additive, kg/t							
	Refined deodorized, flavored	Salad deodorized, flavored	Acid number, mg/KOH/g		Chromaticity, J_2%		Humidity, %	
			Experiment	GOST	Experiment	GOST	Experiment	GOST
With an olive smell	0.15-0.35	0.15-0.35	0.10	0.30	2	6	0.010	0.017
With a laurels smell	0.05-0.10	0.05-0.10	0.12	0.30	3	7	0.011	0.017
With a basil smell	0.15-0.30	0.15-0.30	0.12	0.30	3	7	0.011	0.017
With a rosemary smell	0.15-0.30	0.15-0.30	0.10	0.30	4	8	0.011	0.017

Additive of different types of fragrances along with improvement of flavoring properties of samples of the refined, deodorized and salad cotton oil are characterized by high quality indicators and physical and chemical data (see the Table). It testifies their high nutrition and physiological value. The received samples of the refined and deodorized cotton oil were rationally and effectively used for production of fat-and-oil products.

FEATURES OF THE MICROWAVE OVEN FOR DRYING OF PREPARATIONS

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Due to lack of the control of microwave energy flow the drying of materials may be not well, and sometimes dried materials are overheating or charring.

One of the features of microwave energy supply is the difficulty of changing the microwave field amplitude, so the implementation of products drying can use a discrete mode of power supply.

By formalizing of the computer model of the materials drying process and experiments on laboratory and computer model, we have developed a program for discrete control of microwave heat supply.

For this purpose, we have developed a computer model of the materials drying. Analysis of incorporating automation elements shows the desirability of using the relay mechanisms. On the basis of the computer model automatic control system of the drying process using the relay technique was investigated. The computer model of the system is made on the basis of the applied program MATLAB.

By conducting of experiments in the laboratory physical model on preparations drying conditions were determined. Each drug may be limited by the extent of the heat. The results of the experiments of material drying at a maximum temperature are shown in Fig. 1.

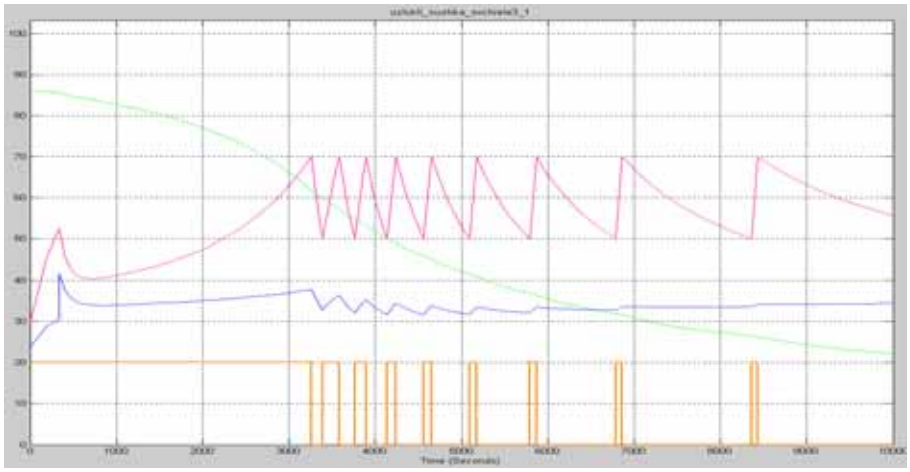

Fig. 1. Results of the experimental on materials drying. Enable and disable the microwave heat-lower curve, the change in temperature of the material (red line) and the change in the equilibrium temperature (blue), and changing moisture of the material (green).

On the basis of the obtained results the device for microwave drying of moist material is developed.

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THE COMPARATIVE STUDY ON ACONITINE FROM *Aconitum karacolicum,* ITS PURIFICATION AND STABILITY BY HPLC

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For many centuries *Aconitum* plants (*Ranunculaceae*) have been known for their biological activity. *Aconitum* alkaloids have been used as the poison, the toxicity is mainly due to C_{19}-norditerpenoid alkaloids such as aconitine, a diterpenoid alkaloid. In addition, *Aconitum* roots are used in Chinese medicine for their anti-inflammatory and analgesic effects that are also partly attributed to aconitine. Currently, two main topics about aconites are investigated: i) the development of aconite-based treatments monitored by chromatographic techniques in order to avoid the poisoning of the patients, and ii) the identification of new aconites derivatives that present the same pharmacological activity without the toxicity, such as lipo-alkaloids or C_{20}-diterpenoids. These molecules have been either found in *Aconitum* plants, but frequently in low quantity, or synthesized from natural aconites. Indeed, due to the complex structure of this molecule, the total synthesis of a large quantity of aconites has never been achieved. Such studies present a real interest, but require a prior access to a large quantity of aconitine or derivatives. The *Aconitum* genus gathers more than 100 species. *Aconitum karacolicum* species grow on the north of Kirghiz Republic (Alatau area). Different aconites were identified in this plant, including aconitine at a rate of 0.8–1%. In this poster, we have report the purification of aconitine from *Aconitum karacolicum* extract using several chromatographic methods and the study of aconitine stability in analytical solvents.

COUMARINS FROM *Pulicaria gnaphaloides*

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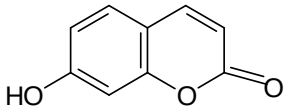
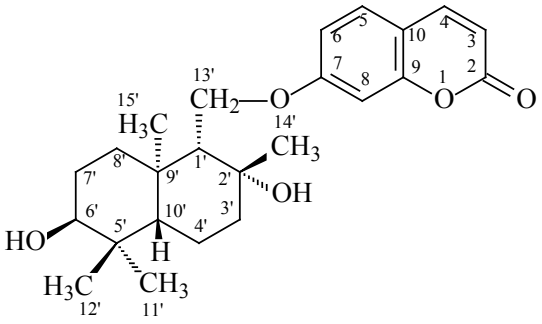
Perennial grassy plants of *Pulicaria* genus (*Compositae* family) widely distributed in the Central Asia and are the rich source of terpenoids and flavonoids.

We have studied the chemical composition of aerial part of *Pulicaria gnaphalodes* Boiss grows in the Samarkand region of Uzbekistan in flowering period. *P. gnaphalodes* used in traditional and non traditional medicine as antifugal activity. It contains carbohydrates, essential oils, organic acids, alkaloids, coumarins, tannin, diterpenoids, flavonoids.

Extracts of *P. gnaphalodes* possess by strongly pronounced antihyperglycemic and hypolipidemic activity.

We have isolated two compounds from butanol fraction by column chromatography. Structures of isolated compounds have been established on the basis of their physical and chemical properties and the analysis of their spectral data IR, UV, ^{1}H, ^{13}C NMR, DEPT. HMBC, COSY, HSQC. The isolated compounds have been identified as umbelliferon $C_9H_6O_3$, mp 222–224°C (**1**) and feshurin, $C_{24}H_{32}O_5$, mp 214–216°C (**2**).





These compounds have been isolated from *genus Pulicaria* for the first time.

TERPENOID COUMARIN FROM *Ferula ovina*

H. Sh. Kamoldinov[1], K. A. Eshbakova[1], Kh. M. Bobakulov[1], A. Yili[2], H. A. Aisa[2], N. D. Abdullaev[1]

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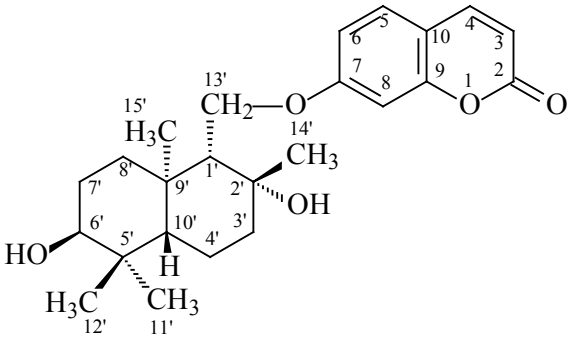
Perennial herbs *Ferula* L. (*Apiaceae* family), including 150 species, are widely distributed in the world. The Flora of the Central Asia includes about 100 species, widely used in the folk medicine as anticancer, antimicrobic, against various diseases and estrogen means. The coumarins, flavonoids and sesquterpenoids were isolated from genus *Ferula*.

Ferula ovina (Boiss) – a perennial herbaceous plant grows on 50–120 cm gravelly slopes, scree, rocks, in bushes, mountain steppes up to 3000 m above sea level. Previously essential oil and sesquterpens were isolated from this plant.

We have studied the roots of *Ferula ovina*, collected during the flowering period in Surkhandarya region of Uzbekistan. From the alcoholic extract by column chromatography on silicagel, eluting with hexane–ethyl acetate a new terpenoid coumarin isolated and identified as feshurine. $C_{24}H_{32}O_5$, mp 216.4°C.

Structure of **1** have been established on the basis of its physical and chemical properties and the analysis of spectral data IR, UV, ^{1}H, ^{13}C NMR, DEPT, COSY, HMBC, NOESY and X-rays.



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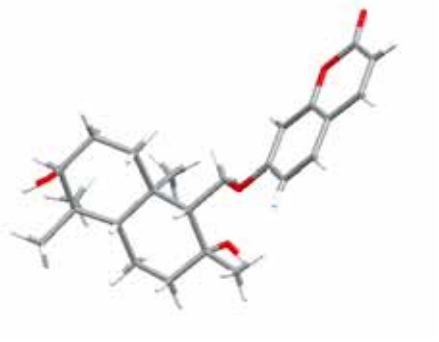

FLAVONOIDS FROM *Inula caspica*

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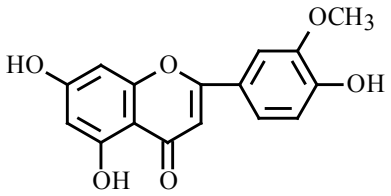
Genus *Inula* (*Asteraceae* family) – one-, two- or perennial herbs, including 100 species, widely distributed in the world. The flora of Uzbekistan includes about 9 species and used in the folk medicine as anticancer, antimicrobic, antibacterial, neurosis, epilepsy, gastritis, diabetes, in gynecology and others diseases.

It flowers in July and August. It grows in saline, brackish, swampy areas, meadows, riparian forests, sometimes a weed, to the middle mountain zone. The roots are used for therapeutic purposes. Carbohydrates and inulin derivative, essential oil, alkaloids in founded the roots, in the aerial parts of the plant – rubber alkaloids. A decoction of the roots is used as an expectorant.

We have study the chemical composition of aerial part of *Inula caspica* grows in the Namangan region of Uzbekistan, in flowering time, and isolated by chromatographic method two compounds from ethylacetate fraction.

Structures **1** and **2** have been established on the basis of their physical and chemical properties and analysis of spectral data IR, UV), ^{1}H, ^{13}C NMR. The compounds were identified as 5,7,4′-trihydroxy-3′-methoxyflavone (chrysoeriol) (**1**) and 5,7,3′,4′-tetrahydroxy-flavone (luteolin) (**2**).



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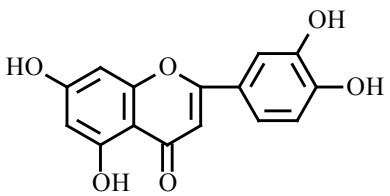

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These compounds have been isolated from *genus Inula* for the first time.

RESEARCH OF THE BIOLOGICAL ACTIVITY OF NATURAL COUMARIN SYNTHESIZED ANALOGS AND DERIVATIVES WITH HETARYL FRAGMENTS

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We synthesized the novel derivatives of coumarin and some 3-heteroaryl-coumarins [1–3] studied *in vitro* for antimycobacterial activity against M. tuberculosis strains $H_{37}Rv$ (Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF), Southern Research Institute, USA) in comparison with rifampicin as standard (effective dose of 6.25 mkg/mL).

The study of TB activity of coumarins derived from a series of aromatic aldehydes, indicates some promising research in this direction. So, out of the 3-heteroaryl-coumarin compound with 1,5-benzodioxypan fragment showed 86% of TB activity. Its bromine-substituted coumarin led to a sharp diminishing of TB activity (29%). Unsubstituted coumarin with 1,3-benzodiooxol fragment shows TB activity by 76%, while the compound with 1,4-benzodioxan fragment (49%). Substituted compounds with 1,4-benzodioxan fragment display low activity (from 36 to 13%).

It should be noted, that the unsubstituted coumarin with 1,5-benzodioxan fragment is more active, than 1,3-benzodioxol and 1,4-benzodioxan fragments, and less active in the studied dose, than control rifampicin (90–95%). Substituted coumarins are less active. Changing the nature of the substituents does not increase the value of efficiency. Apparently, in this case, in the manifestation of high-TB activity (86%) a big role plays the hetaryl fragment 1,5-benzodioxypan interaction to the membrane surface of the tubercle bacillus of Koch.

Thus, the study of the biological activity of synthetic analogues of natural coumarins has shown that they exhibit a significant pharmacological effect. It indicates the perspectives of biologically active compounds search among analogues of coumarines.

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EFFECTS OF PROLINE ON CARDIOSPECIFIC ENZYMES ACTIVITY IN THE BLOOD SERUM IN EXPERIMENTAL ACUTE MYOCARDIAL INFARCTION

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It is known that the necrotic lesion in myocardium during its infarction is replaced by connective tissue. One of the main components of connective tissue is the amino acid proline and its oxidized derivative hydroxyproline. In this connection, there was interesting the effect of proline injection on the rate of substitution of necrotic lesion by connective tissue in the myocardium after infarction. Intensity of the experimental myocardial infarction (EMI) is proportional to the cardiomyocytes specific enzymes activity – creatine kinase–MB (CK-MB), lactate dehydrogenase (LDG) and aspartate aminotransferase (AsAT) in the blood serum.

The experiments were conducted on 15 male rabbits of 2.6–3.0 kg weight. EMI was induced by ligation of the descending branch of the left coronary artery. After the ligation two rabbits died, one of them in one hour after ligation, and the second one after 3 hours. The mortality rate was 27%. Immediately after the ligation proline (product of Vitaline, USA) was administered orally though gavage to six rabbits it was in dose 30 mg/kg. Then every day animals received proline orally at the indicated dose. Five animals were included to the control group. The blood from the ear vein of the animals was taken into heparinized tubes in 30 min, 1, 3, 6, 12 hours and 1, 3 and 7 days of EMI dynamics. The activity of cardiac enzymes in the blood was determined by autoanalyzer "Daytona" Randox (UK). Digital data were processed statistically.

The results showed that the proline at early stages of disease (30 min, 1, 3, 6, 12 and 24 h) did not significantly affected on the dynamics of CK-MB activity, but after 48 hours, the absolute values of CK-MB activity were slightly lower in compare to the control. The study of LDG showed that the introduction of proline to rabbits with EMI increased ones till 3 days of the disease almost at the level of the control group. On the 3rd day the absolute values of LDG activity was slightly lower than the control, and the 7th day – it was significantly lower in compare to the control on 33.4%. In the activity of AsAT no significant changes in compare to the control were identified.

Thus, the studies have shown that proline in dose 30 mg/kg did not significantly affect to the dynamics of cardiac enzyme activity at an early stage of myocardial infarction. In the later stages (3 and 7 days of the disease) there is a positive influence of proline for EMI repair.

The work was carried out under the applied grant No.30.3 “Development of a method for enhancing the healing of necrotic myocardial lesions in the experiment” of the Ministry of Health of the Republic of Uzbekistan.

THE ENZYMATIC ISOLATION OF PECTIN SUBSTANCES FROM SUNFLOWER (*Heliantus annuus* L.) BASKETS

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Obtaining of food pectins from food industry wastes is a cheap and considers actually problems in food industry. *Heliantus annuus* L. of *Asteraceae* family (sunflower baskets) after seed seeds removal is a good source of pectin in a fat-oil industry.

Method of pectin obtaining using mould culture *Trichoderma harzinium* is processed in this work. The mean of work is concludes, that before extraction the raw materials treated with the mould culture, which produce main cellulotical enzymes at temperature 36°C, for 10 day. Then free pectin substances were extracted by water in ratio 1:5 at the room temperature for 2 h. The obtained extract was filtered, centrifugated with ethanol in ratio 1:2. Yield of pectins was 4% from initial mass of dried baskets.

The obtained pectin is an amorphous substance, light-yellow color, dissolved in water, contained no starch. The relative viscosity of pectin 1% solution is η = 1.06 sPz, the comparative rotation $[\alpha]_D^{20}$ +190°. The molecular mass is 26600.

To determine the monosaccharides content the pectin samples were subjected to acid hydrolysis. Galacturonic acid, galactose, arabinose, rhamnose, mannose and a little of glucose and xylose were determined in pectin hydrolysate.

To determine free carboxyl groups and degree of esterification the titration was used. The obtained results are provided in the Table 1.

TABLE 1. **Physico-Chemical Characteristics of Pectin Substances from Sunflower Baskets**

Raw materials	The water solution of pectin of 1%			Titrametrical data, %			
	$[\alpha]_D^{20}$ *	η	pH	K_c	K_e	K_o	λ
Pectin substance	+190°	1.06	4.8	1.26	3.69	4.95	74.54

where, $[\alpha]_D^{20}$ – comparative rotation; η – relative viscosity; K_c – free carboxyl groups; K_e – etherificated carboxyl group; K_o – total carboxyl group; λ – esterification degree.

From table data it is obviously, that the obtained by enzymatic hydrolysis pectin is high degree of esterification.

NEW METHOD OF DETERMINATION OF CRUDE CELLULOSE IN ARID PLANTS

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According to zootechnik analysis, all carbohydrates are classified into two groups: crude cellulose and nitrogen free extractive substances.

Crude cellulose is consisted of cellulose itself, parts of hemicelluloses and from such substances as lignin, cutin, and suberin.

Crude cellulose considered as a factor of normalizing the digestion in the rumen. It is split under the impact of microorganisms of proventriculi of rumen and intestine. Crude cellulose in the diet is favorably influence to the content of fat in the milk of ruminants. However, its excess in diet of animals reduces digestion and efficiency of nutrition use. Requirement of animals to crude cellulose is taken into account in feeding norms.

New method of determination the content of crude cellulose in arid forages is represented in simplification of filtration process and reduction of the time for analysis. It includes taking the sample of crushed dry matter arid fodder, processing it by sulfuric acid at boiling, dividing the sediment with distilled water, drying washed sediment until stable weight, weighing and accounting content of crude protein by known methods. Into the sample of arid fodder with a amount of 1 g it is included solution of sulfuric acid of 6%, warmed up to 60–65°C, boiled during 3–4 min, washed sediment by water solution of strong sodium of 7%, boiled during 3–4 min, taken sediment is washed triple by distilled water during 5–7 min and divided by centrifugation at 2800–3000 rotation per minute during 2–3 min, then dried washed sediment until stable weight at 104–105°C.

The essence of a new method is that arid fodder is processed by more concentrated solutions of sulfuric acid and sodium hydroxide, and the sediment centrifuged three times. Application of more concentrated reagents taking part in hydrolyze of substances reduces the time of analysis, better removes accompanying carbohydrates (lignin and hemicelluloses) considering the high levels of crude cellulose (up to 51%) in arid fodder.

New method is ecologically clean and wasteless, precise, hydrolysate decantated, sediment centrifuged, and the time of analysis reduced.

DEVELOPMENT OF ORIGINAL MEDICAL-NUTRITION ADDITIVES IN LIVESTOCK BREEDING

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There are plants in grasslands of Uzbekistan, which serve a source of nutritious substances and simultaneously they are medical-prophylactic means through self-treatment during grazing. However, medical properties of these plants are shown only at the certain stages of their vegetative period, but the guaranteed maintenance of livestock animals by medical-nutritional plants is crucial during all seasons of year.

Three plant species were selected for medical-nutritional additives which are widely distributed in all type of desert grasslands – *Artemisia diffusa*, *Peganum harmala* and *Ferula foetida*.

Artemisia diffusa plays a significant role as medical-nutrition plant. In budding period *Artemisia diffusa* contains 7.5% ash, 9.29% protein, 7.8% fiber, 5.2% fat, 29.2% cellulose and 39.2% nitrogen free substances. It contains pitches, tannic substances, alkaloids, essential oils, vitamin C. Consumption of the plant at the early stage of the growth before flowering carries medical-prophylactic character, and after bearing – medical-nutritional, as a strong anthelminthic.

All parts of *Peganum harmala* Z. have medical-prophylactic importance. It contains alkaloids 3–4% in seeds, 2.1–2.7% in roots, 1.6–2.3% in ground part. The plant has antibacterial properties. During flowering period it contains 24.1% protein, 18.0% cellulose, 17.7% ash, 3.6% fat and 30.7% nitrogen free substances.

Ferula foetida Z. has the high significance in medical-nutritional balance of grasslands. It contains during the flowering 18.6–22.8% of a protein, 22–29% cellulose; 8.1–8.9% of fat; 10.9–15.3 ash, nitrogen free substances of 34–35%. Resin, essential oils, free ferulic acid is extracted from cuts of underground parts. It is used for the treatment of pulmonary diseases in sheep. Leaves and seeds can be mixed to the forage against helminthes.

High quality of medical-nutritional additive was developed with the composition of flowering plants in the ratio: 6 parts of *Artemisia diffusa* + 2 parts of *Peganum harmala* + 2 parts of *Ferula foetida*. The crushed nutritional plants were entered at preparing food blocks and in a scattered food mix for 20–30% of weight. Feeding with medical-fodder additives promotes improvement of the livestock health which causes the increase of the animal productivity by 15–20%.

SORPTION-ANALYTICAL PROPERTIES OF CELL WALLS OF YEAST SACCHAROMYCES CEREVISIAE

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We have been studied sorption properties of cell walls of brewing yeast *Saccharomyces cerevisiae* in relation to ions of heavy metals, radioactive nuclides, and toxins. FT-IR (Fig. 1) and ^{1}H NMR (Fig. 2) spectroscopy were utilized to establish structure of cell-walls of yeast – the natural biopolymer representing peptidoglucan complex with specific functional groups, responsible for a biosorption. Potentiometric titration (Fig. 3) of a protonated biomass of yeast was established with pK_a values of 5.52 ± 0.06; 6.70 ± 0.02; 9.48 ± 0.05 for carboxylic, phosphorylic and amino groups, respectively. The contribution of each of these groups in biosorption capability to ions Pb (II), Cd (II), Cu (II), U (VI) and phenol was shown. The role of ξ-potential of a of cell walls surface of yeast and its dependence on the optimum pH values for biosorption was established (Fig. 4)

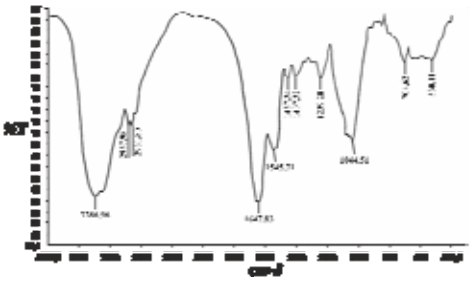

Fig 1. FT-IR spectrum of cell walls of brewing yeast

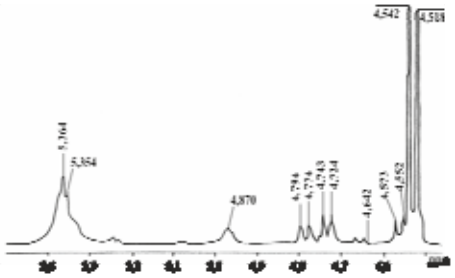

Fig. 2. ^{1}H NMR spectrum of cell walls of yeast

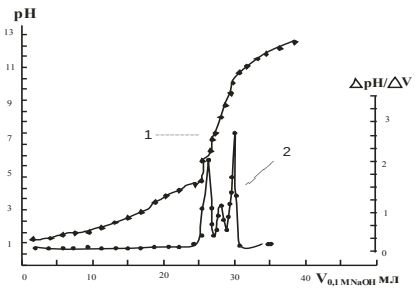

Fig. 3. Integral (1) and differential (2) potentiometric titration curves of cell walls of brewing yeast.

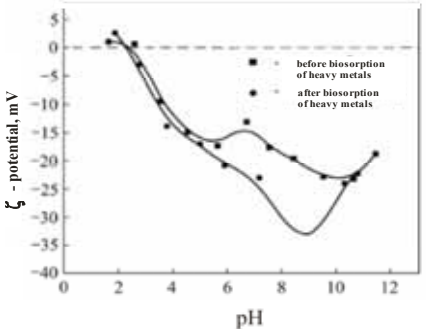

Fig. 4. Dependence of dzetta-potential to pH.

Biosorption dependence on processes as initial concentration of ions in a solution, sorbent doses, pH, activation time, and temperature were established. Key parameters of biosorption were calculated and established maximum sorption capacities of individual substances: Pb (II) – 125.0 mg/g; Cd (II) – 34.48 mg/g; Cu (II) – 25.8 mg/g; U (VI) – 183.3 mg/g and phenol – 18.9 mg/g.

Analytical possibilities of application native biosorbent from cellular walls of yeast for preliminary trace concentration of ions as Pb (II), Cd (II), Cu (II) in natural and waste water with an inverse voltage method were also shown.

COMPARATIVE EVALUATION OF THE ANTIOXIDANT ACTIVITY OF SOME HERBS

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The use of antioxidants (AO), substances that interrupt the radical chain oxidation processes in the objects of organic and inorganic origin is widespread in various fields of chemistry, biology and medicine. Based on individual stock and biologically active substances are novel pharmaceutical preparations and dietary supplements for the treatment and prevention of diseases, normalizing metabolism, etc. In this regard, it is of great practical interest in knowing about the AO activity of various synthetic and natural substances, in particular that of the comparative evaluation of various medicinal plants.

The study presents results of determining the total AO activity of extracts of pharmacy charges, expressed in relation to a 1% aqueous solution of ascorbic acid taken as 100%. The measurements were performed using a specially developed for this purpose an amperometric sensor. Before operation, the transmitter was calibrated by placing resistors readings to "0" in 0.05 M phosphate buffer at pH 6.86 and "100" after introduction into the cell measured amount of an antioxidant such as ascorbic acid. Thus, stock solutions of substances activity can be measured relative to the aqueous solution of ascorbic acid.

Fig. 1 presents results of measuring the AO activity of extracts from a variety of medicinal plants in relation to ascorbic acid.

All samples studied in more or less often AO activity. Comparative analysis in water and 70% aqueous alcoholic extracts showed that the hydroalcoholic extracts exhibit greater AO activity than water extraction, which is apparently due to more complete recovery of biologically active substances of different alcohol extractants. It was also shown that some extracts possessed AO activity exceeds that of ascorbic acid. Among the studied samples aloe, buckthorn, *Rhodiola rosea*, currant leaves, oak bark may distinguish, which have a higher total AO activity, so they can be recommended as herbal remedies of antioxidant action.

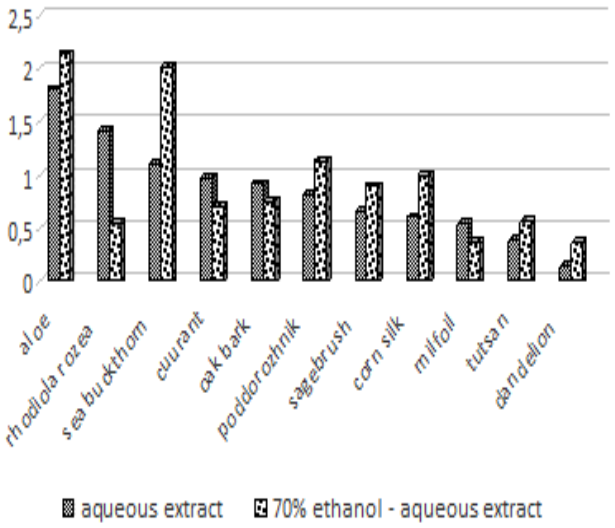

Fig. 1

CHRONIC TOXICITY AND LOCAL IRRITATION OF GREATER CELANDINE SUBSTANCE

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Celandine grass, having a broad and effective therapeutic effect is used in many countries with developed pharmaceuticals. The literature referred celandine belongs to the poisonous plants. In this regard, it was important to establish the dosage of the substance created by the application, as well as its toxicity in humans. Set dosage of substance – 10 mg/kg of body weight (one therapeutic dose).

The study of chronic toxicity of a substance celandine was performed on white laboratory mice for 6 months.

Embodiments of the experience were: a control group of mice received tap water, one experimental group of mice was orally administered 1–3% solution of 1 TD substance (10 mg/kg), 2 experimental groups of mice was injected a solution of 10 TD substance (100 mg/kg), 3 experimental groups of mice administered 100 AP substance (1000 mg/kg).

The experiment showed, that the animals of the control and experimental groups 1 were active, ate good food and some gained weight (1.1 g). With the introduction of 10 TDs and 100 TD mice were depressed, lethargic, reluctantly ate the food and lost weight to an average of 2 g per individual.

Death of the animals during the entire observation period is not fixed. Subject to the dosage of the drug (1 TD) use it for a long time (6 months) was harmless to the body, but the increase in dosages up to 10 APs and 100 TD has the relatively weak toxic effects not result in death.

The establishment of local irritation substance celandine was conducted on rabbits. Substance celandine in aqueous solution at concentrations of 0.5%, 1% and 3% pipette was introduced into rabbit conjunctiva.

The reaction in the conjunctiva was assessed within 24 hours. Pinkness marked conjunctival rabbits when administered to the eye 0.5% solution of the substance, which passed through the 20 minutes, while the 1% solution of the substance pinkness conjunctiva eye after 35 min has passed, with the introduction of a 3% solution of substance pinkness conjunctiva of rabbit eye after 60 minutes has passed.

Thus, it is established that the substance celandine has a weak local irritant effect and a weak chronic toxicity.

STABILITY OF THE SUBSTANCE OF GREATER CELANDINE

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Celandine (*Chelidonium Majus* L.) translation from the Latin means “a gift from heaven”. In fact, this plant has a broad spectrum of action: bactericidal, antispasmodic, analgesic, anti-inflammatory, necrotic tissue, antipruritic, and others. To create modern medicines is necessary to develop the substance of celandine. Scientific-Research Institute “Eastern medicine” created substance celandine, tested it on a specific activity, showed a high therapeutic effect in the treatment of endometritis.

In this regard, it was necessary to establish the stability of the substance celandine, i.e. its shelf life.

Determination of retention substance held in a thermostat TS-80 M-2 at a temperature of 60°C (temperature storage pilot).

For the experiment used bottles of dark glass (30 pcs.), which were placed 5 g of substance celandine. The vials were stoppered tightly screw cap (OST-64-2-87-81) and placed in a thermostat. Analysis of the content of total alkaloids and flavonoids was carried out every 10 days.

In order to establish the shelf life of the experimental storage time in days was multiplied by a constant 16 (K-16).

Found that the shelf life of substance celandine is 1 year and 6.5 months, but on further storage is reduced content of active substances, as evidenced by the findings driven Table.

№	Date of analysis	Authenticity of the project bgh	Humi-dity, %	Quantity ,%		Storage
				amount of alkaloids	flavonoids	
1	05.01.2013	corresponds	4.8	11.2	12.3	120 days
2	05.01.2013	corresponds	4.8	11.2	12.3	120 days
3	15.01.2013	corresponds	4.8	11.2	12.3	280 days
4	15.01.2013	corresponds	4.8	11.2	12.3	280 days
5	25.01.2013	corresponds	4.8	11.2	12.3	340 days
6	25.01.2013	corresponds	4.8	11.2	12.3	340 days
7	04.02.2013	corresponds	4.9	11.2	12.3	400 days
8	04.02.2013	corresponds	4.9	11.2	12.3	400 days
9	14.02.2013	corresponds	4.9	11.2	12.3	560 days
10	14.02.2013	corresponds	4.9	11.2	12.3	560 days
11	24.02.2013	corresponds	5.1	10.0	12.3	720 days
12	24.02.2013	corresponds	5.1	10.0	12.3	720 days

ORIGINAL DESIGN OF IMMUNE PHYTO SYRUP

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Herbal medicine has an important place in the world the practice of medicine due to its multi-activity, low toxicity. They are not only effective in enhancing the adaptability of the organism, but it is reduced in the process of frequent diseases functionality; affect the development of inflammatory processes.

Immunomodulatory syrup is a product based on an aqueous-alcoholic extract of the four types of vegetable raw materials: marjoram finely-flowered, celandine, roots and rhizomes of elecampane, rose hips.

During the study a technology based on a syrup hydroalcoholic extract supplemented with sugar syrup. It is experimentally proved that the production of the syrup should be used as an extraction 40% ethyl alcohol, the ratio of raw material extraction agent 1:10; extraction time of 5–6 days, the multiplicity of mixing 3–4 hours to obtain the extract add sugar syrup density at 1.300–1.310 a volume ratio of 1:2.

The newly developed phyto syrup has been studied in a specific activity:

– inflammatory activity of phyto syrup studies conducted in rats of both sexes weighing 120–140 g in rats induced aseptic inflammation by administering 0.1 mL of 2.5% solution of formalin into the right hind paw. The test drug was administered orally 30 min prior to formalin playback aseptic arthritis doses: 0.25 mL/kg, 0.5 mL/kg, 0.75 mL/kg. The control group received water. Introduction syrup reduced inflammation legs as compared to control animals on: 34.4%, 36.1%, 36.9% in the test groups, indicating that the anti-inflammatory action of the syrup.

– immunological action syrup was studied in rats with experimental reproduction of the model "tracheobronchitis". Control rats desoldering water experienced – syrup in doses of 0.5 mL/kg, 0.75 mL/kg. During the time of the disease and up to 14 days of treatment the study of changes in the composition of blood, to the effectiveness of therapy with syrup conducted. Immunocompetence of the system was evaluated by cell reactivity index, leukocyte index (LI) and immune reactivity index (IPI). LEE during treatment increased by 31.4% and 12.9 MIT, which indicates a favorable course of the disease and increase cellular immunity.

Thus phyto syrup anti-inflammatory action, increases the immune system, it can be recommended as an adjunct to the standard treatment of acute respiratory disease.

ACUTE TOXICITY OF THE SUBSTANCE OF FINELY-FLOWERED OREGANO

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Finely-flowered oregano has the following actions: anti-inflammatory, anti-cold, anti-microbial, analgesic, expectorant, enhancing the secretion of bronchial glands, calming the central nervous system.

Scientific-Research Institute "Eastern medicine" designed and created the substance finely-flowered oregano for the production of modern medicines in usable form.

Studies showed a high specific activity of a therapeutic effect in inflammatory airway diseases. The dosage of treatment and method of administration of the drug was established.

The experiment was performed on white laboratory mice of both sexes weighing 20 ± 2 g. 4 groups were formed from 5 mice in each group of heads by the comparative method. The control group of mice received distilled water. Experimental groups of mice received 1–3% aqueous solution of the substance in doses of 10;100;1000 mg/kg orally.

Research was carried out for 14 days (treatment) on experimental animals in the vivarium.

Observations showed that the mice in all groups were active, happy to accept food and water normally react to external stimuli. Differences between control and experimental animals were observed. By the end of the experiment, all mice were alive, so set the LD_{50} substance oregano failed.

Mice from the control and experimental groups with a maximum dose of the substance administration (1000 mg/kg) etching treatment the end of experiment, macroscopic inspection of the mucous of the gastrointestinal tract and state of parenchymal organs conducted.

Differences between control and experimental animals were founded in these indicators.

Studies have shown that the substance of oregano is non toxic.

THE ROLE OF PECTIN COMBINATIONS IN THE CHILDREN′S ORGANISMS DETOXIFICATION WITH HEAVY METALS

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Nowadays pectin and pectin-containing combinations are recommended by WHO as the most effective and the safest preparations for the prevention of children′s organisms from detoxification by heavy metals and radionuclide.

The problem of children′s organisms detoxification by heavy metals is actual for Uzbekistan too. The recent withdrawal research of healthy children`s hair and blood microelements structure (78 children aged 10–11 years old) showed the heightened content of lead in children′s hair (up to 4.62 ± 1.11 mcg/g) and in children′s blood (up to 1.16 ± 0.05 mg/L). For cadmium and mercury we received the following results: Cd – in hair 0.10 ± 0.02 mkg/g, in blood up to 0.02 ± 0.01 mg/L; Hg – in hair 0.13 ± 0.01 mkg/g, in blood up to 0.02 ± 0.001 mg/L, which is practically corresponding the top level of the biological standard [1, 2].

In the international detoxification practice the following chelates are used: EDTA (Ethylenediaminetetraaceticacid, brand name of Versenate or trade names TrilonB); DMSA (2,3-dimercaptosuccinic acid, trade names "Chemet" and "Succimer"); DMPS (sodium 2,3-dimercaptopropane-1-sulfonate); *D*-peniccilamin and etc. The following preparations are considered as more light preparations: different coal-mineral entero-sorbents like «СУМС», «Альгисорб», «Белыйуголь».

Although classical chelates may bring to possible collateral effects as they withdraw many useful elements and microelements (together with heavy metals). That may bring to the development of repeated deficit of the most important and essential elements such as Zn, Cu, Ca, Mg, Fe.

In this respect pectin as an effective complex-former can be used for prevention from lead, cadmium or mercury detoxification without collateral effects. According to the WHO recommendations the daily dose of pectin should be at least 4–5 g, and in radioactive pollution at least 15–16 g a day.

Pectin is a polymer of galacturonic acid that is principally found in the cell walls of plants. It can be extracted from fruit pips, the pulp and the peel of apples, sugar beet, sunflower and even seaweed. It is a branched anionic polysaccharide, the molecular weight of which can vary from 20 000 to 200 000 (≈50 to 150 kilodaltons). The backbone of pectin is mainly composed of *D*-galacturonic acid units linked together by α-(1→4) glycosidic bonds.

As opposed to Uzbekistan, much attention is paid to preventive arrangements with the help of pectin-containing preparations in the following countries as Russia, Ukraine and Belorussia. There is a whole series of entero-sorbents, for example: «Pectolakt», «Pectomol», «Yablopect», «Medetopect», «Pepidol», «Vitopectin» and etc.

On the base of a big analytical information we proved the effectiveness of pectin preparations application for prevention of pupils of Uzbekistan from toxification by heavy metals.

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Ca^{2+}-DEPENDED HAEMOSTSTIC EFFECT OF DITERPENOIDS ON THE BASIS OF *Lagochilus* GENUS PLANTS

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Estimating of coagulation haemostasis condition *in vitro* and *in vivo* in the present of lagochilin and its some derivatives revealed that their action observed only in the existing of Ca^{2+} ions.

Comparatively analysis of blood coagulation condition in the existence of the studied diterpenoids shows that all parameters of haemostsis for membrane active lagochilin derivatives are passive, than lagochilin and comparative preparation lagoden, which had not membrane effects. Thus, action of the studied diterpenoids definite by the non Ca^{2+}-ionophoretic activity, but their structural features, which acting in the present of Ca^{2+} ions common action on coagulate ability of the plasma, activating in this case internal pathway of coagulation haemostasis and practically do not introducing directly on the external cascade of blood coagulation systems initiation.

Hence, artificial creating Ca^{2+}-ionophoretic activity of the diterpenoids and possible destroy of normal Ca^{2+}-permeability phospholipid membranes of platelets by them does not able increasing of their haemostatic activity. Mechanism of effective coagulating action of the diterpenoids on the base of *Lagochilus* genus plants mainly determining by their function on the side of phospholipid membranes of platelets, when introduction of diterpenoid molecules into the hydrophobic area of lipid matrix with having ionophoretic activity relatively to Ca^{2+} ions decreasing coagulation effect of the studied compounds.

Wholly, creating of haemostatic preparations by the way modification with hydrophobic substitutes having membrane activity of hydroxyl groups in lagochilin molecule is able to introducing the studied compounds into hydrophobic area of lipid bilayers displaying ionophoretic activity relatively to Ca^{2+} ions, but leads to decrease their haemostatic effect, which depend on hydrophilic-hydrophobic part relation of the diterpeniod molecules. Thus, research of haemostatics on the base of lagochilin with possible maximal number of hydroxyl groups (as by the way of obtaining its complexes with polymers and other respective organic molecules, so by the way of synthesis its derivatives or salts, which in case solution in water shall be disconnect with formation hydroxyl group) is moreover one of the actual tasks in creating a new effective and bioavailable haemostatics.

COMPLEXANT PROPERTIES OF SOME LABDAN SERIES DITERPENOIDS

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The basic acting source from *Lagochilus* genus plants that grow in Central Asia and which have haemostatic effect is lagochilin and its derivatives that belong to Labdan series diterpenoids. As we had earlier shown that two diterpenoids: 3,18-*O*-isopropylidenlagochilin and 3,18-*O*-ethylidenlagochilin, synthesized from lagochilin, induce ion conductivity on planar lipid bilayers and have a high selectivity to bivalent cations. In this regard, complexation features of 3,18-*O*-isopropylidenlagochilin and 3,18-*O*-ethylidenlagochilin with cations of zinc and alkali-earth metals have been investigated by conductometry and IR-spectroscopy methods.

It has been shown by the researches of changing electrical conductivity of different solution of metal salts in presence of the studied diterpenoids. By the curves of titration the quantitative characteristics of complexation features of the diterpenoids with bivalent cations were calculated. These parameters are complexation constant (K), Gibbs free energy (ΔG), Stock′s radiuses of complexes (r). The analysis of indicated thermodynamic values has shown that investigated direrpenoids are capable of forming the complexes with metal ions, also are the complexon of alkali-earth metal ions. Stechiometry of complex forming with metal ions is differentiated and in the most cases depends on the nature of a solvent. Different values of complex forming constants indicate of the selectively to separate cations. The changes in Gibbs free energy (ΔG) point that the process of complexation of diterpenoids with cations of bivalent metals is done with no energy consumption, i.e. spontaneously.

To confirm the diterpenoids complexant features IR-spectrums of 3,18-*O*-isopropylidenlagochilin and its complex with Ca^{2+} ion (in the relation 3,18-*O*-isopropylidenlagochilin–Ca^{2+} 1:1) have been registered. There are adsorptions of bands at 1250, 1200 cm^{-1} in the IR-spectrums occurring as a result of fan-shaped oscillation of methyl groups and bands at 1080 and 860 cm^{-1} indicating presence of isopropyl group in the molecule.

The band of adsorption at 3100 cm^{-1} occurring from valent oscillation of hydroxyl groups is displaced toward the high frequency oscillation until 3180 cm^{-1} and that is explained by the weakening of intermolecular hydrogen bonds formed by hydroxyl groups because of presence of couple of methyl groups in 3,18-*O*-isopropylidenlagochilin molecule and that create steric obstacles. In IR-spectrum of complex 3,18-*O*-isopropylidenlagochilin with Ca^{2+} ions on comprise pure molecule of 3,18-*O*-isopropylidenlagochilin there are no bands of adsorption at 3180 cm^{-1} and 1300 cm^{-1}. Apparently, Ca^2 ions form coordination bonds with oxygen of hydroxyl groups and thus destroy intermolecular hydrogen bonds.

ACTION OF MEMBRANE ACTIVE LAGOCHILIN DERIVATIVES ON BLOOD COAGULAION SYSTEM

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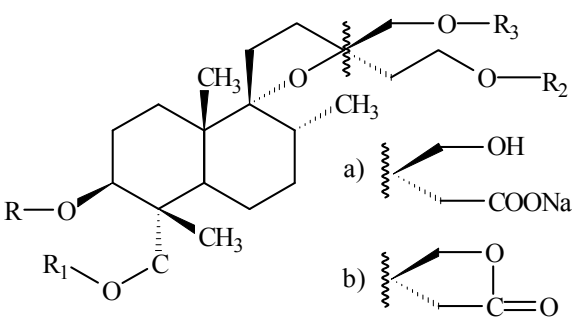
Eight analogical in structure diterpenoids were used in the research: lagochilin and its derivatives. The main difference through them is nature of functional groups and substitutes in positions C_3 and C_{18}, C_{15} and C_{16}, in that order studied compounds can differing to four groups: I) compounds, having free functional groups in positions C_3 and C_{18}, C_{15} and C_{16} lagochilin (**1**) and lagoden (**2**); II) compounds, which hydroxyl groups in position C_3 and C_{18} are blocked 3,18-*O*-isopropylidenlagochilin (**3**) and 3,18-*O*-ethylidenlagochilin (**4**); III) compound, which hydroxyl groups in position C_{15} and C_{16} are blocked lagochirzin (**5**); IV) compounds, which all hydroxyl groups in positions C_3 and C_{18}, C_{15} and C_{16} are blocked 3,18;15,16-di-*O*-isopropylidenlagochilin (**6**), lagochirzidin (**7**) and 3,18-*O*- isopropyliden-lagochirzin (**8**).



1. $R= R_1= R_2= R_3= H$
2. $R= R_1= H$; and part (a)
3. $R + R_1= C(CH_3)_2$, $R_2= R_3= H$
4. $R + R_1= CH(CH_3)$, $R_2= R_3= H$
5. $R= R_1= H$; and part (b)
6. $R + R_1= C(CH_3)_2$, $R_2 + R_3= C(CH_3)_2$
7. $R + R_1= CH(CH_3)$; and part (b)
8. $R + R_1= C(CH_3)_2$; and part (b)

Diterpenoids of the II ultimate group (compounds **3** and **4**) revealed membrane active properties, when other six compounds had not so activities.

Also action of the diterpenoids on blood coagulation system was depended on structural feature of the studied compounds. So, relating of blood coagulation system parameters change on the action of studied compounds shown that these introduction degree on haemostasis was different. It connects with that haemostatic activity of studied compounds depended on their structural feature. Data analysis shown that action of two membrane active lagochilin derivatives on blood coagulation system in clearly degree definite having their ionophoretic properties on alkali-earth metals cation road, because Ca^{2+} ions play important role also in coagulation and platelet haemostasis.

REGISTER SETTINGS OF THE FUNCTIONAL STATE OF MICROBIAL IMMOBILIZED CELLS MITOCHONDRIA

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Currently, there is no doubt that the action of many biologically active compounds, including microbial origin (antibiotics) is realized by modulating the permeability of biological membranes. There is a large group of so-called membrane-compounds with varying selectivity influencing the structure and properties of biological membranes and models.

The effect of compounds of this type generally amounts to accelerate the transfer of substances and ions through the membrane by forming a lipid complex comprising the ion and the molecule transferred ionophore (or chelator).

It should be noted, that the polyene antifungal antibiotics formed ion channels in the membranes of eukaryotes contain ergosterol are natural and fungicides as selectively increased the permeability of membranes.

According Brierley, mitochondrial membrane permeability can be quantified on the kinetics volatile swelling of mitochondria in different salt environments. Study of the properties of membrane-immobilized microbial cells and biologically active substances synthesized by them (polyene antibiotics) shown, that at concentrations of 15–60 ug/mL they induced the significant mitochondrial inner membrane permeability for a number of ions, which accelerates the penetration of the substances needed in the cell.

The data indicate, that in the absence of added compounds the ionophoric inner mitochondrial membrane has low permeability to potassium (K^+), but adding the aforementioned components has been a significant acceleration organelle swelling kinetics proportional concentration used.

A similar pattern is observed in the study of protonophore activity, the results of which can be assumed, that the objects being studied may induce potassium and proton permeability of biological membranes.

In this work the ionophoric activity of various concentrations of biologically active substances (polyene antibiotics), extracted from microorganisms, for the various ions (H^+, K^+, Ca^{2+}, Mg^{2+}) was studied. The set-induced changes in the permeability of membranes is quite specific and depends on the ionic composition of active membrane components that exhibit properties similar to those of natural and synthetic ionophore.

The combination in one product the ionophore, antibiotic or fungicidal activity consider its possible use for many microorganisms, including the infectious agents of cotton.

IMMUNOCHROMATOGRAPHIC METHODS FOR QUANTITATIVE ANALYSIS OF ANTIBIOTICS AND DRUGS

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Recent advances in molecular biology, molecular genetics, bioorganic chemistry, and their practical realization led to the development of lateral flow methods of the quantitative analysis of antibacterial drugs and narcotic substances, in particular, cocaine, amphetamines, morphine, heroin metabolites, tetrahydrocannabinol in biological liquids.

In respect to the latter group of substances subject to special requirements with use of special technical means that can satisfy a number of requirements – selectivity, performance, absence of false results.

It should be noted, that the currently developed immunochromatographic analysis methods are aimed to the determination of the presence of certain concentrations of substances in biological materials and based on immersion test in physiological fluid that starts to migrate along a strip on the principle of thin-layer chromatography. Immune complexes formed between antibody immobilized on the chromatographic paper, and free drug presented in the analyzed sample are proportional to its concentration. Then strip is placed in a solution containing: a) conjugate (a certain drug – peroxidase); b) glucose; c) addition of a chromogen substrate.

During incubation conjugate binds with vacant active center of antibodies and interaction with the immobilized glucose oxidase there is a consecutive generation of hydrogen peroxidea which contributes to the substrate oxidation with the formation of insoluble colored product.

The concentration of antigen (defined substances) in the studied sample is inversely proportional to the intensity developed on a strip of color, i.e. the concentration of a substance is determined not by the enzymatic activity of the conjugate, and chromatographic behavior of.

Thus, being an effective method of diagnosis, rapid tests allow you to visually within a few minutes to determine and assess the content of the antigens, antibodies, hormones and drugs in biological fluids. The hematocrit, i.e. the ratio of plasma and formed elements is essential. At high hematocrit reduces the number of plasma with an antigen, migrating along a strip.

Given the above, of particular interest, from a practical point of view, is the use of marked imminoxil radicals of gap tens in determining the concentration of morphine in biological liquids. For the drug antibodies were obtained and used in the test system after joining imminoxil radical.

If the detectable drug contained in the sample, then it blocks the active centres of antibodies. Morphine added as a component of the test system, labeled by imminoxil radical, remained unbound and range of labels coincides with the spectrum of imminoxil in the solution.

THE THERAPEUTICAL PROPERTIES OF BIOCOMPLEXES

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Finding the ways to regulate the various endogenous processes using external factors including by using bio-complexes which are the compounds of metals and active ligands is one of the most important and promising areas of human physiology and biological chemistry.

We have carried out studies aimed to identifying the most important factors that determine the specificity of the studied ligands′ – MetSCL and – MetSOH and bio-complexes with metals Co, Ci, Zn, Ni contribution to the activity of DNA polymerase cores, as well as RNA polymerases I and II.

The experiments were carried out on white rats which were decapitated under the ether anesthesia. Their livers were rapidly removed and placed in an isolation medium.

The mitochondrial and microsomal liver fractions were obtained by differential centrifugation.

The effect of biological preparations were examined at concentrations $10^{-3} – 10^{-7}$ mol/L in the suspension of microsomes or mitochondrial by incubation for 30 min at 37°C. The intensity of free radical oxidation in the mitochondrial and microsomal fractions was assessed by the accumulation of TBA-active products (MDA). The accumulation of lipid peroxidation products were expressed as nmol MDA/mg of protein for 30 min.

Studies have shown that both ligands to a certain degree contribute to increase of the DNA polymerase activity of rat liver nuclei. However, they differ markedly on the quantitative influence on these processes. Unlike to initial ligands, the inhibition of DNA polymerase activity of liver nuclei is typical to biocomplexes. This fact suggests the direct involvement of biometals in enzymatic processes.

At the same time, the effect of biocomplexes on the level of accumulation of DNA polymerase, as in the case of lipid peroxidation, is determined by both the nature of the central atom and a ligand coordinated thereto. This gives the grounds to conclude that the specific impact of bio-complexes on the activity of DNA polymerase occurs with direct involvement of the central atom in these processes.

It was revealed that the effects of ligands and biocomplexes on the activity of DNA polymerase, RNA polymerase I and II are determined by several factors: the nature of the metal, its population of d-sub-layer, the presence of the ligand ions capable to react with the functional groups, such as enzymes and substrates, or increasing their affinity, as well as with the components of nucleic acids, changing biosynthetic processes in the body.

The identified specific activity of biocomplexes for cancer, anemia, radiation injury and pyelonephritis, hepatitis can offer them as therapeutic agents that affect the hematopoietic activity as cytotoxic agents with probable anti-tumor activity.

IMMUNOLOGICAL ASPECTS OF THE PATHOGENESIS OF EPILEPSY

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Neuroimmunogenesis of epilepsy is accompanied by the formation of antibodies to the number of receptors. The study the immunological aspects of epilepsy to predict the disease is one of the main tasks of advanced epileptology.

To study the levels of neurotropic autoantibodies in blood serum of patients with idiopathic and symptomatic epilepsies.

We studied 52 patients with epilepsy at the average age of 36.2 ± 14.7 years old. 38 patients of them had idiopathic epilepsy (I group), 14 patients had symptomatic epilepsy (II group). The control group consisted of 16 healthy subjects matched for age. In all patients we studied cognitive function by using MMSE scale, test to memorize of 5 words, clock drawing test and test for speech activity. Immunological studies were carried out with ELI-Neuro-test 12 by immunoenzymatic analysis. We studied the levels of neurotropic autoantibodies to NF-200, GFAP, S100, MBP, voltage-dependent calcium channels, glutamate receptors, GABA, dopamine, serotonin and *n*-choline receptors, as well as to DNA and β2 glycoprotein (CU). The data obtained were processed using methods of variation statistics.

Our study showed that patients with complex partial seizures were more likely to develop cognitive impairment than patients with secondary generalized and simple partial seizures. Epilepsy was characterized by elevated serum levels of neurotropic autoantibodies. In idiopathic epilepsy, we observed more significant elevation of antibodies to protein NF-200 (22.0 ± 6.7), S100 (54.3 ± 10.3), MBP (14.9 ± 4.9), GABA (22.6 ± 3.5) and dopamine receptors (19.7 ± 3.9), testifying to the role of degenerative and demyelinization processes, as well as apoptosis, emotional dysfunction, GABA and dopaminergic disturbances in such patients. In symptomatic epilepsy, we founded the elevated levels of autoantibodies to GFAP (13.9 ± 7.9), GABA (21.9 ± 3.9) and dopamine receptors (18.9 ± 2.1), as well as to DNA (25.3 ± 13) and reduced levels of antibodies to serotonin receptors (5.1 ± 3.7), indicating GABA, dopamin and serotoninergic disturbances, proliferation of astroglial cells (gliosis) and barrier dysfunction of the hematoencephalic barrier, as well as non-specific immunoactivation, possibly, connected with non-specific infectious-inflammatory process.

Thus, autoimmune disturbances play the important role in the pathogenesis of epilepsy. More severe attacks are accompanied by worsening of neuroimmune dysregulation. The degree and duration of autoimmune process can serve additional diagnostic and prognostic criteria for epilepsies. Along with appropriate antiepileptic drugs, timely correction of autoimmune aggression and local inflammation, considering investigated markers of neuroimmune dysregulation, should be recommended in treating of epilepsy patients.

CHEMICAL COMPOSITION OF *Tanacetum pseudachilleae* C. WINKL ESSENTIAL OIL

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Nowadays the medicinal plants tested in the folk medicine are used together with other agents for the treatment of parasitic diseases. Preparations of plant origin are available, cheap and low toxic.

Tanacetum pseudachilleae C. Winkl is the Central Asian endemic plant, allied species of a *Tanacetum vulgare* L. widely used as an anthelmintic agent – was studied by us in order to use it in medical practice together with a *Tanacetum vulgare* L. Natural stocks of *Tanacetum pseudachilleae* C. Winkl are quite large and may well meet the needs of the pharmaceutical industry of the Republic of Uzbekistan for the raw materials.

The purpose of our investigation was to determine and identify the component composition of essential oil of flowers of *Tanacetum pseudachilleae* C. Winkl growing in the Republic of Uzbekistan was established experimentally.

Essential oil of *Tanacetum pseudachilleae* C. Winkl flowers was obtained by distillation with water according to the SP XI procedure (technique). Combined gas liquid chromatography and chromato-mass spectrometry methods were used to identify the constituent components of the essential oil obtained. Determination was performed using the HP GC/MS 6890/5973 under the following conditions: column – HP-5MS 5% phenyl methyl siloxane capillary 30.0 m × 250 mm × 0.25 mm nominal; mobile phase – He (helium), mobile phase rate – 0.5 mL/min; precision (10:1), in the Split mode; vaporization chamber temperature – 275°C; detector temperature – 230°C; AUX – 280°C; column temperature is gradually increased from 70°C to 270°C; temperature increasing rate –5°C/min, isothermal mode (270°C) is kept till the end of analysis for 25 min. For this purpose 0.5 mL of essential oil was placed into 25 mL volumetric flask and 10 mL of hexane was added, then the solution volume was made up to the mark with the same solvent and stirred. The obtained solution was passed through a separation funnel and filtered through a paper filter with layer of anhydrous sodium sulfate into a conical flask. The first part of the filtrate was discarded. Injection sample volume was 2 mL. Willey-275 software database was used to identify the substances.

The presence of more than 40 components having more than 80% probability of coincidence with Willey-275 software database was established by means of conducted researches in the composition of *Tanacetum pseudachilleae* C. Winkl flowers essential oil. 24 components of them are the most prevalent and have been identified.

Retention time of main components in aforementioned conditions at the chromatogram of the test sample solution: camphene – 4.93 min (43.78%); sabinene-6,19 min (0.96%) 1,8-cineole – 7.46 min (7.65%), lavandulol – 10.78 min (4.43), *trans*-kariofilen – 17.50 min (2.05%); germakren – 19.00 min (3.79%), haranil acetate – 17.98 min (0.15%), α-amorphen – 19.80 min (0.42%), Δ-cadinene 19.96 min (0.46%).

On the basis of researches conducted for the first time the primary component composition of the essential oil of flowers of *Tanacetum pseudachilleae* C. Winkl growing in the Republic of Uzbekistan was established experimentally.

EVALUATION OF THE EFFECTS OF ALFALFA MOSAIC VIRUS ON CAROTINOIDS IN THE LEAVES OF ALFALFA PLANT

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Relevance of the study determined that in recent years suggested that vitamin A affects the immune system, has a protective antioxidant properties, and its use reduces the risk of cancer, an important aspect in recent situation regarding the frequency of data pathological processes. The highest amount of vitamin A in the liver of animals and fish, and a precursor contained in fruits and vegetables of yellow and orange, are pro-vitamins – β-carotinoids. Carotinoids are generally contain only in products of plant origin and in human organism conversed to vitamin A by the enzyme carotinase. Vitamin A deficiency is the cause of blindness and xerophthalmia, so vitamin A is an essential factor of human nutrition.

The functions of carotinoids in plants are very diverse. Theories explaining the functions are based primarily on these function oxygen scavenging compounds, as well as light energy in the blue region of the visible spectrum. Carotinoids are involved in general metabolism processes in photosynthetic oxidant reduction reactions affect the growth process and plant developed on sexual functions plants etc. (Lebedev, 1948; Lukovnikova, 1966 Manuelyan, 1967 Merzlyak, 1989; Merzlyak, Gtelson, Chivkunova et al, 2003). In connection with this study the effect of alfalfa mosaic virus infection to the content of carotinoids in the leaves of the plant is of great practical and scientific value.

To study we used 50 mg of alfalfa leaves of a plant grown in natural conditions, classified on the degree of infection and extracted in a porcelain mortar in 5 mL of 100% acetone. Acetone mixture of pigments was filtered through a glass filter (№2) and transferred to the test tube. From received pigment liquid 0.2 mL was taken, mixed with 2.8 mL of acetone, and measured with a spectrophotometer (SPEKOL-1300) at a wavelength of 440.5 nm. The pigment was calculated using the P. Wettstein formula.

Investigations have shown that carotinoids in the healthy alfalfa plants is 70.81 mg/L, and in low infected by mosaic virus alfalfa is 65.13 mg/L, in the medium infected plants – 50.17 mg/L, and in a highly infected – 41.40 mg/L. And the study of carotinoids in the ratio of fresh weight depends on the degree of infection, the amount of carotinoids in healthy plants is 7.38 mg/g, slightly damaged – 6.51 mg/g, in the medium infected – 5.02 mg/g, and in high infected – 4.14 mg/g. It was founded that the amount of pigment in relation to the fresh weight decreased increase relative to the control depending on the degree of infection.

Based on these results the following conclusions can be made. In alfalfa plants in dependence of the ratio of the degree of infection with virus, the amount of carotinoids decreased from 11.76% to 43.93%. This leads to a reduction of important physiological properties of the growth, development and flowering plants.

CONCENTRATION-DEPENDENT EFFECTS OF THE FLAVONOID QUERCETIN ON MITOCHONDRIAL PERMEABILITY TRANSITION PORE

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Recent investigations indicate that mitochondrial permeability transition pore (MPTP) has a significant role in cell physiology and cause mitochondria dysfunction in pathological conditions. Different toxic compounds, pH of matrix, changing potentials, adenine nucleotide translocase inhibitors, some heavy metals, thyroid hormones caused exposing process of MPTP, membrane permeabilization. Besides MPTP turns to open conformation in pathological conditions and provides high conductivity of cell membrane. Studying MPTP dysfunctions in pathological conditions and correcting them with plant compounds is one of significant problems of pharmacology and medicine.

Following the above mentioned problems we studied *in vitro* the effects of the flavonoid quercetin on MPTP conditions of rat liver.

Mitochondrias from the livers of rats were isolated by centrifugation. The swelling kinetics of mitochondrias was determined in 3 mL cells with the optical density in 540 nm.

Researches show that quercetin reveals membrane activity properties directly dependent on concentration studied. In our investigation quercetin in low concentrations (10 μM, 20 μM, 30 μM) increased the swelling process of mitochondria comparing to control, and this gives evidence about MPTP turns to open conformation.

High concentrations effects of quercetin (100 μM, 150 μM ва 200 μM) were opposite to the effects in low concentrations, high concentrations led locked conformation of MPTP. Comparing to control, high concentrations of quercetin decreased the swelling process of mitochondria. Our investigations showed that, quercetin reveals membrane activity dependent only on concentration. Thus, quercetin active influence to MPTP: low concentrations lead to membrane permeabilization and high concentrations lower permeabilization process, consequently stabilizes the membrane.

The obtained results were very significant to understand the effects of quercetin on the action mechanism in cell and mitochondria processes and membrane correction in pathological conditions.

COMPLEX USE OF LOCAL MICROFERTILIZERS AND MICROELEMENTS

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In order to study the effect of microbial preparations on plants experiments on the farms and in the fields of public institutions carried out.

Since 2009 to present the mirobiological fertilizer “Baikal EM1” has been tested in many of the farms and showed the following results on the yield increase: for cotton in the Institute of seed breeding – for 12.6 c/ha, Agrofayz " farm in Tashkent district – 11 c/ha, "Nasar" farm in Kashkadaryua district – 10.9 c/ha; "Quvasoy" farm in Fergana district – 13.4 c/ha; for wheat in "Zilolmomo" farm in Surkhandariya district – 11.4 c/ha, Plant Protection Centre MAWR RU in Surkhandariya district – 11 c/ha; for potatoes in “Cora-arik lands" farm – 5 t/ha; for tomato in the Institute of vegetables, melons and potatoes – 133.4 c/ha and watermelons – 3.4 c/ha. The Institute of General and Inorganic chemistry of Uzbek Academy of Sciences noted that the application of microbiological fertilizer "Baikal EM1" transform insoluble phosphates into soluble form, improves the fertility of the soil and the environment as well as its physical and chemical properties. Treatment of the preparation during years supported increasing of crops yields by 50–60%, vegetables – by 90%, cotton up to 35–40%. Thus, for 2-year use of the preparation in the soil the nitrogen content increased for 2.7 times, the phosphorus for 3 times, potassium for 15%.

In the Tashkent State Technical University research laboratory the concentrate including more than 36 macro and micronutrients was obtained by processing the minerals underground saline water of Chartak area. The preparation was named "Bio-Iodine-Bromine" and used as a plant growth stimulator. For the first time the studies of this complex elements effect on the germination and growth of several species of cultivated plants. Positive results were obtained by soaking the seeds of plants in 24 hours in a 1% solution concentrate "Bio-Iodine-Bromine". Germination acceleration (3–4 days), increase rice yield of 10% relative to the control field were observed. Germination was determined by the method of Interstate standards for seed crops.

On laboratory experiments with seeds of cotton variety "Farovon MT-3" experiments on the complex influence of "Bio-Iodine-Bromine " and " Baikal EM1" on germination, growth and yield. Acceleration of germination for 3 days, increasing of yield for 35% has been obtained.

Integrated application of both methods will undoubtedly increase the natural fertility of our land.

THE DYE PLANTS OF TURKISTAN MOUNTAIN RIDGE

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The area of Uzbekistan is tremendously rich for various plants, among them herbal, fodder crops, bee breeding sorts are of crucial importance. Especially, nowadays dye (paint, ink) plants growing in our country are becoming more and more of high demand, because artificial dye (paint, ink) elements may negative impact on the quality of food products.

The Turkistan mountain range forming Hisar–Oloy system of mountains is situated within the confines of Uzbekistan and Tajikistan. 1200 varities of high plants can be founded on this territory. The dye plants of this regions have yet to be studied thoroughly. The dye plants of Uzbekistan have been researched by such scientists as S. H. Cheverenidi, S. M. Mustafoyev (1964), S. Solihov (1977, 1985), G. Karimov (1981). Nonetheless, the dye plants of Turkistan mountain range have not been investigated deep enough.

According to our estimations, there are 27 plant families, 56 varities and 71 types in Turkistan ridge. The families which include most dye plants are *Asteraceae* (8), *Fabaceae* (7), *Boraginaceae* (6), *Papaveraceae* (5), *Polygonaceae* (5), *Salicaceae* (4). In this area there are 16 annual plants, 6 biennial plants, perennial plants, 6 bushes, 2 half-bushes, 6 types of trees. The dye plants of Turkistan range spread in steep highland areas as follows: 38 types in desert, 62 types in highlands, 39 types in mountains and 3 types in meadow lands.

The list of life forms of dye plants in Turkistan ridge.

S.n.	Families	The number of varities	The number of types	S.n.	Families	The number of varities	The number of types
1	*Asteraceae*	7	8		*Polygonaceae*	3	5
2	*Berberidaceae*	1	3	15	*Punicaceae*	1	1
3	*Boraginaceae*	5	6	16	*Moraceae*	1	1
4	*Cruciferae*	4	4	17	*Plumbaginaceae*	1	1
5	*Chenopodiaceae*	2	2	18	*Ranunculaceae*	1	2
6	*Datiscaceae*	1	1	19	*Resedaceae*	1	1
7	*Elaeagnaceae*	2	2	20	*Rutaceae*	1	1
8	*Fabaceae*	7	7	21	*Primulaceae*	1	1
9	*Guttiferae*	1	3	22	*Rubiaceae*	2	3
10	*Lamiaceae*	3	3	23	*Salicaceae*	1	4
11	*Liliaceae*	1	1	24	*Tamaricaceae*	1	1
12	*Malvaceae*	2	2	25	*Scrophulariaceae*	1	1
13	*Papaveraceae*	3	5	26	*Zygophyllaceae*	1	1
14	*Peganeaceae*	1	1	27	Total	56	71

So, the Turkistan mountain range is significantly abundant in dye plants, and identification of brand new peculiarities is indispensable.

THE ALKALOIDS OF TOXIC LANTS OF TURKISTAN MOUNTAIN RIDGE

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The Turkistan mountain range forming Hisar–Oloy system of mountains are situated within the confines of Uzbekistan and Tajikistan. 1200 varities of high plants can be found in this territory, majority of which are alkaloid-bearing plants.

To date, 5000 alkaloid-bearing plants have been sorted out; the structural composition of 3000 types have been defined. Initially, the alkaloid plants were studied by A.P. Orehov; his researches were successively taken up by academic S. Yunusov in Uzbekistan. He studied over 4500 types of high-plants in Central Asia and determined that 2000 of them are alkaloid plants.

The alkaloid-bearing plants of the flora of Central Asia have been studied by E. E. Korotkova and her pupils and disciples T. Odilov, S. Holodkov, K. Toyjonov, S. Hamidhujayev, U. Rahmonkulov and O. Nigmatullayev. Most of the alkaloid-bearing plants are considered to be venomous (toxic). Among venomous (toxic) plants *F. communis* and *F. Marmarica* types from *Ferula* L. varieties contain alkaloids and coumarins, and, therefore, they possess poisonous effect on cattle (M. F. Infante, 1965; S. N. Kamel, M. T. Boyoumi, 1972). Men and animals who consume them may get poisoned.

According to our evaluations, 20 types of plants in Turkistan mountain ridge are regarded as poisonous (venomous, toxic) plants of alkaloid-containing plants of first type. They are as follows: Poppy from *Papaveraceae* family, *Papaver somniferum* L., *P. pavoninum* Schrenk, *Delphinium semibarbatum* Bienert, *Glaucium fimbrilligerum* Boiss., *Roemeria refracta* DC.; *Parpi* from *Ranunculaceae* family, *Aconitum talassicum* M. Pop., *A. zeravschanicum* Steinb.; *Amarilidaceae*, *Ungernia Bunge; Fabaceae, Vexibia pachycarpa Goebelia* Bunce, *Melilotus officinalis* Desr.; *Boraginaceae*, *Heliotropium dasycarpum* Ldb., *Trichodesma incanum* (Bunge) DC.; *Zygophyllaceae*, *Tribulus terrestris* L.; *Equisetaceae, Equisetum arvense* L.; *Peganiaceae, Peganum harmala* L.; *Solanaceae, Hyoscyamus niger* L., *Datura stramonium* L.; *Apiaceae, Conium maculatum* L.; *Asteraceae, Xanthium spinosum* L.; *Campanulaceae, Codonopsis clematidea* Schrenk.

THE TYPES OF *Ferula* L. GROUP, THE TERPENOIDS PECULIARITIES′ SOURCE AND THE POTENTIALS OF RATIONAL APPLICATION

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Ferula L. group includes utmost number of types (170) in *Apiaceae* family. There are 106 types in Central Asia and Kazakhstan. The types of this group include: volatile oils, fodder, bee, herbal, starch-sugar, aromatic herbs, food and technical plants.

The chemical components of the members of *Ferula* L. group have been profoundly studied by the scientists of the Institute of Plant Elements′ Chemistry G. P. Nikonov, A. I. Saidhodjayev, V. M. Malikov.

More 50 types of *Cousinia microcarpa* Boiss studied in Uzbekistan, approximately 250 terpenoid elements have been sorted out (Saidhodjayev et.al, 1974; Sagitdinova et.al, 1977, 1978; Melibayev, Rahmankulov, Saidhodjayev, 1980).

Presently, nearly 100 *Cousinia microcarpa* Boiss types have been defined as containing sesquiterpenes matters. 66 (54.7%) *Cousinia microcarpa* Boiss terpenoid coumarins, 40 (35.5%) type is ester, 15 (12.4%) type is sesquiterpene lactone. Mostly sesquiterpene lactones can be found in monocarp types present in desert areas; perennial policarp types in mountain zones contain coumarins and esters.

As a result of complex study of *Cousinia microcarpa* Boiss found in Central Asia, brand new preparation and medicines are being created (Saidhodjayev, et. al, 1974; Melibayev, Rahmankulov, Sayidhodjayev, 1980; Malikov et. al, 1998; Kurmukov, Ahmedhodjayeva, 1994). It has been identified that *F. tenuisecta* plant contains oestrogen matters. Thus, on the grounds of this exploration tefestrol medicine apllied in gynaecology and panoferol drug used in veterinary science have been created.

F. varia plant preserves lyuteolin-7-*O*-β-*D*-glucopyranozide. It has been stated that this substance under Refrosizin name have been undergoing clinic tests (Maksumova et.al, 1993).

It should be noted, that currently from *F. foetida, F. kuhistanica* plants′ roots glue (resin, pitch, tar) extracted and hundred tons of raw materials are being exported abroad. This fact is resulting in diminishing plant reserves. To our mind, if new medicines are created from these resins in our country, instead of exporting raw material, the plant reserves would be preserved for good. We think that our scientists possess enough scientific potential and facilities.

THE PRESERVATION OF NATURAL RESERVES OF THE TYPES OF *Ferula* L. GROUP AS A CRUCIAL PROBLEM

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The members of *Ferula* L. group are put into *Apiaceae* family. There are over 170 types in the world. Above 110 types of the group spread in Central Asia (Rahmonkulov, 1999).

The members of *Ferula* L. group are the plants with volatile oils, sweet tasting, containing rezin, herbal, terpenoids preserving, honey (sweet) emitting, fodder, food, starch and sugar-born.

The types of *Ferula* L. group have been applied in curing various deseases since ancient times as they have volatile oils, starch and resin in their composition. The solid mass (substance) extracted from them were called as kina, sapagen, asafetida, galbanum, sumbul, ammoniakum, etc. by aborigines.

The root and glue of *Ferula* L. were used in confectionery and perfumery in such ancient eastern countries as Iran, India, Pakistan and Afghanistan.

The scientists of the Institute of the Chemistry of Plant Matters created such medicines as tefestrol applied in curing gynaecological disorders and panoferol used in veterinary medicine from the chemical substances extracted from *Ferula* L.

Out of over 50 types of *Ferula* L. growing in Uzbekistan, one third is endemic type and occur only in certain territories. For instance, *F. nuratavica, F. helenae* types happen in Nurota mountain ridge.

It should be highlighted that adoption of new lands, inundation of desert areas (the Aydar-Arnasoy lakes system), overpasturing is leading to diminishing the natural fields of *Ferula* L.

Hundred tons of resin (pitch) extracted from *Ferula* L. had been exported in the last decades. As a negative result of incorrect extraction of glue and resin from plants *F. foetida* and *F. kuhistanica* plant types are getting rare in the natural reserves in the southern territories of Uzbekistan.

In order to conserve the types of *Ferula* L. group, the following activities need to be carried out:

– to diminish the number of ranch cattle grazed in pastures;
– to completely abide by the rules of collecting and preparing herbal substances;
– to provide chances and conviences for them to regenerate by using fields by turns;
– to prepare the soil in every 4 or 5 years in order to extract glue;
– to maximum use drugs (medicines, preparations) extracted from resin (pitch) instead of raw resin (pitch) itself.
– to discontinue harvesting over the allocated quota;
– to make preparations for growing (increasing) plants from their seeds.

ANALYSIS OF THE INFLUENCE OF MICROWAVE RADIATION ON THE ALTERATION OF COTTON CAKS UNDER MOIST-HEAT TREATMENT

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Gossypol is a valuable raw material for obtaining of medicinal products containing gossypol, and therefore, conducted extensive research on its extraction from cottonseed oil.

Analysis of manufacturing technology of cottonseed oil on a "pre-press-extraction" shows that the bulk of the free gossypol undergoes a change, i.e. communicates with other related triacylglycerols substances (proteins, phospholipids, etc.) occurs when moisture-heat treatment meal in harsh conditions. This occurs in high (100–105°C) temperature, presence of moisture and oxygen. Due to the hard regime of moisture-heat treatment of meal on cottonseed oil destruction of volatile substances, the formation of hydroperoxides and secondary products of oxidation, hydrolytic cleavage of triacylglycerols, phospholipids changes, the interaction of gossypol with proteins, sugars, etc occur [1].

All this items dictate the need for moisture-heat processing of cotton meal under mild conditions, in particular with the use of microwave radiation.

Applying the latest allows in the shortest time produce surround induction heating cotton meal the smallest change in the content of gossypol and its derivatives.

Certainly, the use of microwave radiation requires the selection of the optimal conditions of moisture-heat processing of cotton meal that ensures maximum yield of gossypol from pressed oil [2].

We have conducted a comprehensive study of the process of moisture-heat treatment of cotton with different husk content of meals (5 to 15% by weight meal) using microwave radiation at a frequency of 2450 MHz. Experiments carried out within from 2 to 20 minutes to determine the optimal time of microwave radiation [1].

It was found that microwave radiation at a frequency of 2450 MHz optimal time moisture-heat processing of cotton meal is 12–15 minutes. Thus, husk content of meal should not exceed 10%, and humidity – 13–15%.

Thus, these studies allow us to recommend this technique for maximum clearance in pressing cottonseed oil which is extracted gossypol on the pharmaceutical industry.

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STUDY OF EASILY OXIDIZED COMPONENTS OF FAT PHASE IN MARGARINE PRODUCTS

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It is known that easily oxidized components in margarine products are those highly unsaturated fatty acids (such as linolenic acid, linoleic and etc.) which in the presence of catalysts (copper, iron etc.) easily attach to themselves the oxygen.

Despite the presence of naturally occurring antioxidants in margarine products an oxidation process is very fast, especially at increase of the temperature. This results in formation of oxidized fatty acids with some unpleasant odor and taste. Also carcinogens are harmful for consumers′ health, difficult for digestion and have negative impact on the quality of produced margarine products.

Those synthetic antioxidants that applied in practice are not yet thoroughly studied and not always effective during inhibition of oxidative processes (depending on the type of margarine product).

We have studied some naturally occurring antioxidants derived from vegetable oils as a result of preservation process of different types of margarine products. In particular, phosphatide concentrates, tocopherols and other naturally occurred antioxidants received from margarine production and during their long-time preservation have been studied.

For example investigated tocopherol derived from soybean oil in various forms. A comparative study of margarine in their long-term storage had been carried out.

Stability of margarine products was determined by the variation of the index of peroxide value of fat phase.

It was determined that consumption of the above-mentioned antioxidants depends on the content of unsaturated fatty acids and their position in the structure of triacylglycerol′s fat phase as well as on the conditions of their input in the compound of produced margarine products. As such, for example, multiple deodorization of fat phase causes strong decrease of natural antioxidants level in margarine products that calls for re-consideration of the existing technology in producing of oil-based margarine.

The complexity of oxidation mechanism in margarine products during its long-term storage time requests for new researches in terms of efficient composition of natural antioxidants derived from vegetable oils. By this, we have studied various compositions of antioxidants derived from natural tocopherol, sesamol and β-carotene in the preparation of various types of margarine.

It is determined that by introduction of antioxidants composition consisting of “tocopherol–sezamol” at a proportion of 50:50, a peroxide value of margarine decreases at 25–30%, whereas with the composition of “tocopherol-β-carotene” is makes 15–20%. This shows that the first composition of antioxidants is more efficient in terms of increasing margarine oxidation value during its long-term preservation time compared to the last one.

As such, researches conducted on easily oxidized components of margarine fat phase products show the necessity in individual selection of natural antioxidants and rational ways of their use.

NUTRITIONAL INDEX OF SOME DOMINANT PLANTS FROM CENTRAL KYZYLKUM AREA

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Biochemical content of forage plants is the evaluation criterion of their nutritional value. The nutritional value of the studied plants was analyzed by determination of hygroscopic moisture, ash, crude protein, crude cellulose, crude fat and nitrogen-free extractives. The researches included the study of the content of the main components during growing season of some commonly dominant forage plants from Central Kyzylkum area – *Calligonum leucocladum* (Schrenk) Bunge*, Artemisia diffusa* H. Krasch*., Astragalus villosissimus* Bunge, *Haloxylon aphyllum* (Minkw.) Iljin.

The Nutrition of Dominant Plants

Season	Hygroscopic moisture	Ash	Crude protein	Crude fat	Crude cellulose	Nitrogen-free extractives
			Calligonum leucocladum			
Spring	6.7	9.1	13.3	2.6	9.4	58.8
Summer	6.6	10.6	9.3	1.3	27.7	44.4
Autumn	5.1	10.6	7.2	2.1	34.6	40.4
			Artemisia diffusa			
Spring	6.9	16.7	20.1	9.5	15.6	31.1
Summer	7.8	17.4	11.6	5.5	34.7	22.9
Autumn	6.5	16.9	9.3	6.5	43.5	17.1
			Astragalus villosissimus			
Spring	7.4	7.7	17.8	2.9	22.8	41.3
Summer	6.8	6.1	19.2	1.6	38.0	28.2
Autumn	4.8	6.0	19.3	1.0	39.9	28.9
			Haloxylon aphyllum			
Spring	5.5	26.7	11.0	2.4	14.1	40.1
Summer	7.7	29.0	7.4	1.1	22.9	31.8
Autumn	7.9	29.6	5.3	1.9	26.9	28.3

The results of these researches concern that the studied dominant forage plants are highly nutritious in spring. The low amount of cellulose and ash, and the relatively high amounts of protein, fat and nitrogen-free extractives in the spring provide a high nutritional value of plants in this season. The high content of cellulose in *Artemisia diffusa* and *Astragalus villosissimus* during the growing period does not diminish their nutritional value, as high amounts of crude protein in their composition has a positive effect on plants palatability by animals.

PARTIAL CHARACTERIZATION OF PROTEOLYTIC ACTIVITY IN *Sabal minor* AND *Sabal bermudana* SEEDS

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The present study was undertaken to investigate the changing of total proteolytic activity in seed germination process in Sabal species. Also the effect of presoaking of seeds in gibberellic acid was revealed. The experiment was carried out under laboratory conditions during 30 days using 2% casein in phosphate – citrate buffer (pH 8). Protease activity was assayed spectrophotometrically, the amount of enzyme was calculated a unit on 1 mg of protein per hour.

Obtained results shown that the synthesis and release of proteases begin in 6 days from starting the experiment: 0.6–2.87 u/mg of protein in control (distilled water) and 0.4–2.83 in test (GA) (Table). The proteolytic activity in *S. minor* cotyledons was maximal on the eighteenth day of seedling – 6.56 units in control, 5.73 – in test. In month of seedling the level of protease falls, reaching 1.4–2.8 units.

TABLE. **Proteolytic Activity in Seeds (unit/mg protein per hour)**

Days of seedling	2	6	10	14	18	22	26	30
				S. minor				
Control	0.6	2.87	4.7	5.8	6.56	5.62	4.2	2.8
Experimental	0.4	2.83	3.32	4.56	5.73	4.3	3.1	1.45
				S. bermudana				
Control	0.16	0.35	1.32	2.7	4.3	5.3	4.2	1.85
Experimental	0.23	0.56	2.25	3.56	4.7	5.89	4.1	2.86

A similar trend in dynamic of proteolytic activity can be observed in *S. bermudana* species. The maximum accumulation of protease fall on the 22-th seedling day: 5.3–5.89 units.

The results demonstrate that GA treatment did not cause the protease level. Biochemical changes in test almost identical to those in control. This is the fact that the soaking in water stimulates biochemical processes without using chemical enhancers in viable seeds. So, the most beneficial method was soaking the cleaned seeds in water.

SYNTHESIS AND PHARMACOLOGICAL ACTIVITY OF MONOTHERPENYLSULFANYLTRIAZOLES

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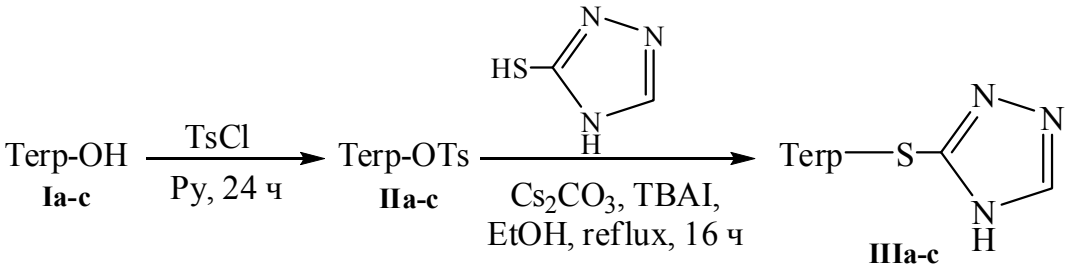
Natural monoterpenoids represent one of the most interesting and promising from the viewpoint of their synthetic possibilities. Important direction of chemistry monoterpenoids are functionalization of the starting substrates in order to obtain pharmacologically active compounds.

In this paper we synthesized new sulfanyltriazoles **IIIa–c** on the basis of pinane and carane monoterpenoids (Scheme 1). Initial terpene alcohols **Ia–c** were converted to tosylate derivatives by interaction with merkaptotriazole which gave the desired product. Monotherpenylsulfanyltriazoles were isolated in pure form by silica gel column chromatography and characterized by NMR and IR spectroscopy.



Terp= (**a**); (**b**); (**c**)

Toxicity of ethanol solutions of the monotherpenylsulfanyltriazoles was evaluated by the ability of compounds to induce hemolysis of red blood cells of laboratory mice (*in vitro*). Membrane protective and antioxidant activities were determined by the inhibition level of H_2O_2–induced hemolysis, deceleration of accumulation of secondary products of lipid peroxidation and the oxidation of oxyhemoglobin of red blood cells. Despite the low cytotoxicity at the concentration 100 μM all the studied compounds exhibited high membrane protective and antioxidant activities. That is perspective and requires more detailed studies of biological activities of these compounds in various model systems.

This work was supported by the Russian Foundation for Basic Research (RFBR Project №13-03-01312a) and by the Ural Branch of RAS (12-U-3-1015).

PLANT METABOLOMICS: RESOLUTION OF ELUSIVE PEAKS OF BIOACTIVE TRITERPENOID SAPONINS IN LC-MS PROFILES FROM *Barbarea vulgaris* AND IMPLICATIONS FOR PLANT-INSECT INTERACTIONS

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Plant metabolomics is a state-of-the-art approach in identification of plant bioactive compounds towards various biotic/ abiotic stresses and play a key role in natural product discovery (Fig. 1).

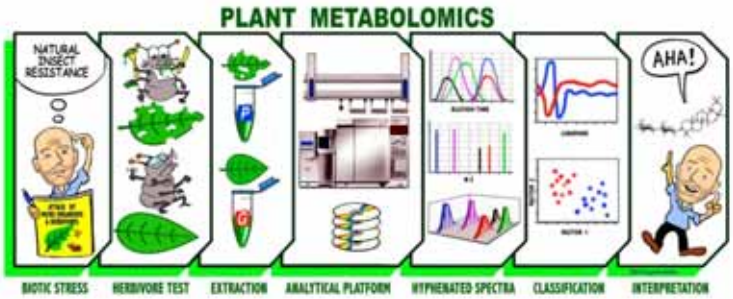

Fig. 1.

Previous studies on metabolomic profiling of 127 F2 *Barbarea vulgaris* plants derived from a cross between a parental glabrous (G) and pubescent (P) type by LC-MS, revealed four bioactive triterpenoid saponins (hederagenin cellobioside, oleanolic acid cellobioside, epihederagenin cellobioside, and gypsogenin cellobioside) that correlated with resistance against the insect herbivore, *Phyllotreta nemorum* [1]. Our work demonstrates the application of a novel multi-way decomposition technique Parallel Factor Analysis2 (PARAFAC2) [2] for resolving complex LC-MS data obtained from the 127 F2 *Barbarea vulgaris* plants. PARAFAC2 enabled resolution and quantification of several elusive (e.g. overlapped, elution time shifted, low s/n ratio and severely hindered under noise peaks) chromatographic peaks, which could not be detected and quantified by conventional chromatographic data analysis methods. In order to evaluate metabolite-insect resistance relationship, PARAFAC2 scores of triterpenoid peaks and plants' resistance level were used for developing partial least squares (PLS) regression models. This approach allowed identification of five additional possible natural insect deterrents that were structurally similar to those previously identified bioactive triterpenoid saponins (based on LC-MS/MS fragmentation patterns). More structural information of these natural pesticides of *Barbarea vulgaris* and application of PARAFAC2 method are described in detail in [2].

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THE VEGETATION OF GEORGIA – A POTENTIAL SOURCE OF THERAPEUTIC DRUGS

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A number of plants rich in certain classes of natural compounds were identified by preliminary phytochemical study of Georgian flora.

Salvia officinalis, Astragalus falcatus, Urtica dioica, Pueraria hirsuta, Trifolium trichocephalum were selected by further study. Crude purified phenolic compounds were obtained and purified. Further chemical study revealed the presence of kaempferol, quercetin and luteolin derivatives and condensed tannins in *Salvia officinalis*.

34 individual flavonoids were isolated and identified from the investigated plants. Five of them were new. They were characterized as falcoside C – quercetin-3-*O*-β-*D*-galactopyranosyl-(6→1)-*O*-α-*L*-rhamnopyranosyl-(3→1)-β-*D*-glucopyranoside, 7-*O*-β-*D*-glucopyranoside; falcoside D – isorhamnetin-3-*O*-β-*D*-galactopyranosyl-(6→1)-*O*-α-*L*-rhamnopyranosyl-(3→1)-β-*D*-xylopyranoside, 7-*O*-α-*D*-rhamnopyranoside (*Astragalus falcatus* Lam.); urticyanine 1-pelargonidin-3-*O*-glucodigalactoside; urticyanine 2-pelargonidin-3-*O*-[ξ (vanylil)-xylosyl] ξ-xyloside; urticyanine 3-pelargonidin-3-*O*-β-*D*-xyloside (*Urtica dioica* L. var. *rubescens* Gvin. et Kav.)

The establishment of the structures were carried out on the basis of study of the products of chemical transformation and IR, UV, ^{1}H and ^{13}C NMR, HSQC, HMBC, DEPT, COSY data and mass spectrometry.

Pharmacological study of these substances *in vitro* and *in vivo* experiments showed a high leukopoietic, diuretic, hypoazotemic, cardiotonic and antispasmodic activity.

Based on the results of the chemical and pharmacological experiments the development of novel drugs has been started, as well as technological and validation methods.

ALKALOIDS OF *Catharanthus* F. ALBUS (SWEET) G. DON, INTRODUCED TO WESTERN GEORGIA

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Genus *Catharanthus* six species a medicional plants comprise. *Catharanthus* F. albus (Sweet) G. Don is the one of species of *Apocynaceae* family. In a present articale the separation process of pharmacological active total alkaloids from *Catharanthus* F. albus, introduced in Western Georgia was studied. Separation of alkaloids from herbal material was realized with microfiltration through laboratory ftoroplast F-4 membrane at descending flow rate 200→50 mL/h and pressure 0.12 atm. The obtained two fractions: A_1, A_2. In all cases gum fractions A_1 and A_2 were dissolved in chloroform and extracted with posphate buffer pH 7.0; 5.0; 3.0; 2.0: the buffer layer was extracted chloroform and then basified with ammonia solution to pH 10 again extracted with chloroform.

GC/MS analysis revealed that ajmalicine (M^+ 352 (100%)), akuammicine (M^+ 322, *m/z* 121 (100%) and viudoline (M^+ 456) gc/ms predominate in buffer fractions of sum A_2 when compared with GC/MS chromatograms of authentic samples. Vincaleucoblastine was obtained by preparative TLC and was confirmed spectroscopically (IR, ^{13}C NMR). Catharantine and lenrosine was confirmed by TLC comparisons with autentic samples.

The fraction A_2 were method separation procecds by the principle of extraction of the target alkaloids. As a result of the research concluded following: the A_1 fraction is enriched dimeric alkaloids: vincaleucoblastine, leurosine, the A_2 fraction is enriched monomeric alkaloids: vindoline, catharantine, akuammicine, ajmalicine. Thus exthraction of alkaloids from *Catharanthus* F. albus procecds selectively. Alkaloids ajmalicine, leurosine, akuammicine, vindoline were used as authentic samples.

FLAVONOIDS AND TRITERPENOIDS OF *Cephalaria media* FROM AZERBAIJAN FLORA

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With the aim of finding new sources of bioactive substances, we studied the aerial parts of *C. media* L. i t v, fam. *Dipsacaceae*. It should be noted that *C. media* is an endemic species for the Caucasus. Currently, chemical composition and pharmacological properties aren′t studied.

1.0 kg of dried flowers was extracted with 80% ethanol in the ratio 1:8 twice, extracts were evaporated till aqueous residue and treated successively with chloroform, ethyl acetate and *n*-butanol. From the ethyl acetate extract flavonoids were received by preparative paper chromatography cynaroside and quercimeritrin. Cynaroside – luteolin 7-*O*-β-*D*-glucopyranoside structure $C_{21}H_{20}O_{11}$, mp 250–252°C (ethanol). UV spectrum (MeOH, λ_{max}, nm): 255, 267 melt., 349. Products of acid hydrolysis (4% H_2SO_4, 4h.): luteolin, *D*-glucose. Quercimeritrin – quercetin-7-*O*-β-*D*-glucopyranoside $C_{21}H_{20}O_{12}$, mp 252–254°C (ethanol). UV spectrum (MeOH, λ_{max}, nm): 254, 370. Products of acid hydrolysis (4% H_2SO_4, 4h): quercetin, *D*-glucose.

Quercimeritrin wasn′t detected in the leaves. Only one flavonoid cynaroside was isolated from leaves.

For purification of *n*-butanol extract from polyphenolic compounds it waspassed through aluminium oxide. *N*-butanol solution is evaporated to dryness and subjected to acid hydrolysis (7% H_2SO_4, 5 hours). Then, the hydrolyzate was cooled and treated with chloroform. From the chloroform extract by column chromatography on aluminium oxide oleanolic acid: $C_{30}H_{48}O_3$, mp 303–305°C (ethanol), $[\alpha]_D^{20}$ +79 ±2° (with 1.2; pyridine–methanol) and hederagenin: $C_{30}H_{48}O_4$, mp 322–324°C (ethanol), $[\alpha]_D^{20}$ +76 ±2° (with 1.0; pyridine–methanol) (eluents: chloroform and ethanol) was obtained.

After neutralization of hydrolyzate with barium carbonate sugars glucose, galactose, arabinose and rhamnose were founded by paper chromatography.

All isolated substances were identified by their physic-chemical properties and spectral data. In some cases the comparison of standard samples used.

Note, that cynaroside and its aglycone luteolin decrease cholesterol and triglycerides in the blood. In addition, luteolin has anti-oxidant, anti-inflammatory, anti-allergic and anti-carcinogenic properties.

STUDY OF SYNTHESIS OF SOME 20-HYDRAZONES OF 16α,17α-EPOXI-5α-PREGNAN-3β-OL-20-ONE

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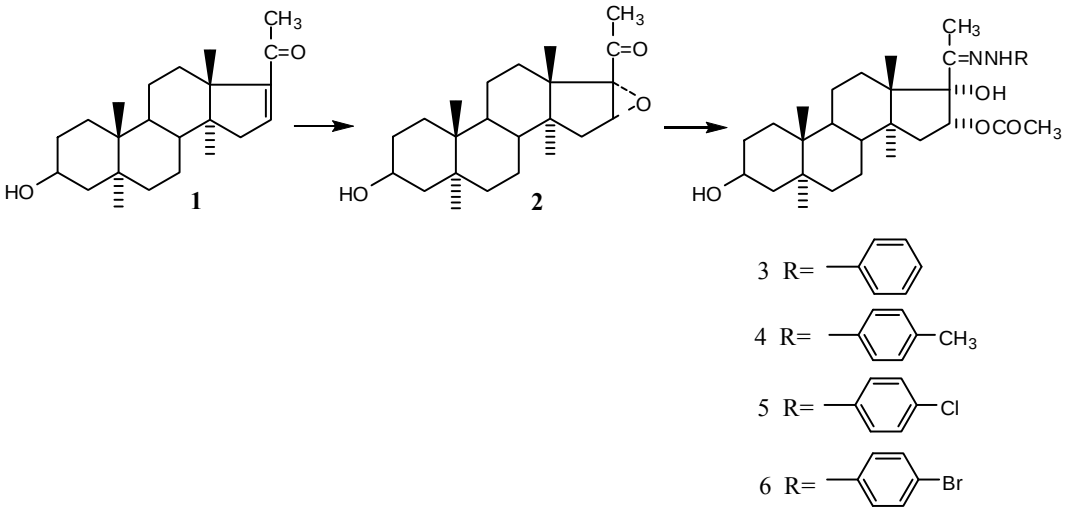
The interest towards the chemical modification of steroidal compounds is due to the broad biological activity typical to their derivatives. Tigogenineis obtained from the *Yucca gloriosa*, which has been introduced in Georgia. The intermediate products of the tigogenine transformation are 5α-steroidal ketones. Studying the interactional reactions of these ketones with differenthydrazines and acid hydrazides is of both theoretical and practical importance.The obtained hydrazones and pyrazolines exhibit high antibacterial and antiviral activities.



5α-Pregn-16-en-3β-ol-20-one (**1**) was obtained from tigogenine, which reacts with hydrogen peroxide in the area of alkaline methanol giving 16α,17α-epoxi-5α-pregnan-3β-ol-20-one (**2**). The ability to synthesize 20-hydrazones (**3–6**) by steroide (**2**) and hydrazines (phenilhydrazine, *p*-methyl-, -chlor-, -bromphenilhydrazine) condensation in anhydrous acetic acid at 25°C and 118°C has been studied. These hydrazones are interesting as potentially biological active compounds.

RECEIVING AND PHYSIOLOGICAL ACTIVITY OF NEW OXYHUMIC PREPARATIONS FROM PEAT

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Humic acids and products of their chemical modification are important for use in various areas of a national economy. They find the main application as growth factors and fertilizers in agriculture. Considerable interest in the applied plan is presented by oxyhumates substances which are recommended for application as humic growth factors, fertilizers and is superficial – active agents. It is offered [1] to receive oxyhumates from peat by its oxidation by hydrogen peroxide in the alkaline environment in rather severe constraints at 125°C in the autoclave within 4 hours in the presence of cobalt and copper salts as catalysts. Such ways allow to receive humic fertilizers with an exit of 75–93% from the organic weight of the peat, containing cobalt and copper as microcells. We developed a new way of receiving oxyhumates preparations at peat oxidation by hydrogen peroxide in water ammonia in the conditions of cavitational processing [2].

Receiving process nitrogen of containing humic preparations from peat carried out as follows. Hinge plate of initial peat humidity of 50% weighing 2.0 kg process in the rotor cavitational device with a frequency of rotation of a rotor of 3000 rpm within 30 min in suspension 0.5–5.0% water solution of ammonia, and then oxidize hydrogen peroxide (in calculation of 2.5–20% of H_2O_2 from the weight of absolutely dry peat) at a temperature of 60°C in the conditions of cavitational processing during from 15 to 60 minutes at the hydromodule 2 × 4. The cooled reactionary mix unload and centrifuge, separating a liquid phase (a target product) from the firm rest. Then a liquid phase concentrate in vacuum at 50°C before receiving the dry rest. In the received dry rest define the content of the general nitrogen. In a liquid phase determine the content of carbon of organic substances by Tyurin′s photocolorimetric method (in g/L). The liquid oxyhumates preparations containing in the structure of 9.5% of nitrogen and to 157 g/L of humic substances are received.

For clarification of effect of possible stimulation or growth inhibition when using the received oxyhumates products as growth factors of crops, determination of viability of seeds of a spring-sown field by a method of vegetative experiment was carried out. It is shown that additives oxyhumates ammonium (from peat) in concentration of 0.01 and 0.03% lead nitrogen of containing humic preparations to increase in viability of a spring-sown field in comparison with control on the average for 10.0–12.5%.

Thus, it is established that the received products of oxidation of peat hydrogen peroxide and the water-ammoniac environment in the conditions of cavitational processing are effective growth factors of plants.

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THE USE OF 3-PHASE EXTRACTION FOR ALCALOIDS OBTAINING

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For the first time the method of a 3-phase extraction is used in the production of several alkaloids. For the first time are deduced equations that allow to describe the extraction process in the 3-phase system. Previously, we proposed a method for 3-phase extraction for the preparation of some biologically active compounds from plant materials. The method of 3-phase extraction (system: raw material – water or water containing solvent – liquophobic solvent) allows to combine the processes of extraction of target compounds from raw materials and converting them into an organic solvent, using one vessel or reactor, which greatly simplifies the process of obtaining. Some reduction in the coefficient of mass transfer in time is compensated by the addition of new portions of the organic solvent, which plays a role of the kind of pump. This work shows the possibility of using this method to obtain alkaloids. The dependence of the yield of the desired alkaloids (F) of a number of parameters: the process time (t), the dispersion of raw material (d), the ratio of solid and aqueous phases (n), the ratio in the liquid-liquid system (m), number of stages of separating the organic phase and adding the new amount of organic solvent (k), the intensity of mass mixing (f), is described by a linear equation of the type: $F = A\ t^a\ d^b\ n^c\ m^d\ k^e\ f^g$, where A, and a, b, c, d, e, g, us – are the coefficients, specific to each alkaloid. Simplifications of the scheme, wetting the raw material with organic solvent during extraction increase the yield. Receiving of colhamin and colchicines. Into the extraction vessel are placed shredded tubers of Colchicum Speciosum Stv., water, 1,2-dichloroethane or chloroform, in a ratio of 1:6:3. The process is conducted at room temperature for 1 hour. After separation of the organic phase and addition of its new quantity the extraction is repeated. Isolation of alkaloids from the organic phase is conducted by usual methods. Output increases by an average of 30%. Receiving of platifillin. Into the extraction vessel are placed underground or overground parts of Senecio rhombifolius, 2–4% sulfuric acid, 1,2-dichloroethane or chloroform, in a ratio of 1:9 (for underground parts), 1:17 (for the overground):4. Extraction is carried out for 1 hour, after which the metallic zinc is added, and then 25% ammonia solution. The total process time is 2 hours, the process is carried out twice. The yield increases of 25–30%. Receiving of hyoscyamine. Into the extraction vessel is placed grass of the *Atropa belladonna* L., 25% ammonia solution and 1,2-dichloroethane or chloroform in the ratio 1:2:6. Extraction is carried out for one hour, is carried out twice. The isolation of alkaloid is carried out by the usual method. Output of hyoscyamine is increased of 18–22%.

In all schemes is provided the complete removal of the organic solvent from the end-product.

PHENOLIC CONSTITUENTS OF *Helleborus caucasicus* LEAVES A.Br.

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Helleborus species (*Ranunculaceae*) distributed in Europe and Asia, mostly for their content in steroidal compounds are studied. In recent years phenolic glycoside derivatives and quercetin glycosides have been reported from the aerial parts of some European spp [1–3].

For the first time *Helleborus caucasicus* A. Br. was researched for its phenolic profile.

Phenolic fraction (40% MeOH) from *Helleborus caucasicus* leaves was subjected to the column chromatography (LiChroprep RP-18, 40-63 μm, Millipore Corp., Bedford, MA), followed by washing with distilled water and then with increasing concentration of aqueous methanol (2.5% increments from 0% to 100% MeOH). Fractions containing 1–3 major compounds were purified on a 2 cm × 50 cm, 25–40 μm RP-18 glass column using an isocratic system (ACN-1% AcOH) optimized for each one based on the analytical separation. This allowed to isolate 7 individual flavonoides: quercetin-3-*O*-β-*D*-xylopyranosyl-(1→2)-*O*-β-*D*-galactopyranosyl-7-*O*-β-*D*-glucopyranoside (**1**), kaempferol-3-*O*-[2-(*E*-caffeoyl)]-β-*D*-xylopyranosyl-(1→2)-β-*D*-galactopyranosyl-7-*O*-β-*D*-glucopyranoside (**2**); quercetin 3-*O*-[2-(*E*-caffeoyl)]-β-*D*-xylopyranosyl-(1→2)-β-*D*-galactopyranosyl-7-*O*-β-*D*-glucopyranoside (**3**); quercetin-3-*O*-[2-(coumaroyl)]-β-*D*-xylopyranosyl-(1→2)-β-*D*-galactopyranosyl-7-*O*-β-*D*-glucopyranoside (**4**); quercetin-3-*O*-[3-(*E*-caffeoyl)]-β-*D*-xylopyranosyl-(1→2)-β-*D*-galactopyranosyl-7-*O*-β-*D*-glucopyranoside (**5**); quercetin-3-*O*-β-*D*-galactopyranosyl-(3-hydroxy-3-methylglutaroyl)-7-*O*-β-*D*-glucopyranoside (**6**) and quercetin-3-*O*-β-*D*-xylopyranosyl-(1→2)-β-*D*-galactopyranoside (**7**). The former six flavonoides (1–6) are novel for plant kingdom and the latter one (**7**) for *Helleborus* genus. The structures of single compounds were elucidated by spectrometric (ESI-MS) and spectroscopic (UV, NMR) means.

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The authors declare no competing financial interest.

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THE SYNTHESIS, PHYSICAL AND CHEMICAL PROPERTIES OF DERIVATIVES OF 3-(4-METHYLPHENYL)-8-[2-(4-PHENYL-5-SULFANYL-4*H*-1,2,4-TRIAZOL-3-YL)ETHYL]XANTHINE – POTENTIAL BIOLOGICAL ACTIVE COMPOUNDS

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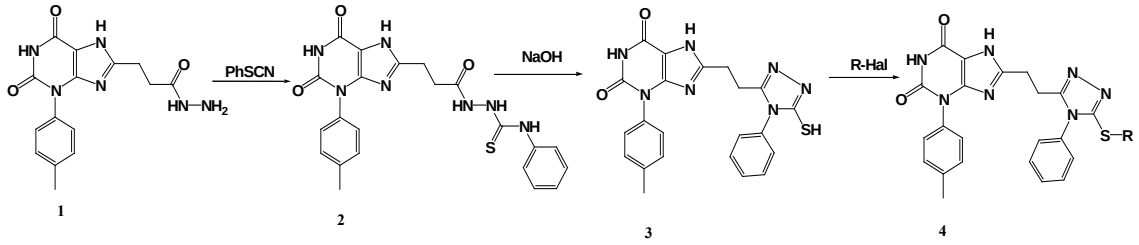
The purine ring system undoubtedly belong to the most ubiquitous heterocycles in nature, as they represent the main structure of many biologically significant compounds, including nucleosides and nucleotides. Substituted xanthine derivatives are an important class of pharmacologically active compounds with well-known activity as adenosine receptor antagonists, phosphodiesterase inhibitors and inducers of histone deacetylase activity etc. This has led to a wide range of medical applications including the treatment of asthma, bronchitis and chronic obstructive pulmonary disease, and their use as diuretics, cardiac stimulants and renal protective agents. At the same time, 1,2,4-triazole derivatives are known to exhibit various pharmacological properties such as antimicrobial, antitubercular, anticancer, anticonvulsant, anti-inflammatory, analgesic and antiviral.

In our opinion, combination of these heterocycle systems in one molecule is promising in terms of creating of novel biological active compounds different active fragments in one molecule.

With this purpose we made a synthesis of 3-(4-methylphenyl)-8-[2-(4-phenyl-5-sulfanyl-4*H*-1,2,4-triazol-3-yl)ethyl]xanthine (**3**) and its *S*-substituted derivatives (**4**). As initial compound we used hydrazide of β-[3-(4-methylphenyl)xanthin-8-yl]propionic acid (**1**). Compound **2** was obtained by condensation of hydrazide **1** with phenylisothiocyanate, by the subsequent cyclization of it in NaOH solution we have got (triazol-3-ylmethyl)xanthine 3. By the next alkylation of it, we have synthesized the *S*-substituted derivatives **4**. It should be noted that under the reaction conditions, electrophilic substitution occurs exclusively on the sulfur atom.



The structures of all synthesized compounds were unambiguously confirmed by physicochemical methods (IR and PMR spectroscopy and mass spectrometry) and their individuality – by the method of thin layer chromatography.

The data of primary pharmacological screening showed that synthesized compounds exhibit antioxidant, diuretic and antibacterial properties that confirmed the perspective of search of potential bioactive substances among (triazol-3-ylmethyl)xanthine derivatives.

SYNTHESIS AND BIOLOGICAL ACTIVITY OF ANNELATED XANTHINE DERIVATIVES

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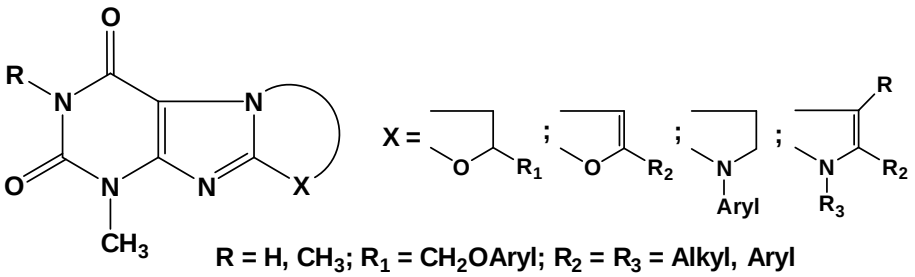
A variety of 1,3,7,8-tetrasubstituted and condensed on the edge "f" xanthine derivatives has been known to have diverse pharmacological effects due to their impact on the purinergic receptors. Since condensed xanthine derivatives are less researched in biological aspect than N- and C_8-substituted of xanthine, there was syntesized a range of previously undescribed oxazolo[2,3-f]- and imidazo[1,2-f]xanthine derivatives of general formula:



R = H, CH_3; R_1 = CH_2OAryl; R_2 = R_3 = Alkyl, Aryl

Oxazolinoxanthines were obtained from the reaction of 8-bromoxanthines with the respective oxiranes in the presence of excessive tertiary aliphatic amines. Oxazolo- and imidazoxanthines were synthesized through 7-acylmethyl-8-bromoxanthines cyclization, whereas imidazolinoxanthines derivatives were obtained by 7-β-chloroethyl-8-bromoxanthines interaction with primary aromatic amines.

The structure of synthesized compounds has been proved by the data of elemental analysis, IR-, NMR- spectroscopy and mass-spectrometry, the individuality has been confirmed through thin layer chromatography method. Acute toxicity, diuretic, analgetic and anti-inflammatory activities have been studied for the synthesized substances.

Acute toxicity was studied with the application of Kerber method. Experience has shown that the obtained substances fall into Toxicity Class 4. The study of diuretic activity of synthesized compounds was performed following E. Berkhin method (with Hydrochlorothiazide and Furosemide used as benchmark standard). The obtained data indicate of prospective viability of the given compounds class as a diuretic.

Analgetic activity of synthesized compounds has been studied applying Acetic acid writhing model, with anti-inflammatory activity researched using Carrageenan-induced Paw Edema model. For benchmark standard were used Sodium Diclofenac and Metamizole. The analysis of received data has proved that synthesized substances are highly competitive as per pain-relieving and anti-inflammatory activity criteria, in some cases even outperforming the benchmark standards. In addition, specific regularities have been established in a "structure–biological activity" row.

SYNTHESIS, PHYSICAL-CHEMICAL AND BIOLOGICAL PROPERTIES OF 8-AMINOSUBSTITUTED 7-β-HYDROXY(OXO)ALKYL(ARYL)-XANTHINES

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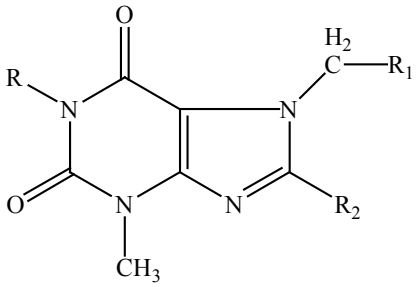
For hundreds of years, mankind uses tea, cacao and coffee to improve mental and physical performance. The main active ingredients of this plants are alkaloids, xanthine derivatives – caffeine, theophylline, theobromine, which have found wide application in medical practice as drugs with CNS stimulantion, antihypertensive, diuretic, bronchodilation activity (such drugs as: pentoxifylline complamine, etofylline, diprofylline, kordabromine etc.). It should be noted that the xanthine alkaloids are part of many drugs combined, and therefore the search for new biologically active compounds, xanthine derivatives certainly is perspective direction for development of new drugs.

The aim of our work is a search of new bioactive compounds in a range of xanthine derivatives. Considerable number undescribed in the literature of compounds has been synthesized of general formula:



R=H, CH_3
R_1=CH(OH)alkyl(aryl); C(O)alkyl(aryl); $CH(OH)CH_2O$alkyl(aryl)
R_2=NHalkyl; NHoxyalkyl; NHalkoxyalkyl; NHaryl; NHalkyl N$(alkyl)_2$; cycloalkylamino

These compounds have been prepared by reacting 8-bromo-3-methylxanthine (theophylline) with halogenalkohols, halogenketones in DMF in the presence of $NaHCO_3$. Reaction of 8-bromoxanthines with oxiranes substituted in the presence of catalytic amounts of triethylamine or dimethylbenzylamine have been prepared corresponding 7-β-hydroxy-γ-alkyl (aryl)-8-hydroxypropyl bromoxanthines. 8-Aminosubstituted xanthines have been obtained from the reaction of the corresponding bromoxanthines with primary or secondary aliphatic in aqueous dioxane or ethoxyethanol.

The structure of the compounds has been confirmed by elemental analysis IR, NMR spectroscopy and mass spectrometry, identity has been confirmed through TLC method.

The study of the potential hypotensive, diuretic, actoprotective, anti-inflammatory, analgesic effects established that most compounds are more active than benchmark standarts.

The dependence of biological activity on the structure of the obtained compounds is discussing now.

SESQUITERPENE LACTONES OF *Centaurea scabiosa* L. AS A PROMISING DRUG CANDIDATES

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The modern pharmaceutical industry is experiencing a great shortage of biologically active chemical compounds promising for use in preventive and therapeutic medicine. Despite the fact that nowadays there are tools for chemical structure modeling depending on the material properties of the molecular target the screening of natural molecules did not lose its relevance still because it is the source of many molecules of candidate drugs. This is mainly due to the fact that native chemical structure of these compounds can provide effective pharmacological interaction, along with a low undesirable side reactions probability.

The group of sesquiterpene lactones produced by plants of the *Asteraceae* family is one of the best examples of biologically active substances that have found very wide application in medical practice. Of greatest interest are antiparasitic (opisthorchiasis, giardiasis, malaria) and antitumor activity of sesquiterpene lactones views.

At the Pharmaceutical Chemistry department of Siberian State Medical University (Tomsk) for a number of years basic and applied research of sesquiterpene lactones of the plants *Centaurea* genus growing in Siberia were carried out. Among these plants *Centaurea scabiosa* L. was the most well studied. By column chromatography on silica gel of this plant lipophilic extracts three sesquiterpene lactones of guaianolide type: cynaropicrin, grosshemine and repin have been isolated and identified. The presence in *C. scabiosa* in prevailing proportion of cynaropicrin allowed to refer this plant to prospective sources anti-opisthorchiasis drug because it is known that this compound has a strong anthelmintic activity against *Opisthorchis felineus* and *Opisthorchis viverrini*. These worms belonging to the class of trematodes form the two largest opisthorchiasis hearths in the world: *O. felineus* – in the Ob-Irtysh basin in which the Tomsk region territory is the most severely contaminated; and *Opisthorchis viverrini* – in Asian countries such as Thailand and Laos.

Anti-opisthorchiasis activity of cynaropicrin isolated from *C. scabiosa*, was confirmed in chronic opisthorchiasis experimental model on golden hamsters. It was observed that cynaropicrin has not adverse effects on the liver biochemical parameters and its efficiency was comparable with that of the reference preparation – Biltricide® (Bayer, Germany).

In addition to this a cycle of applied research was carried out with a result of pharmaceutical substances and dosage forms (tablets and capsules) based on *C. scabiosa* sesquiterpene lactones complex technology development and draft of normative documentation for quality control elaboration.

The experimental results are protected by two Russian Federation patents and show great scientific and practical potential of Siberian flora medicinal plants in the search for new effective drugs for the treatment of socially significant diseases.

COMPLEX PROCESSING OF GRAPE SEEDS AS A NEW SOURCE OF RAW MATERIAL FOR GETTING MEDICINAL PRODUCTS

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Research of grape seeds as a source of getting medicinal products is one of the advanced search directions in implementation of up-to-date and more effective medicinal preparations in national production.

Grape seeds contain the complex of biologically active substances. Red grape polyphenols are of more interest and possess greater biological activity.

Grape seed polyphenols or proanthcyanids have strongly marked antioxidant activity. Regular dietary intake of polyphenols helps preventing and treating cardio-vascular diseases, atherosclerosis, diabetes, gastro-intestinal diseases, liver ones and diseases of bile passages, pancreas, kidneys, immune system, metabolism disorders. It was proved that proanthcyanids prevent the growth of cancer cells.

There is not enough attention to the issue of grape and grape seed processing and it has not been studied as the source of herbal medicinal product. There are no companies to process wine industry wastes and more than 80% of grape husk and seeds containing up to 26% of grape seeds are used entirely as feeding stuff.

Thus, extraction of biologically active substances out of grape seeds and the study of their pharmacological activity and development of medicinal products on their base are the actual task.

Target of research was grape variety seeds: Rkatsiteli, Cabernet, Saperavi, Riesling, Bayanshirei growing in the South-Kazakhstan oblast. We have developed the new technology of the complex grape seeds' processing to extract biologically active substances. Thus, oil, dry extract and sorbent were extracted from the grape seeds.

The complex grape seeds′ processing was performed in three stages. The first stage comprised getting the grape oil by the method of extraction. The second stage included dry extract getting by 20% ethyl alcohol after extracting the oil from the meal. At the third stage the meal was used to get sorbent after the extraction of grape oil and dry extract. Sorbent extraction was 46.7%.The extracted new sorbent meets the requirements of "Gosudarstvennyi standart" (public standard) 4453-74 "activated, refining, powdered charcoal" with coal rank OU-B OKP-21 6236 0200.

We studied the physicochemical and technological properties of extracted substances from the grape seeds such as oil, extract and sorbent. Pharmacological tests were carried out while testing animals, from which we got positive results in defining safety and anti-inflammatory effect of oil and extract of the grape seeds.

Thus, the use of non-waste technology of processing wine industry wastes gives a go-ahead to extract new raw material sources for getting medicinal products.

THE GRIGNARD REACTION IN SYNTHESIS OF 18α*H*-OLEANANE A-SECO- AND A-PENTACYCLO-DERIVATIVES

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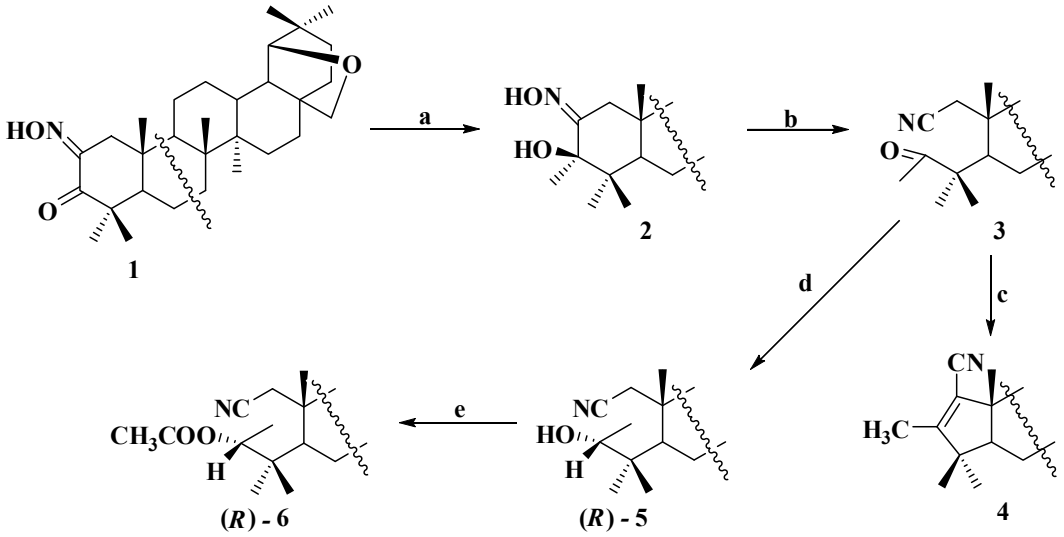
3-Methylsubstituted hydroxyoxime **2** was prepared by interaction of the Grignard reagent (CH_3MgI) with oleanane α-ketoxime **1** [1], by the Beckmann fragmentation of which 2,3-secotriterpene methylketone **3** was synthesized (Scheme 1). β-Substituted pentacyclic A-ennitrile **4** was prepared by chemoselective oxonitrile cyclizations of methylketone **3**.



Reagents and conditions: (a) $CH_3MgI/(C_2H_5)_2O$; (b) $SOCl_2/CH_2Cl_2$; (c) *t*-C_4H_9OH/*t*-C_4H_9OK; (d) $NaBH_4/CH_3OH$; (e) $(CH_3CO)_2O$.

Scheme 1.

18α*H*-Oleanane methylketone **3** effectively inhibits replication of herpes simplex virus type I (HSV, C1 strain), and of HIV-1 (EC_{50} 22.5 ± 19.9 and 7.20 ± 2.8 μg/mL, respectively). Experimentally confirmed are: inactivity of 3(*R*)-hydroxy compound **5** prepared by reduction of methylketone **3** against said viruses, and selective antiviral activity of 3(*R*)-acetate **6** against herpes virus (EC_{50} 21.6 ± 18.9 μg/mL).

This work was financially supported by the Program of Presidium of the RAS "Basic Sciences for the Medicine" (№12-P-3-1009), by the RFBR Grant №13-03-00629, and by grants of the Ministry of Education of the Perm Region for implementation of the research project in the framework of the "International Research Groups" program.

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HETEROCYCLIZATION REACTIONS OF TRITERPENE α-HYDROXYIMINOKETONES

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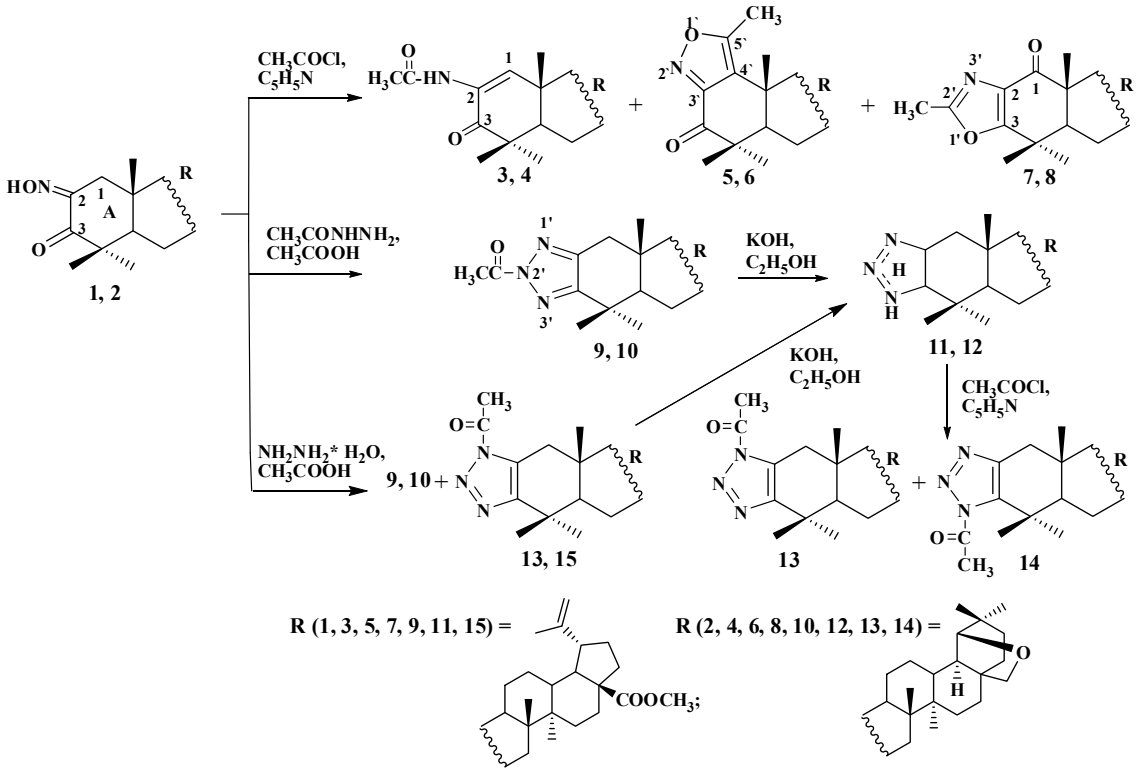
Lupane and 18α*N*-oleanane α-hydroxyiminoketones **1**, **2** [1] are a promising basis for the synthesis of azoles condensed with the A-ring of triterpene skeleton. For example, boiling of α-hydroxyiminoketones **1**, **2** in pyridine with an excess of acetyl chloride leads to a mixture of enamines **3**, **4** with C(1)-C(2)-anellated 5-methylisoxazole **5**, **6,** and with C(2)-C(3)-annelated 2-methyloxazole **7**, **8**. Conditions for the synthesis of *N*-substituted 1,2,3-triazoles **9**, **10** and **13–15**, hydrolysis of which affords a high chemical yield of unsubstituted 18α*H*-oleanane 1,2,3-triazole **12** and of lupane 1,2,3-triazole **11** (IC_{50} 8.4–16.8 μM) cytotoxically active against the RD TE32, A549 and MS cell lines, have been selected.



This work was financially supported by the Programme of the Presidium of RAS "Basic Sciences for the Medicine" (Nr. 12-P-3-1009) and by the RFBR Grant Nr. 12-03-31060_mol_a.

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POLYMERIC DERIVATIVES OF BETULIN

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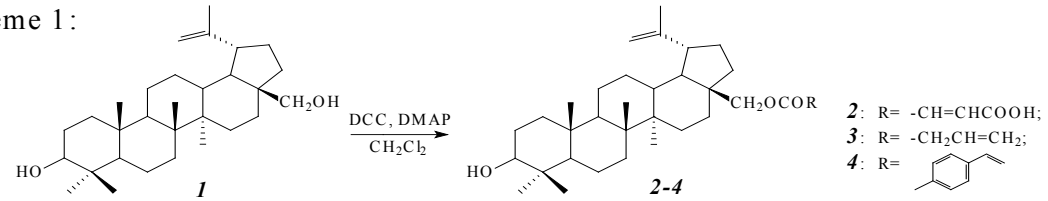
Triterpene derivatives of lupane type are of significant interest due to the broad spectrum of their biological properties and availability of nature compound – betulin for their obtaining. Betulin and its derivatives, betulinic and betulonic acids, have proved to possess antitumoral and antiviral activities [1, 2]. Triterpene introduction into soluble polymer matrix is undoubtedly of present interest.

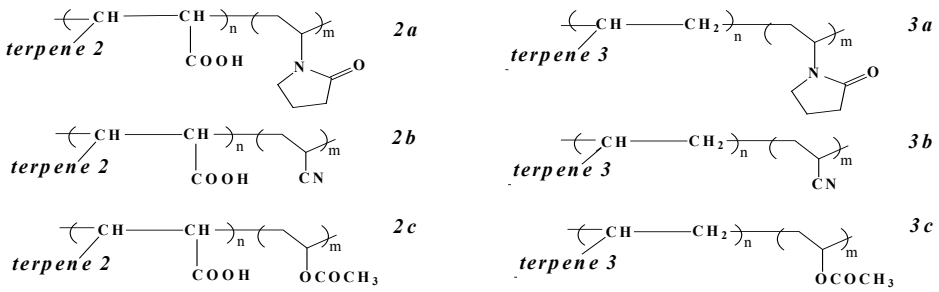
It was found that betulin reacts with maleic, vinylacetic and vinylbenzoic acids with formation of 28-*O*-ethers of betulin **2–4** (Scheme 1).

Scheme 1:



28-*O*-ethers of betulin **2, 3** were found to be copolymerized with *N*-vinylpyrrolidone, vinylacetate, acrylonitrile in the presence of free-radical initiator – AIBN. The structure of new copolymers (Scheme 2) was identified by ^{1}H and ^{13}C NMR spectroscopy. The copolymers obtained are soluble in organic solvents owing to the absence of intermolecular crosslinks.

Scheme 2:



Investigation of biological properties of copolymers shows that copolymer of 28-*O*-maleic ether of betulin with vinylacetate possess cytotoxic activity against rhabdomyosarcoma tumor cells RD TE32.

Financial support by the Russian Foundation for Basic Research (Grant №11-03-96003-r_ural_a) and youth Grant UB RAS (№13-3-NP-59) is gratefully acknowledged.

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RESEARCH OF THE ANTICONVULSANT ACTIVITY OF MEMBERS OF *Betulaceae*, *Lamiaceae*, *Fumariaceae*, AND *Oleaceae* FAMILIES

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Epilepsy is one of the most serious chronic diseases. Irrational treatment of epilepsy can cause deterioration of patient, mental, cognitive and behavioral disorders, personality disorders, or even death. Currently there are a number of synthetic anticonvulsant remedies, but long application of these drugs can cause serious disorders of the central nervous system, the cardiovascular system, musculoskeletal system, endocrine system, etc.

One of the most important areas of pharmaceutical science is search and development of new high-performance drugs. It is known that herbal remedies take a leading position due to their mild assimilation by the human body, application performance, breadth of therapeutic action, along with a minimal risk of side effects, especially during long-term treatment of chronic diseases, which include epilepsy. But currently pharmaceutical markets of Ukraine and other countries of the world have practically no facilities for treatment of epilepsy by herbal remedies.

Analysis of the literature data has shown that some members of *Lamiaceae*, *Betulaceae*, *Fumariaceae* and *Oleaceae* families can provide an anticonvunsant activity. Members of these families are well-spread in Ukraine, so it solves the problem of search of herbal resources. Therefore the scope of our research was determination of the anticonvulsant activity of extracts of *Lamiaceae*, *Betulaceae*, *Fumariaceae* and *Oleaceae* families.

That end extracts of *Ocimum basillicum* L. (Purple and Genovese) herb, *Leonurus cardiaca* L. herb*, Origanum vulgare* L. herb, *Corylus avellana* L. leaves, *Fumaria officinalis* L. herb, *Fumaria shleicheri* Soy.-Will. herb, *Syringa vulgaris* L. herb, *Jasminum officinale* L. herb, and *Forsythia europaea* Degen. leaves were prepared. Analyzed samples of herbal material were collected in different regions of Ukraine. Air-dried and crushed herbs were powdered and exposed to the extraction by water, ethanol 96% and ethanol 50%. Then obtained liquid extracts were dried under a vacuum to dryness.

Screening study of anticonvulsant activity was carried out using pentylenetetrazol model of seizures in albino mice. Animal experimental groups received extracts were intragastrally as preventive maintenance within 2 days, and 30 minutes before the administration of pentylenetetrazol. Results have shown that extracts of *Ocimum basilicum* L.*, Leonurus cardiaca* L. and *Fumaria shleicheri* Soy.-Will. have a pronounced anticonvulsant activity. Thus further study prospective was defined for herbal extracts.

Obtained results can be used for development of the original phytotherapeutic remedy with the anticonvulsant activity.

UNUSUAL FRAGMENTATION DERIVATIVES OF 16-ACETOXY-22-OXOCHOLESTEROL IN REACTION WITH METHYLENETRIPHENYLPHOSPHORANE

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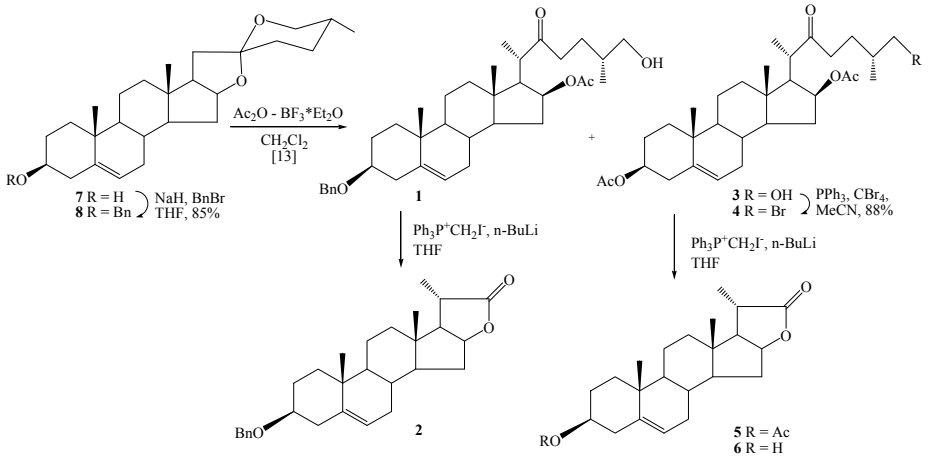
Methylenetriphenylphosphorane (CH_2=PPh_3) is widely used in synthetic practice for a terminal methylenation of ketones, aldehydes, esters and other. Unusual fragmentation reaction we found while olefination of steroidal ketone **1** with methylenetriphenyllphosphorane, in situ generated from $Ph_3P^+CH_2I^-$ action of *n*-BuLi in THF. As a result the lactone **2** was isolated with a moderate yield. Similar reaction of the alcohol **3** and bromide **4** with CH_2=PPh_3 led to the known lactone **5** [1]. By deprotection 3β-hydroxy group of lactone **5** natural *bis*-norcholanic lactone vespertilin **6** which has anti-cancer activity and also used in the partial synthesis of steroids [2]. Benzyl ether **8** was received in result in benzylation of 3β-OH group of a commercially available steroid diosgenin **7** (BnBr, NaH) and then was introduced into the previously developed for 3β-acetate diosgenin acetolysis reaction with Ac_2O–$BF_3 \times Et_2O$ [3]. The obtained compound **1** and **3** (~ 3.4:1) were separated by column chromatography on SiO_2. Ketone **3** was synthesized on the basis of **7** with using a known method [3].



The study was performed under the financial support of the Russian Foundation for Basic Research (Project №11-03-00780).

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THE REACTION OF *N*-[TRI (HYROXYMETHYL)METHANE] ACRYLAMIDE WITH DECYLAMINE IN CONDITIONS OF INVERS PHASE TRANSFER CATALYSIS. FRACTAL STRUCTURE OF THE REACTION PRODUCT

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In organic synthesis very often arises necessity to carry out a reaction between water and oil soluble reagents. There are different ways for solving this problem. One is "Inverse Phase Catalysis" (IPTC), in which case the substrate is transferred from organic phase into aqueous phase [1]. The idea is: the two-phase system is used, one phase is water which contains surfactants in concentrations higher than critical micelle concentration as a transfer agent for substrate from organic phase into aqueous phase [2].

The aim of this work is study the reaction of water soluble *N*-[tri(hydroxymethyl)methane] acrylamide (TA) with oil soluble decylamine (DA) in two-phase system water-heptane in accordance with model "oil-water".

It was shown that the initial rate of reaction TA + DA in two-phase system water-heptane is described by following:

$$W_0 = k[TA]_0[DA]_0$$

The constant of TA + DA reaction rate in the system water-heptane is $1 \cdot 10^{-5}$ L·mol^{-1}·s^{-1} at T = 293 K, W_m = 100 s/min, S = 2 cm^2.

At the high rate of mixing (W_m = 1400 s/min) and in the presence of surfactant until 10% the transferred emulsion doesn′t stabile and the initial rate of reaction is increased on one order. Then stabile emulsion is forming and the reaction is stopped. But, in that case, only monoadduct′s of reaction is formed-*N*-[tri(hydroxymethyl) methane] amide of 3-decylaminopropionic acid (DATPA). That principle can be used for getting pure monoadduct.

It is very interesting the reaction at low rates of mixing. The product of TA + DA reaction isn′t soluble both in water and heptane and during the reaction the DATPA is allocated between water and heptanes as "chemical sandwich". It is shown that DATPA at the interface of phases water-heptane forms tongue-type fractal structure.

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STUDY OF THE ANTIMICROBIAL ACTIVITY OF A LIPOPHILIC SUBSTANCE FROM *Lamium album* FLOWERS

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The white dead-nettle is an non-officinal plant used only in folk medicine. However, different groups of biologically active substances have been well investigated in the plant, in particular, flavonoids, iridoids, phenolcarbonic and hydroxycinnamic acids.

From white dead-nettle flowers, we obtained a lipophilic substance in the Soxhlet apparatus, chloroform had been used as an extracting agent. By chromatographic analysis iridoids, lipids and chlorophylls have been identified in the substance.

To study the fatty acid composition, an internal standard (50 μg of tridecane in hexane) and 1.0 mL of a methylating agent – 14% BCl_3 in methanol, Supelco No. 3-3033 were added to 0.50 mg of dried substance in a 2 mL vial. The mixture was kept in a sealed vial for 8 hours at 65°C. During this time, fatty oil was extracted completely from the substance and the fatty acids had undergone the re-etherification. The reaction mixture was decanted and diluted with 1 ml of distilled water.

To obtain methyl ethers of fatty acids, 0.2 mL of dichloromethane was added, the mixture was shaken for 1 hour and subjected to chromatographic study. Fatty acids′ methyl ethers were analysed using chromatography mass-spectrometer 5973N/6890N MSD/DS Agilent Technologies (U.S.A.). Fatty acids′ methyl ethers were identified by calculating the equivalent length of the aliphatic chain (ECL) and using data from mass spectra libraries NIST 05 and Willey 2007 with the total amount of spectra exceeding 470,000, and identification programs AMDIS and NIST. The internal standard mass was used for quantification of components.

Nineteen fatty acids were identified in the white dead-nettle flowers′ substance. In the total number of acids, the dominating ones were the palmic, stearic, oleic, linolic and linolenoic acids.

The antibacterial activity of the white dead-nettle lipophilic substance was studied at the Mechnikov Institute of Microbiology and Immunology. Mueller-Hinton agar was used to determine the antibacterial activity of the preparation. Nutrient agar and Sabouraud′s medium were used to cultivate microorganisms. The following test strains of microorganisms were used: *Staphylococcus aureus* 25923, *Escherichia coli* 25922, *Proteus vulgaris* 4636, *Bacillus subtilis* ATCC 6633, *Pseudomonas aeruginosa* ATCC 27853, and *Candida albicans* ATCC 885/563. The antimicrobial activity was studied using the agar diffusion method (the 'well′ diffusion method).

The substance demonstrated a pronounced antibacterial activity with respect to *Staphylococcus aureus* ATCC 25923, with a diameter of growth inhibition zone d = 30.3 ± 0.4 mm, and to *Pseudomonas aeruginosa* ATCC 27853 with d = 24.3 ± 0.2 mm; and an antifungal effect with respect to *Candida albicans* 885–563 – 18.1 ± 0.4 mm.

The investigation results are a prerequisite to developing medicinal drugs from white dead-nettle raw material with antimicrobial and antifungal activity.

FLAVONOIDS OF SEVERAL SPECIES OF BLACKBERRY

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Blackberry (*Rubus*) is well known genus from family *Rosaceae*. There are about 19 species of genus *Rubus* which found in Ukraine. The most spread species is *Rubus hirtus* Weldstet Kit, *R. eurythyrsiger* Juz, *R. caesius* L., *R. candicans* Weihe.

Extract from blackberry fruits are known as diaphoretic agent. Leaf extract is recommended to treat respiratory system and as anti-tussive agent. Remedies from shouts produce anti-inflammatory action in case of gingivitis, stomatitis and angina. Phytoremedies which made on the base of leaves recommended as diuretic agent.

The goal of research was to investigate flavonoid composition of leaves and shouts of some blackberry species: *R. eurythyrsiger* Juz., *R. hirtus* Weldstet Kit, *R. candicans* Weihe. The samples of herbal drugs were obtained by cutting the shouts in Crimea (Ukraine) in 2011–2012. The samples were dried at 32°C and stored in paper sacks in a dark, cool and dry depository.

To investigate flavonoid composition in detail it was obtained from every herbal drug sample 70%-alcohol extract. The concentrated extract was left for 10 hours at a temperature of 5–10°C to separate chlorophyll and resins. Dark green gummy precipitate separated from the aqueous residue by filtration. Purified extract consistently was treated by chloroform, ethyl acetate and *n*-butanol. Each fractions were concentrated to completely removing of solvent. Thus was obtained the following fraction: chloroform, ethyl acetate and *n*-butanol extracts and water residue. The qualitative composition of each fraction was analyzed by paper chromatography and thin layer chromatography using chromogenic reagents.

To isolate individual components used columns chromatography of sorbent: polyamide, silica gel grade LS 100/250 and preparative paper chromatography and thin layer of sorbent rechromatography, fractional crystallization. For the separation of ethyl acetate fraction of individual components using column chromatography on polyamide sorbent. Concentrated ethyl acetate extract (20.0 g) was applied to the column of polyamide sorbent (d = 5 cm, h = 90 cm) and elution was carried out with chloroform and its mixture with ethanol, increasing the concentration of the latter. Qualitative content of each factions was controlled by paper chromatography in systems of *n*-butanol–acetic acid–water (4:1:2), 15% acetic acid, *n*-benzene–ethyl acetate–acetic acid–water (50:50:1:1) formamide–ethanol (1:3). Fraction with same composition were joined, evaporated to a dry residue, which was dissolved in a minimum amount of 96% ethyl alcohol or methanol and left for crystallization. Major flavonoids, which were included of the fractions isolated by repeated chromatography on polyamide column, fractional crystallization and preparative chromatography on paper. Eight flavonoids has been discovered as a result, conventionally designated as substances **1–8**.

Isolated compounds were identified by physicochemical (UV, IR, PMR spectroscopy), chemical and biochemical methods of analysis. Comparison of the obtained data from the literature and with authentic samples allowed identification of compound **1** with kaempferol, **2** – with quercetin, **3** – astragalin, **4** – kaempferol-3-*O*-arabinoside, **5** – with luteolin, **6** – isoquercetrin, **7** – hiperoside, **8** – rutin. All flavonoids are new for all three species of Rubus genus.

CHEMICAL COMPOSITION OF ESSENTIAL OIL FROM LEAVES OF *Iris versicolor*

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Iris versicolor L**.** (*Blue Flag*) belongs tothe *Iridaceae* family and is a flowering herbaceous perennial plant, growing 10–80 cm high, with a thick creeping rhizome. Leaves radical, well-developed, sword-shaped form. The rhizomes contain a volatile oil; a glycoside, iridin; acids including salicylic and isophthalic; amonocyclic C, triterpenoid; sterols, gum, resin, xanthonesmangiferin, organic acids. Rhizomes of *Iris* are used in homeopathy as anti-inflammatory, astringent, cholagogue, laxative, diuretic, antiemetic, blood and lymph purifier, alterative for sluggish conditions of liver, gallbladder and glandular system. Phytochemical composition of leaf of *Iris versicolor* has not been studied previously. The present investigation describes the chemical composition of the essential oil from leaves of *Iris versicolor.*

Leaves of the *Iris versicolor* had been collected in spring of 2012 in Botanical Garden′s territory of V. M. Karazin, Kharkiv National University. For investigation used chromatography-mass-spectroscopy method. Conditions of research: chromatograph Agilent Technology 6890 N, equipped with mass-spectrometric detector 5973N, capillary chromatographic column INNOWAX with inner diameter 0.25 mm and in length of 30 m. In order to identify the individual components the data of mass spectra libraries NIST 05 and WILEY 2007 had been used.

According to the results of the research the quantitative content of 31 compounds of the essential oil from leaves of *Iris versicolor*has been established. It was determined that the plant raw material contains 0.1% essential oil. Components are present in an amount from 0.1% to 22%.

The dominant components among terpenoids were triterpenoids gualene (16.17%), which has immunostimulating activity; diterpenephytol (22.40%), which is part of chlorophyll and therefore are the most common plants in the isoprenoid, neophytadiene (3.93%); sesquiterpenoids – hexahydrofarnesyl acetone (4.38%), farnesyl acetone (0.99%), farnesyl acetone C (1.68%), monoterpenoids – geranilacetone (0.50%); aromatic compounds – eugenol (0.34%) (stimulator of cell proliferation), phenylacetaldehyde (1.47%), 2-methoxy-4-vinylphenol (1.52%), 2,3,6-trimethyl phenol (0.43%), 3-phenyl pyridine (0.11%), bensylbensoat (0.11%); norterpenoids – β-damascenone (1.11%), 5,6-epoxy-β-ionone (0.41%), β-ionone (0.09%); ketones – megastigmatrienone (0.10%), benzophenone (0.66%) and aldehydes (octanal, decanal), fatty acids (myristicand palmitic acids)and their esters, hydrocarbons.

Component composition of essential oil from leaves of *Iris versicolor* obtained by hydrodistillation showed the presence of mono-, seksviternoidov, diterpenoids and esters contained in small amounts but causing the plant flavor.

Aromatherapy recommends the use of *iris* oil for bronchial inflammation, coughing, as well as in mixtures for the care of the skin. Essential oil of *iris* normalize function of the brain, has a detoxifying, diuretic, expectorant, strengthens the immune system.

The obtained results indicate the prospects of using leaves of *Iris versicolor* as a source for essential oils and medicines.

CARBOXYLIC ACIDS OF *Veronica longifolia* L.

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Veronica longifolia L. belongs to the family *Plantaginaceae*. According to the scientific sources iridoids and flavonoids are most studied groups of biological active substances (BAS) of *Veronica* L. genus.

The aim of our study was to identify and quantify organic acids in the leaves and flowers of *Veronica longifolia* L. by means of chromatography-mass spectrometry.

The objects of the study were herb, leaves and flowers of *Veronica longifolia* L., that have been harvested in the flowering stage in the Kharkiv region in 2012.

The analysis of acid′s methyl esters had deen performed using chromatography-mass spectrometer 5973N/6890N MSD/DS Agilent Technologies. To 0.50 mg of herbal drugs in 2 mL vial internal standard (50 mg of tridecane in hexane) and 1.0 mL of methylating agent – 14% BCl_3 in methanol have been added. The mixture was kept in a sealed vial for 8 hours at 65°C. Sample injection (2 mL) in chromatographic column was performed in a mode *splitless* (without breakdown of flow), the rate of sample injection – 1 mL/min, the period – 0.2 min. The identification of acid's methyl esters was performed by calculating the equivalent length of the aliphatic chain (ECL); using data from the mass spectra library NIST 05 and Willey 2007 combining with programs for identification AMDIS and NIST; the retention time was compared with the retention time of standard compounds (Sigma).

8 aromatic acids, including 5 acids in flowers and 7 – in leaves have been identified and quantified.

Among the identified compounds were: aromatic acids: benzoic, phenylacetic, salicylic, 3-phenyllactic, vanillic, 4-hydroxyphenylacetic, 4-hydroxybenzoic and ferulic acids. In leaves phenylacetic, salicylic and hydroxyphenylacetic acids were found, which weren′t found in flowers. In leaves dominant acids were aromatic ones (mg/kg) benzoic (168.3) and ferulic (332.1); in the flowers – benzoic (243.8), ferulic (219.6), 4-hydroxybenzoic (141.8) and vanillic (344.0) acids dominated. The original acid for flowers was 3-phenyllactic. The total content of aromatic acids in the leaves was 685.7 mg/kg. The total content of aromatic acids in flowers was 1008.0 mg/kg.

In the results of study 13 mono-, dicarboxylic and hydroxycarboxylic acids have been identified and quantified, 12 acids were found in flowers, 11 of them – in leaves. Among them were: caproic (hexanoic), 3-hexenoic, 2-hexenoic, oxalic, malonic, fumaric, succinic, 10-methylundecanoic, suberic, azelaic and 3-hydroxy-2-methylglytaric, malic and citric.

The dominant acids in herbal drugs were (mg/kg) malonic 1325.4 and 1234.4; 3-hydroxy-2-methylglutaric 1441.9 and 1084.3; malic 1139.7 and 2211.3; citric acids 2259.9 and 6235.3 in the flowers and leaves, respectively.

The total content of aliphatic acids in flowers was 6657.4 mg/kg. The total content of aliphatic acids in leaves was 11427.4 mg/kg.

PROSPECTS OF DEVELOPMENT OF ORIGINAL HEPATOPROTECTIVE DRUGS BASED ON EXTRACTS FROM LADY'S BEDSTRAW'S HERB

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In folk medicine in treatment of liver and biliary tract diseases infusion and decoction of Lady's Bedstraw's herb (*Galium verum* L., Madder family (*Rubiaceae* Juss.) are used.

Hepatoprotective activity of raw materials is explained by the presence of biologically active substances (BAS) with significant antioxidant and anti-inflammatory properties – quercetin and luteolin derivatives, hydroxycinnamic acids.

From *G. verum* herb we obtained two dry extracts: from 70% ethanolic extract purified from lipophilic compounds (BCC-T) and from an aqueous extract purified from polysaccharides (ОПК-Т).

In these extracts hydroxycinnamic acids (chlorogenic, neochlorogenic and caffeic) and flavonoids (rutin and cynaroside) had been identified. The content of hydroxycinnamic acids in extracts BCC-T and ОПК-Т were 10.12% and 9.93%, respectively; the content of flavonoids – 3.77% and 3.54%, respectively.

Taking into account the high concentration of hepatotropic BAS in obtained extracts, the study of hepatoprotective activity of substances was phytochemically supported. The study was carried out on a model of acute tetrachlormethan-induced hepatitis on white male rats weighing 0.18–0.25 kg. Animals had been kept in accordance with sanitary standards on a standard diet and with the principles of humane treatment to laboratory animals. Animals were treated (subcutaneous administration) with studied extracts and reference drug "Silibor" in dose of 25 mg/kg were before 1 h and after 2 h after hepatotropic poison administration.

In the group of animals, that were treated with extract ОПК-Т, activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) decreased in 3.5 and 3.4 times, respectively; the activity of alkaline phosphatase decreased in 1.3 times; the activity of cholinesterase increased in 1.4 times comparing with the control group. In the group of animals, that were treated with extract BCC-T, the activity of ALT and AST decreased in 2.7 and 2.4 times, respectively; the activity of alkaline phosphatase decreased in 1.2 times; cholinesterase activity increased in 1.3 times comparing with the control group. Thus, the more pronounced hepatoprotective activity was intrinsic to the extract ОПК-Т.

Since, the qualitative and quantitative contents of flavonoids and hydroxycinnamic acids in the studied substances are comparable, it is necessary to carry out further comparative study of BAS of obtained extracts in order to establish correlative relationships between composition of BAS and hepatoprotective activity of extracts.

The results of preclinical studies create preconditions for further pharmacological screening of dry purified aqueous extract from *G. verum* herb to develop on its basis the original home-produced hepatoprotective drug.

AMINOACID COMPOSITION OF *Asperula octonaria* KLOKOV HERB

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It is known that genera of *Asperula* and *Galium* (*Rubiaceae* Juss.) were originally distinguished in morphology of corolla. But even as of 2013 attempts to distinguish these two genus on the basis of morphology, including the presence or absence of floral bracts or DNA analysis, were unsuccessful: their taxonomy is still not solved. *Asperula octonaria* Klokov (*Galium octonarium* (Klokov) Pobed.) is highly polymorphic species. It is often identified with the western european species *Galium glaucum*. Nowadays there are from four to six species which are close to *Galium glaucum*. On the territory of Russia, Ukraine and Kazakhstan they are *G. biebersteinii* Ehrend., *G. octonarium* (Klokov) Soy, *G. tomentellum* Klokov and also recently described *G. hexanarium* Knjazev, *G. turgaicum* Knjazev. *Asperula octonaria* is close to the dye bedstraw *Galium tinctorium* (L.) Scop.

Asperula octonaria is not an official plant, but is widely used in folk medicine as a diuretic, sudorific and sedative agent.

In order to clarify the taxonomy of genera *Asperula* and *Galium*, as well as the standardization of *A. octonaria* herb as a source of pharmacologically active substances the content of groups of biologically active substances such as phenolic compounds and iridoids had been determined.

The goal of the present research was to study the amino-acid composition of *A. octonaria* herb, samples of which were collected during flowering in May–June 2012 in Kharkiv region, Ukraine.

The content of total N was determined on an EA-3000 elemental analyzer (Euro Vector, Italy) using a thermal-conductivity detector (TCD). The analyzed raw material contained 2.5% of N. The protein content calculated using the common factor of 6.25 was 15.63%.

Quantification of free and bound amino acids in the studied samples was performed on an Agilent Technologies Model 1100 liquid chromatograph, connected to a G1379A, flow vacuum de-gasser, a G13111A 4-channel low-pressure gradient pump, a G1313A automated injector, a G13116A column thermostat and a G1316A diode-matrix detector. Detection was made using an UV detector with measurement scale 1.0, scan time 0.5 s., detection wavelength 265 nm. Amino acids were identified by retention time and by comparison with standard samples of amino acids.

The study identified in the herb 20 free and bound amino acids, 9 of which were essential ones. Dominant compounds (mg/100 g) were asparaginic (1005.4) and glutaminic (1092.3) acids, arginine (601.9), serine (514.4), alanine (505.0), proline (460.8), glycine (449.3) and tyrosine (442.2). The content of free amino acids was 0.04%; of bound – 0.96%.

CHEMICAL RESEARCH OF HAWTHORNS FLOWERS LIPOPHILIC COMPOUNDS FROM UKRAINIAN FLORA

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We have investigated phenolic, lipophilic and volatile compounds of fruits, flowers and leaves of hawthorn species from different botanic sections. During experiment flavonoids, terpenoids, fatty acids and their esters, hydrocarbons was established.

Continuing the phytochemical research of *Crataegus* L. genus representatives, we used chromatography-mass-spectrometric method for comparative study of lipophilic compounds from flowers of some hawthorn species from Ukrainian flora.

For determination of qualitative and quantitative content the lipophilic compounds we used chromatography Agilent Technology HP6890 GC with mass spectrometric detector 5973N. Sample (5 g) were placed to vial of 20 mL and added internal standard – trydekan, and then use the resulting concentration of internal standard for calculations.

Studies conducted by conditions of analysis: quartz chromatography column, capillary HP-5MS. Column length 30 m, internal diameter 0.25 mm. Carrier gas – helium. The velocity of carrier gas 1 mL/1 min. Volume tests – 2 mcl. Entering sample splitless, it is without splitting the flow. The speed of sample 1.2 mL/1 min during 0.2 min. Temperature of thermostat 50°C with programming 4°/min. to 220°C. Temperature of detector and evaporators 250°C. The obtained spectrs are seen as based on the general laws of the fragmentation of the molecules of organic compounds under electron impact, and comparing the results with mass-spectral libraries NIST05 WILEY and 2007 with a total of over 470000 spectra in conjunction with programs to identify AMDIS and NIST.

In result of investigation in flowers of *Crataegus monogyna* was identified and established quantitative content of 42 lipophilic compounds; *Crataegus ambiqua* – 32 compounds; *Crataegus fallacina* – 42 compounds. Content of compounds is calculated in terms of the total number of compounds.

In the flowers of *Crataegus monogyna* identified aromatic compounds (2.16%), terpenoids (4.9%), higher hydrocarbons, aldehydes, alcohols (82.1%), derivatives of fatty acids and their esters (10.8%).

Among terpenoids on quantitative content dominated squalene (80.2%) and *cis*-linalool oxide (6.8%).

In the flowers of *Crataegus ambiqua* identified terpenoids (15.5%), derivatives of fatty acids and their esters (23.1%) and higher hydrocarbons (57.7%).

Among terpenoids on quantitative content dominated squalene (64.2%) and eugenol (17.8%).

In the flowers of *Crataegus fallacina* identified aromatic compounds (22.3%), terpenoids (15.8%), derivatives of fatty acids and their esters (33.1%) and higher hydrocarbons (48.7%).

Among terpenoids on quantitative content dominated squalene (78.3%) and β-terpineol (1.8%).

Common terpenoids compounds of this species are squalene, limonen, eugenol.

RESEARCH OF FATTY ACID COMPOSITION OF *Artemisia annua* L., *Artemisia abrotanum* L. AND *Artemisia dracunculus* L. HERBS

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We have previously examined the components of essential oils of some species of the *Artemisia* L. genus, lipophilic extracts – chloroform and ethyl acetate–alcohol (8:2) – were obtained, the main biologically active substances (BAS) – terpenoids, organic acids, hydrocarbons were identified. Pronounced antimicrobial and antifungal activity of the obtained substances against strains of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Proteus vulgaris*, and *Candida albicans* were established. Further research of BAS and physiological activity of these raw materials and pharmaceutical substances based on them is quite promising.

The aim of this research was to investigate the fatty acid composition of *Artemisia annua* L. (sweet wormwood or annual wormwood), *Artemisia abrotanum* L. (southernwood) and *Artemisia dracunculus* L. (tarragon) herbs.

The objects of study were examples of herbs of these species harvested at the budding stage in the summer of 2011 in the Kharkiv region (Ukraine).

The study of the qualitative and quantitative composition of fatty acids was carried out by GC-MS method. Fatty acid methyl esters obtained by adding to the plant material BCl_3 solution in methanol were analyzed by chromatograph Agilent Technology HP6890 GC with the mass spectrometric detector 5973N. Their identification was performed using the data of mass spectra libraries NIST 05 and Wiley 2007 combined with the software for identifying AMDIS and NIST. Quantitative calculation of fatty acids was carried out by the internal standard method.

As a result, in the herbs of studied species 19 fatty acids were identified, 14 of which are saturated (caproic, lauric, myristic, pentadecanoic, palmitic, heptadecanoic, stearic, arachidic, heneykosylic, behenic, tricosylic, lignoceric, pentakosylic and cerotic), 3 monounsaturated (3-hexenoic, palmitoleic and oleic), 2 polyunsaturated (linoleic and linolenic acids). In the *Artemisia annua* L. herb 15 acids, in the *Artemisia abrotanum* L. herb – 15 acids, in the *Artemisia dracunculus* L. herb – 18 acids were identified. 14 acids were detected in all species. 3-Hexenoic, myristic, pentakosylic acids were detected only in the tarragon herb, heneykosylic acid – only in the southernwood herb, lauric acid – in the sweet wormwood and tarragon herbs. The total fatty acid content in the sweet wormwood herb was 8453.45 mg/kg, in the southernwood herb – 9342.75 mg/kg, in the tarragon herb – 11148.20 mg/kg.

GC-MS research of the fatty acid composition of the *Artemisia annua* L., *Artemisia abrotanum* L. and *Artemisia dracunculus* L. herbs of Ukraine flora was carried out for the first time.

CHEMICAL ANALYZIS OF *Scorzonera hispanica* L.

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Scorzonera hispanica L. family *Asteraceae* is a plant that contains many biologically active substances (proteins, polysaccharides, sugars, tannins, vitamins and minerals) and also has nutritional properties. *Scorzonera* is grown in many countries as an ornamental and agricultural plant. Due to the high content of inulin, *Scorzonera* roots could be used as part of the diet of patients with diabetes, also it could be used in the case of obesity, vitamin deficiency, atherosclerosis, reduced levels of hemoglobin. Using roots of *Scorzonera* improves metabolism, helps to eliminate radionuclides and increases the number of bifidobacteria in the gastrointestinal tract. Scorzonera′s dietary fiber have therapeutic and preventive value. Such substances as water-soluble inulin, pectin concentrate, freeze dried powder, original coffee-like drinks and polysaccharide concentrates, which have antibacterial and hypoglycemic activity, are used in the the food industry. Almost all studies apply only to underground organs of *Scorzonera*. Study of *Scorzonera* overground organs is not developed in modern scientific literature.

The study, made at the base of National Pharmaceutical University, made it possible to determine the content of organic acids in *Scorzonera hispanica* leaves. In the experiment there were used first year leaves of *Scorzonera hispanica* collected in the period of full development of the rosette before the beginning of flowering period. For the determination of organic acids was used chromatography-mass spectrometry method. For the extraction of fatty acids methyl esters was used methylene chloride (0.2 mL). Chromatographic analysis was performed on Agilent Technologies 6890 chromatograph with mass spectrometric detector 5973. Chromatographic column – INNOWAX capillary with an inner diameter of 0.25 mm and 30 meters length. During the study in the sample material were established and identified 30 organic acids, among which are 7 carboxylic acids, 6 phenolic acids and 17 fatty acids. Among the carboxylic acids accumulates the maximum amount of citric (4807.3 mg/kg), malic (1385.9 mg/kg) and malonic (1068.5 mg/kg) acids, which improve energy metabolism in the tissues of the body, involved in the redox reactions of mitochondria, and also used in medical practice. Among the dominant phenolic acids are fumaric acid (79.7 mg/kg) and salicylic acid (71.3 mg/kg); among fatty acids – palmitic acid (2397.2 mg/kg).

Dynamics of content of organic acids is presented in a following order:

for carboxylic acids: citric > malic > malonic > oxalic > hept-2,4-dienic > succinic > dimethoxyacetic;

for phenolic acids: fumaric > salicylic > ferulic > benzoic > vanillic > phenylacetic;

for fatty acids: palmitic > linolenic > linoleic > oleic > myristic > arachidic > behenic > tetracosanic > palmitoleic > pentadecanoic > heptadecanoic > hexacosanoic > tricosanoic > hexanoic > caprylic > heneicosanoic > stearic.

The study of the presence and content of organic acids is necessary to determine the dynamics of plant metabolism, which are perspective for the treatment of the diseases, related with metabolic disorders. The obtained results make Scorzonera hispanica a perspective herbal drug and envisaging further development of research in this direction.

HYDROXYCINNAMIC DERIVATIVES IN MEDICINAL PLANTS

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Many pharmacopoeia′s medicinal plants and herbal drugs are rich in hydroxycinnamic acid and its derivatives. Caffeic, chlorogenic, ferulic acids and others belong to this phenolic group of compounds. Rosmarinic acid which is an ester of caffeic acid and 3,4-dihydroxyphenyllactic acid also attract our attention. It is commonly found in species of the family *Boraginaceae* and *Lamiaceae*. However, it is also found in several species of other higher plants and in some fern and hornwort species. Rosmarinic acid has a number of interesting biological activities, e.g. antiviral, antibacterial, anti-inflammatory, antioxidant and also is used to treat thyroid problem.

The goal of investigation is to determine the content of hydroxycinnamic derivatives among well-known herbal drugs for the following creation of new medicine with antiviral, antibacterial, anti-inflammatory effects. The samples of herbal drug were obtained by cutting the herb in Botanical garden of National University of Pharmacy. The herb was dried at 32°C and stored in paper sacks in a dark, cool and dry depository. Identification of rosmarinic, caffeic and chlorogenic acids in 50%-alcohol extract of herbal drug was carried out by paper and thin-layer chromatography in different solvent system in comparison with the solution of references compounds.

Analysis was carried out using HPLC method on chromatograph "Waters" with manual injector Rheodyne 7725i and the following processing of the results by “Multichrom for Windows”. Detection was made with the help of UV-detector “Water 2486”, $\lambda = 320$ nm. The column was a Zorbaz Eclipse_XDB, 4.6 × 250 mm long. Mobile phase: methanol–10 g/L phosphoric acid (40:60). Flow rate: 1.0 mL/min, column temperature 30°C. Results are represented in Table 1.

TABLE 1. **Hydroxycinnamic Derivatives in Medicinal Plants**

Herbal drug sample	Rosmarinic acid, %	Caffeic acid, %	Chlorogenic acid, %
Melissa herb	2.50	0.039	0.064
Melissa flower	3.30	0.026	0.05
Melissa leaf	2.80	0.048	0.078
Rosemary leaf	3.10	0. 053	0.034
Common thyme herb	2.10	0.070	0.021
Creeping thyme herb	2.25	0.060	0.030
Peppermint herb	0.38	0.09	0.058
Peppermint leaf	0.50	0.078	0.045
Sage leaf	1.45	0.048	0.039
Lavender flower	0.09.	0.089	0.011
Common plantain leaf	0.35	0.024	0.047
Ribwort plantain leaf	0.40	0.039	0.055

Rosmarinic acid was discovered in common plantain and ribwort plantain leaf at first. Different organs of mellisa, rosemary leaf, herb of two thyme species are highly rich in rosmarinic acid. Herbal drugs from these plants may be recommended as perspective sources of antiviral remedies. In java leaves, marjoram herb and skullcap root rosmarinic acid was not identified.

CARBOXYLIC ACID FROM *Aronia melanocarpa* LEAVES ALCOCHOLIC EXTRACT

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Black Chokeberry (*Aronia melanocarpa* (Michaux) Elliot) from the *Rose* family (*Rosaceae* Juss.) is widely cultivated in Ukraine as a fruit, medicinal, and ornamental plant. Previously we studied essential oil, macro-and micronutrients, carbohydrates and carboxylic acids from leaves of this plant. The aim of this work is to study acid composition of alcoholic extract from leaves of Black Chokeberry that were harvested in May 2012 in the botanical garden of National University of Pharmacy. For studying viscous alcoholic extract was obtained by extraction material with 50% ethanol by the method from State pharmacopoeia of USSR, 11TH Edition, vol. **2**.

Determination of carboxylic acids was conducted by a modified method on the chromatograph Agilent Technologies 6890 with a mass spectrometer detector 5973. We prepared sample for analysis as specified in [V. A. Samoilova, V. N. Kovalev, V. A. Rybak, Ye. V. Krivoruchko, Chem. Nat. Compd., 637 (2013)]. For quantitative calculations we used the internal standard method. The results of research are presented in Table 1.

TABLE 1. **Carboxylic Acids from *Aronia melanocarpa* Leaves Alcoholic Extract**

Acid	Retention index*	Content, mg/kg	Acid	Retention index*	Content, mg/kg
Oxalic	1359	57.2	Stearic	2384	31.1
Malonic	1477	277.8	Oleic	2402	54.7
Fumaric	1516	25.6	Linoleic	2443	245.3
Succinic	1575	124.6	Linolenic	2490	412.8
Benzoic	1600	1474.2	Vanillic	2522	39.3
Phenylacetic	1746	57.8	*p*-Coumaric	2729	303.6
Salicylic	1757	84.9	*p*-Oxybenzoic	2780	56.7
Malic	2008	379.3	Purple	2793	47.6
β-Oxy-phenylacetic	2218	743.9	Gentisic	2805	103.4
Citric	2367	1241.9	Ferulic	2919	307.8

*Retention index of methyl ester of acid.

As seen from the received results in the alcoholic extract of the leaves of chokeberry the content of 20 carboxylic acids was identified. Benzoic (1474.2 mg / kg) and citric (1241.9 mg /kg) acids prevail, in contrast to the previously studied leaves of chokeberry, where linolenic (3779.2 mg/kg), oxalic (2864.6 mg/kg), palmitic (2047.6 mg/kg) and apple (1506.9 mg/kg) acids prevail.

Pharmacognostic study of leaves of Black Chokeberry will be continued.

LUPINE MULTIVALENT-PERSPECTIVE SOURCE OF BIOLOGICALLY ACTIVE SUBSTANCES

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Genus *Lupine* (*Lupinus* L.) of the legume family (*Fabaceae*) includes about 200 species of annual and perennial herbaceous plants. In CIS countries they cultivate annual three species: lupine yellow (*L. luteus* L.), l. white (*L. albus* L.), *L. angustifolia* (*L. angustifolius* L.) and one perennial species - l. multivalent (*L. polyphyllus* Lindl.). Lupine is valuable legume of multi-purpose use. Analysis of scientific references indicates the presence in lupine of different groups of biologically active substances: organic and fatty acids, amino acids, reducing sugars, polysaccharides, minerals, vitamins, saponins, tannins, flavonoids, isoflavonoids, and hydroxycinnamic acids and alkaloids.

In medical practice, the various organs of lupine is recommended to use as drugs that decrease cholesterol and blood sugar, normalize blood pressure, regulate the bioenergy activity, as well as enhance immunity, activity of the heart, reduce the risk of cancer and prevent cataract. By the qualitative reactions and various chromatographic methods in the roots of lupine multivalent founded reducing sugars, starch, polysaccharides, flavonoids, isoflavones, hydroxycinnamic acids, tannins, saponins, indicated of perspective studies of this herbal drug for the development of drugs of various kinds of pharmacological action. Using the method of gas chromatography-mass spectrometry in the roots of Lupinus polyphyllus were identified 14 fatty acids. The research was carried out on Agilent Technology 6890N chromatograph -mass spectrometer detector 5973N.

The results are shown in the Table.

Fatty acids	Content, mg/kg	
	free acids	bound acids
	Saturated	
Caproic acid	6.7	51.3
Palmitic acid	665.3	925.6
Heptadecanoic acid	–	59.3
Stearic acid	7.9	99.8
Lauric acid	38.8	
Myristic acid	97.1	
Nonanoic acid	65.5	
Capric acid	19.4	
Pentadecanoic acid	46.4	
	Unsaturated	
Linoleic acid	70.5	744.4
Linolenic acid		172.9
Oleic acid	44.2	181.2
Palmitoleic acid	74.6	
11-Octadecenoic acid	–	80.4

Summary according to the results of analysis the roots of lupine contain 11 free and 8 bound fatty acids, 5 of which belong as to free as to bound one.

CHEMICAL COMPOSITION AND ANTIFUNGAL ACTIVITY OF ESSENTIAL OILS OBTAINED FROM *Abies sibirica* L., GROWING IN THE REPUBLIC OF KAZAKHSTAN

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Basing on the analysis of literature it was revealed that a comprehensive study of etheric-oil plants, essential oils and search for ways of their new applications in various sectors of the economy are not only urgent in this century, but are also acquiring a special importance, scientific and practical significance. Among coniferous attar plants the most widely spread in the Republic of Kazakhstan is *Abies sibirica* L., which grows in the East Kazakhstan region, mountain forests of the Altai, the Tarbagatai and the Dzhungarsky Alatau.

The aim of this work is the comparative research of the component composition of the essential oils samples obtained by means of steam distillation and microwave heating from *Abies sibirica* L., collected in the Altai mountain forests of the East Kazakhstan region, and their antifungal activity towards *Candida albicans*.

Samples of the essential oils of *Abies sibirica* L. were obtained by methods of steam distillation and microwave heating in a «STARTE Microwave Extraction System» device. Qualitative and quantitative analyses of the essential oils samples composition were performed with an «Agilent Technologies 7890A GC System, 7683B Series Injector, 5975C VL MSD with Triple-Axis Detector» device. To identify the components the library of NIST 02 and Willey mass spectra was used.

The antifungal activity of the essential oils of *Abies sibirica* L., obtained by means of steam distillation (sample WM) and microwave heating (sample MW), was determined with a «SPECTRO star Omega» device.

Comparison of the data above with the available data on the chemical composition of the essential oil of *Abies sibirica* L., obtained by steam distillation, shows that the essential oil of *Abies sibirica* L., obtained by microwave heating, has a richer component composition. Bornyl acetate content of this oil is 34.26%.

Thus, our studies of the essential oils of *Abies sibirica* L. have revealed dependence of the oils properties on the ways the oils are obtained: the essential oil of *Abies sibirica* L., obtained by microwave heating, has a richer component composition and displays a higher antifungal activity towards *Candida albicans* than that one obtained by means of steam distillation.

ACETYLCHOLINESTERASE INHIBITING CHARACTERS OF *Salvia* spp.

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Salvia is one of the most numerous genera within the family *Lamiaceae* (around 900 species) which grows in many parts of the world. About 250 species are distributed in Central Asia and Mediterranean regions. At least 17 species of the genus are found in Uzbekistan, 22 species in Ukraine. The common species for these states comprise *Salvia splendens, S. aethiopis, S. sclarea, S. virgata*.

Salvia officinalis has been evaluated (Ozarowski M. et al., 2009) using different *in vitro* and *in vivo* models to prove their efficacy in the management of patients with Alzheimer′s disease and the studies have demonstrated that extracts are active in inhibition of AChE or β-amyloid deposits inhibition *in vitro*. An 80%-ethanolic extract from sage leaf exhibited dose-dependent cholinesterase-inhibiting activity (Kennedy D.O. et al., 2006). Essential oil of *Salvia officinalis* inhibited 46%, ethanolic extract – 16% of acetylcholinesterase activity at a concentration of 0.5 mg/mL, its decoction – 57% at 5 mg/mL (Ferreira A. et al., 2006).

The inhibition of anticholinesterase *in vitro* by a 95% ethanolic extract of *S. officinalis* (2.5 mg/mL) was 68%, and by steam distilled oils of *S. officinalis* and *S. lavandulifolia* (0.1 mg/mL) 52% and 63%, respectively (Perry N. et al., 1996). The IC_{50} value of *S. lavandulifolia* oil is reportedly 0.03 mg/mL; the monoterpenes 1,8-cineole and α-pinene from the oil have been identified as the inhibitors of acetylcholinesterase with IC_{50} values of 0.67 and 0.63 mmol/L, respectively (Perry N. et al., 2000).

The acetone, ethanol, butanol and water extracts of *Salvia sclareoides* were screened (Rauter A. et al, 2007) for the *in vitro* inhibitory activity of acetylcholinesterase; all these extracts inhibited acetylcholinesterase activity at 10 μg/mL, a remarkable activity since the standard drug rivastigmine does not inhibit acetylcholinesterase at the same concentration.

Four AChE inhibitory compounds, dihydrotanshinone, cryptotanshinone, tanshinone I and tanshinone IIA were isolated (Ren Y. et al., 2004) from an acetone extract of the dried root of *Salvia miltiorhiza*. The inhibitory activities of dihydrotanshinone and cryptotanshinone were dose-dependent, their IC_{50} values being 1.0 microM and 7.0 microM, respectively.

Fraction, characterized by the presence of sesquiterpenes as major components of *Salvia leriifolia* extract (Loizzo M.R. et al., 2010) was the most active against AChE (IC_{50} = 0.05 mg/mL).

Anticholinesterase activity was also determined for the essential oil and hexane extract of *S. chionantha* (Tel G. et al., 2010), the essential oil and ethanol extract of *S. potentillifolia* (Kivrak I. et al., 2009), *S. poculata* (Kolak U. et al., 2009).

Considering an increasing interest and demand in the anti-neurodegenerative phytopharmaceuticals, plants of the genus *Salvia* may become the promising sources of new natural biologically active agents for treatment of Alzheimer′s disease.

THE PROSPECTIVITY OF RESEARCH OF A SUMMER SQUASH GRASS

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A squash (*Cucurbita*) is a genus of one-year and perennial plants of gourd family which number about 20 types which are wildly growing only in America. This genus stimulates interest because its cultural forms are widespread everywhere where agriculture, except for the northern areas lying outside 62–63 N.W. is developed. A squash is not only the major food culture, but also a source of pharmacological active substance around the world (for example, carotenoids). The seeds of a squash are well studied. The preparations made of them are widely applied both in official, and in folk medicine. But in folk medicine there are used not only seeds and fruits, but also flowers, leaves, stalks, fruit stems for treatment of urogenital system diseases, digestive ones, when you have gout, diabetes, for healing of wounds.

There are grown 4 types of a squash in Ukraine: firm (*C. pepo* L.), large-fruited (*C. maxima* Duch.), muscat (*C. moschata* Duch. ex. Poir.), fig-leaved (*C. ficifolia* Bouche). From all types of a squash a summer squash is more widespread (*Cucurbita pepo* L.). These are trailers with the stalks covered firm and thorny hairs. They have five-laciniate leaves with the acute-angled ends of blades and deep serrated edge. The flowers are campanulate: the sepals are narrow, almost linear; the petals are adnate at 2/3 lengths of a corolla, their ends are sharp. The cultural forms have large, no drawing or striped fruits; the seeds are cream, oval, with a clear scar at the edges. In June we gathered a grass during flowering before fruiting, dried up at the room temperature and crushed for studying of overhead part of a summer squash.

The definition of quantitative and qualitative content of organic acids was carried out with a chromatography-mass spectrometry method. As a result of researches 12 organic acids from which citric, siccine, malic acids have dominating value are identified in grass. The greatest number of citric acid (11842.9 mg/kg) and malic acid (3012.5 mg/kg) is revealed in stalks, siccine acid (1647.8 mg/kg) – in flowers.

The qualitative and quantitative content of fatty acids were determined with a gas-liquid chromatography method. During the research there were found both saturated fatty acids, and unsaturated ones. Among saturated fatty acids the dominating place is taken by palmitic acid, its greatest number is contained in flowers (6422.1 mg/kg), and among unsaturated fatty acids the dominating one is linolenic, its greatest number is contained in leaves. Though, the highest content of unsaturated acids (12784 mg/kg) is mostly revealed in flowers. The qualitative analysis of fatty and organic acids show the importance of further studying of a summer squash grass. The received results can be used in future for MKQ creation.

COMPARATIVE ANALYSIS OF COMPONENT STRUCTURE OF A NUMBER OF GROUPS OF BAS, BUDS AND *Alnus glutinosa* (L.) GAERTN

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The object of our researches was the widespread plant of a temperate climate. It is a black alder *Alnus glutinosa* (L.) Gaertn of birch *Betulaceae* family. The plant is rather studied. The official raw materials are collective fruits (cones), possessing astringent, styptic, antimicrobic action. In Ukraine the original preparations "Altan" and "Altobor" are issued from this type of raw materials. Bark, leaves, catkins (male inflorescences) of this plant had been applied long since in folk medicine when you have haemorrhoids, allergies, stomatitises and bleeding of gums, dysentery, pulmonary tuberculosis, stomach pains, rheumatism, gout, the rheumatoid arthritis, pruritic rashes, scrofula, dermatitis and burns.

However the comparative analysis of component structure of some BAS groups of buds and leaves practically didn't carry out. Therefore the comparison of qualitative structure of compounds and the quantitative maintenance of a number of the BAS groups is actual from the point of view of the expansion of a source of raw materials.

The qualitative structure is defined and the quantitative maintenance of components of the substances which are overtaking with water vapor, and also a number of groups of phenol compounds is established. As in qualitative, and in a quantitative sense these types of raw materials on these groups of connections differ. The analysis of the substances which are overtaking with water vapor was carried out with a method of a gas chromatography. In the buds of black alder 47 compounds were found out, 45 compounds were identified; in the leaves 48 compounds overtaken with water vapor were found out, 46 from which were identified. The general for both types of raw materials were 35 substances. The dominating components both buds and leaves were geraniol (164 mg/kg and 207.5 mg/kg, accordingly) and eugenol (139.3 mg/kg and 152.3 mg/kg, accordingly).

The qualitative structure and the quantitative maintenance of a number of phenol compounds were being determined by the modified HPLC method. There were found out not less than 7 substances in the buds, not less than 4 substances in the leaves, 3 from which are contained also in the buds. It is characteristic the high contents for epicatechin gallate and epigallocatechin (in buds – 3.90% and 3.80%, accordingly; in leaves – 1.64% and 1.63%, accordingly) in both types of raw materials.

Thus, certain regularities in the change of qualitative structure and the quantitative maintenance of components of some BAS groups – essential oil, phenol compounds of buds and leaves of black alder were retraced.

The received results will be used in further researches and when phytopreparations will be worked out.

THE PHYTOCHEMICAL STUDYING OF RAW MATERIALS OF THE SOWING CUCUMBER

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The sowing cucumber – *Cucumis sativus* L., *Cucurbitaceae* family is an annual monoecious grassy plant with a lying rough stalk. The leaves are cordate, pentagonal laciniate. The flowers are unisexual, yellow. The flowers of stamen are gathered in bunches in sinus, the pistillate flowers are single, on a short pedicle.

The cucumber is widely cultivated on all territory of Ukraine. Thanks to its qualities the fruits of a cucumber are used as an aliment, especially dietary one, also in cosmetology. Cucumber juice possesses anti-inflammatory, anesthetic, diuretic and gepatoprotective action. The ratio of the dissolved mineral salts in it has regulating effect on work of heart, kidneys, a liver. Cucumbers and cucumber juice are used as a cough remedy in folk medicine, earlier juice was drunk at pulmonary tuberculosis. The broth made of lashes (stalks) is drunk when you have diseases of a liver and jaundice, the broth of flowers – when you have malaria. The fresh fruits of a cucumber and cucumber juice are one of the most popular components of domestic cosmetology, possessing bleaching and moistening action on skin.

The purpose of our work is phytochemical studying of leaves, stalks, flowers, seeds of the sowing cucumber, sort "Dzherelo".

Raw materials samples from five places of growth are studied. The raw materials were prepared in July–August, 2013 on various phases of vegetation: two cotyledon, 2–3 real leaves, mass flowering and fructification, the end of fructification. The external signs of raw materials are established, the diagnostic ones are: the rigid hairiness of all plant, the form of edge of a leaf plate, the location of honey-cups, the structure of androecium and gynecium.

The distinctive diagnostic anatomic signs were determined during microscopic studying. It is possible to carry to them: various types of hairs and their structure, the type of carrying-out bunches and stalk structure, the location of crystals of a carbonate of calcium, and also various structure of honey-cups of female and male flowers.

The loss in weight when drying, the content of ashes of the general and ashes insoluble in 10% solution of acid hydrochloric were defined according to techniques of the State pharmacopeia of Ukraine of the I edition. The definition of element structure was fulfilled with a method of a nuclear and emissive spectophotometery. The existence of 16 macro - and microelements is established. The high content of potassium is noted. The quantitative and qualitative composition of organic, including fatty acids in leaves, stalks, flowers and seeds is established. There were identified not less than 11 organic and 12 fatty acids in raw materials of a cucumber. In seeds of a cucumber the azelaic acid dominates; in stalks, leaves and flowers citric acid dominates. The greatest content of linoleic acid is observed in seeds; in stalks and leaves linoleic acid prevails, and in flowers palmitic acid dominates.

The chemical composition of *Cucumis sativus* testifies to availability and expediency of further studying of a grass, flowers and seeds of this plant.

INVESTIGATION OF CHEMICAL COMPOUNDS OF LEAVES

Ulmus caprinifolia RUPP. EX G.SUCKOW AND *Fraxinus excelsior* L.

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Leaves as a type of medicinal vegetable raw materials are one of the most available objects. From the point of view of environmental protection and preservation of fund of flora of our planet the correct preparation of leaves practically doesn′t do harm to making plants. Thus, the expansion of the range of this type of medicinal vegetable raw materials is perspective.

In this context our attention was drawn with *Ulmus caprinifolia* (family *Ulmaceae*) and *Fraxinus excelcior* (family *Oleaceae*), widespread not only in Ukraine, but also on all European part of the continent. These plants are sources of several types of raw materials, including leaves which are long since and widely applied in folk medicine of the different countries.

For example, vitamin C, phenol-carboxylic acids, flavonoids (kaempferol, rutin), derivatives of leucopeonidin and leucopelargonidin were found in leaves of an *Ulmus caprinifolia*. The extractions of leaves of an *Ulmus caprinifolia* have astringent, anti-inflammatory, diuretic, healing and antimicrobic action.

The leaves of *Fraxinus excelcior* contain carbohydrates, organic acids, vitamins, essential oils, saponins, flavonoids and tannins. The preparations of *Fraxinus excelcior* have styptic, tonic, febrifugal, astringent, healing, laxative, diuretic, antimicrobial, spasmolytic, antitussive action, antirheumatic and antihelminthagogue action.

The purpose of present research is studying of a chemical composition of leaves of an *Ulmus caprinifolia* and an *Fraxinus excelcior* as perspective types of vegetable raw materials for a pharmaceutical industry.

The qualitative structure and the quantitative content of substances of such BAS groups as organic acids, including fatty acids were determined with the method of a gas chromatography.

In the leaf of *Ulmus caprinifolia* not less than 11 organic acids (dominating components citric acid – 1414.2 mg/kg, oxalic acid – 1801.0 mg/kg and malic acid – 1626.2 mg/kg), and also 14 fatty acids (according to the contents linolenic acid (4691.4 mg/kg), palmitic acid (4261.8 mg/kg) and linoleic acid (2408.7 mg/kg) prevail) are found out.

In the leaf of *Fraxinus excelcior* not less than 11 organic acids from which oxalic acid – 1264.2 mg/kg was a prevailing component, and 10 fatty acids (dominating components are linolenic (6714.6 mg/kg), palmitic (4293.0 mg/kg) and oleic acid (2073.9 mg/kg) are revealed.

The received results will be considered in further researches of these types of raw materials.

SEARCH OF THE COMPOSITION AND STANDARTIZATION PARAMETERS OF HERBAL SPECIES FOR TREATMENT OF JOINT

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According to the statistics of the WHO (World Health Organization) joint diseases are the third most common disease after disease of the circulatory and digestive system, and the first in a number of causes of temporary disability of people. According to studies, every fourth inhabitant of Russia and Ukraine suffers this disease. And among people over 60 years, 97% report joint pain.

Nowadays the reasons for the occurrence of this disease are more numerous. On the one hand, some people suffer the disease in virtue of the patient's genetic predisposition or metabolic disorders.

On the other hand, there are other factors that contribute the progress of these diseases peculiar to modernity: hypodynamia, lack of exercise in the proper amount leads to a weakening of the muscles and increases body weight, respectively, the load on the joints grows too, what does not make them healthier; poor environment and poor diet are the causes of allergies, which can also indirectly influence the growth of inflammatory and degenerative processes in the joints; fast pace of life, expressed in the absence of time to visit to a doctor.

"The articular diseases" take the first place in the world among diseases of the internal organs which (if in neglected case) can lead to temporary and even permanent disability. Raises the concern the fact where these diseases occur to the people in an increasingly young age. Medications that are prescribed to the patients with arthrosis and arthritis have mostly the effect which aims only to remove the pain and inflammation. Thus, these drugs take away only to some extent painful effects, but do not fight the cause of the disease. These are analgesics (including narcotic) non-steroidal anti-inflammatories, corticosteroids, psychotropic drugs and relaxants. They have side effects often. Ointments and external rubbings are also often used. Moderate exercises are often helpful as well.

The use of herbal remedies for treatment of diseases of the joints is effective as herbal preparations possess polyvalent effect, exhibit anti-inflammatory, analgesic, antihistaminic properties, have the ability of partial cytoprotection, i.e. can restore the damaged cartilage. Especially wide specter of activity is applied by many components of herbal species.

Considering the literature data, we have developed structure of herbal species "Artrophyt" composed of the seven components recommended for use in arthritis and osteoarthritis. Most of the medicinal plants components are used in officinal, some apply only in ethnoscience. The composition is protected by patent.

We have set up the authentication settings for macro-and microscopic characteristics by chromatographic methods, methods of assay for the main groups of biological active compounds. The basic numeric indexes of collection such as loss on drying, ash content, bulk density, content of the main active ingredients a determined.

The results of research are used in order to establish methods of quality control of the phytocomposition.

THE COMPARATIVE STUDY OF FRACTIONS OF BILE OF ANIMALS

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Chinese medicine has incorporated the use of bear gall bladders and bile for over 1300 years. The Pharmacopoeia of the People′s Republic of China (1977) indicates that bear gall bladder is useful for cleansing heat symptoms, calming the liver and brightening the eyes. It is also used for treating convulsions, conjunctivitis and pharyngolaryngitis. Pharmacological and clinical studies have confirmed the therapeutic effects of bear bile, especially of its components, ursodeoxycholic acid (UDCA) and chenodeoxycholic acids (CDCA), for the treatment of gallstones and liver diseases. Pig bile has also been found to have antiinflammatory, nticonvulsant and analgesic effects, and can prolong the survival time of mice under hypoxic conditions. The bile of mammals, as well as of other animal species, results from metabolic processes in the liver. Bile consists of approximately 86% water and 14% dry matter. The most important components of the dry matter are free and conjugated bile acids.

The work Is devoted to the isolation and study of bioactive complexes and substances of three kinds of bile: cattle – *Bos taurus* (ZhBt), pigs – *Sus scrofa domesticus* (ZhSs), chickens – *Galus galus* (ZhGg); of technology of complex processing of bile, and creation on the basis of complexes of bile new medications and to the establishment of pharmacological activity in the experiment.

By methods of liquid-liquid extraction and chromatography in the complexes of animals bile the presence of 137 compounds was established: bile acids (45), fatty acids (20), amino acids (17), among them – 9 essential, 14 fatty acids, phospholipids (13), cholesterol (1), porphyrins (16), enzymes (6), macro-and micronutrients (19). By two-dimensional chromatography in the lipophilic complex (LC) of bile revealed 75 substances which by chromatographic mobility, fluorescence under UV-light and the colouring with specific reagents were referred to steroids (46), phospholipids (13), porphyrins (16).

The antimicrobial activity of LC in concentration 0.1% against *Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis* and *Candida albic*ans and antibacterial activity of water remain of bile (WRB) ZhBt towards *Staphylococcus aureus* and *Candida albicans* were established. Pharmacological researches were conducted in vivo and in vitro. It was established that bile glycoprotein complex (GPC) helps absorption of fats, activate lipase in digestion and stimulates peristalsis in experimental animals.

The WRB has expressed antihypoxic action and stabilizes the membranes. LC showes pronounced hepatotropic and antioxidant effects. WRB in a dose of 12 mL/kg, LC – 20 mg/kg, GPC – 25 mL/kg at 30-day intragastric introduction do not have toxic effects on the peripheral blood picture and morpho-functional state of the internal organs in the subacute experiment. Complexes can be recommended as medications to improve digestion, in violation of cerebral and peripheral circulation, redox metabolism in tissues, at hepatitis, as a tonic, stabilizing agent in adverse effects.

INFLUENCE OF ASPHALT CONCRETE MIXTURES ON THE ENVIRONMENT

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The issue of adverse effects of asphalt on the human body studied insufficiently well. The negative impact on humans and the environment have harmful elements stand out as the production and lying of asphalt, and during its operation.

The aim of this work is to modify the binder, i.e. the bitumen polymeric compounds, polymers improve the properties the bitumen, giving his adhesion, which is necessary for road industries. Thus, studies of changes in the properties of the oil in the preparation of road bitumen and asphalt paving are relevant, which means a decrease in toxicity of bituminous mixtures for the environment and human health.

In the experimental part of this work was modified bitumen by heating at boiling temperature ≈ 155°C, and poured into it the necessary quantity of polymer in our cases (0.3%, 0.5%, 0.9%) and the mixture was intensively interfere with constant temperature. Crushed stone fraction 10–20 mm were washed under running water skipping, tying them to the wire and dried in a muffle oven at 130°C, then the furnace temperature was lowered to 110°C and held for 1 hour. After gaining bituminous mixture temperature 155°C, stones lowered into the bitumen blend, about 14–16 sec, and dried in air for exactly 1 hour, then 500 mL of boiled distilled water and dipped in a beaker.

Made by composition the bitumen with amines: polyethylene polyamine, polyethylene mine at 0.3%, 0.5%, 0.9%, we get a different adhesion with crushed stone (Alexis, Almaty region) fractions 5–10, the result is low at 0.3–0.5%, the result was received with a high 0.9%, indicating a high adhesion, and a mean bitumen will behave well in the asphalt mix without causing toxic effects on the environment.

Also making the composition of the asphalt and rosin epoxy resin (ED 20) for 0.3–0.5%, the results were low (not satisfactory), 0.7, 0.9% higher results (satisfactory).

Hence we can conclude that:

– the findings suggest less toxic effects the bitumen at its operation on human health and the environment;

– new compositions obtained are glued strongly and reliable held in a long time the carcass selected mineral particles – mineral load bearing structural basis road surface under dynamic alternating loads in the actual atmospheric influences in a wide temperature range, ultraviolet radiation from the sun, the effect of oxygen.

ON THE QUESTION OF THE ESSENTIAL OIL OF THE HERB *Aristolochia clematitis* L.

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Essential oils are widely used in medicine due to the complex chemical composition and multidisciplinary pharmacological activity. *Aristolochia clematitis* L. are a perennial herb of the family *Aristolochiaceae*.

Above-ground part and roots are used as medicinal plants in the alternative medicine. *Aristolochia clematitis* L. evince a diuretic, anti-inflammatory, adaptogenic, wound healing, analgesic effect. Raw materials used at high blood pressure, which is result after inflammatory diseases of the kidney, and the herb and roots are used at edema of different origin. Antiseptic action of *Aristolochia clematitis* L. determines its effect in tinea, furunculosis, pyoderma, skin itching and mastitis. The plant has an odor, which may be due to the presence of essential oils.

Receiving and examining component of essential oil of the herb *Aristolochia clematitis* L.

The essential oil was obtained from minced raw steam distillation according to the method Klevendzhera. Qualitative and quantitative composition of the components in the essential oil content were determined using chromatography-mass spectrometric method. The study was performed on a gas chromatograph brand Newlett-Packard 6890 GC with a mass selective detector 5973N. The quantitative content of components in essential oil calculated by the ratio of peak area to the sum of squares of components of all peaks in the chromatogram (method of normalization).

Received quantity of essential oil from the herb *Aristolochia clematitis* L. was 0.2%. The essential oil was an oily liquid light yellow color with a pungent odor. The presence of 44 compounds was found in the essential oil composition. Camphor (21.04%), bornilatsetat (9.12%), α-terpineol (3.05%), furfural (3.29%) and 2-methoxy-4-vinilfenol (3.41%) contained the greatest amount of essential oil herb *Aristolochia clematitis* L. 4 unidentified substances was found in essential oils, the quantity one of which was 5.16%. Given the significant accumulation of camphor and bornilatsetat can predict antiseptic and anti-inflammatory action.

Research qualitative composition and quantitative content of essential oil components of the herb *Aristolochia clematitis* L. was conduct by chromatography-mass spectrometric method. 44 compounds identified in the essential oil, some of which are marker may be used for standardization of raw prediction directions for its use.

THE INFLUENCE OF PLANT DIETARY SUPPLEMENT TO CHANGES IN THE SYSTEM "PRO/ANTIOXIDANTS-NO_X" IN AGING

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One of the most important tasks of modern pharmacy is to develop tools that can slow the progression of age-related changes in the body, improving the quality of life and prolonging it. It is established that the medicines with geroprotective properties can prevent peroxidation of biomolecules and the formation of free radicals, normalize metabolic processes, improve cerebral circulation. Therefore, the most urgent is the search for safe and effective herbal geroprotectors.

The purpose of the study – to research the influence of dietary supplements "Vin-Vita" on age-related changes in the system "pro/antioxidants - NO_x" in rat tissues.

The study was performed in rats of two age groups: adult (6–7 month) and old (24 month), treated with "Vin-Vita" intraperitoneally for 30 days.

Under the influence of the "Vin-Vita" was a decrease in the intensity oxidative modification of the protein (5.0–17.2%), and stimulation of the total antioxidant activity and the activity of antioxidant enzymes (19.2–40.2%) in rat tissues of adult and old age. It can be assumed that due to the antioxidant properties of parapharmaceutics exhibits the ability to suppress the peroxide in the initial processes of proteins – the initiating stage of a adult age period. In the later period of ontogenesis bioflavonoids red grapes function as effective "chelators" transition metal ions, where in the inhibitor of protein induced oxidation.

The content of nitric oxide metabolites decreased in the group of adult and significantly increased in the group of old rats (8.8–20.4%). Most authors (Kulchitskiy O. K. 2005, Afanas′ev I. B. 2009) relate the changes in the NO-producing system with age with the formation of peroxynitrite. It is believed that flavonoids act as "traps" and secondary active oxygen species: peroxynitrite, lipid peroxides and free radicals.

It should be noted that the tissues of old rats effect "Vin-Vita" was more pronounced indicators (oxidative modification of proteins, superoxide dismutase and catalase, NO_x) level indicators reached adult organism.

Thus, the possibility of correcting the identified age-related changes with parapharmaceutics "Vin-Vita".

COMPLEXATION OF PECTIN POLYSACCHARIDES WITH *s, d*-METALS CATIONS

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Biologically available water complexes with *s-, d*-metals (Ca^{2+}, Mg^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Mn^{2+}, Zn^{2+}) are synthesized on the basis of biologically active natural biopolymer pectin, perspective for medicine and pharmacology. We used sodium salt of deetherified pectin – sodium pectate with 100% degree of salt-formation – as initial ligand for complexes obtaining. This salt was synthesized by processing pectin with alkaline under controlled values of pH at titrimetric transition from low acid (pH 3.8) to light alkaline region (pH 8.5–9.0). Such approach allowed us to get sodium salt of pectic acid with the exactly known content of sodium ions in polymer and to perform analytical quantitative calculations for obtaining pectic acid metal complexes with the fixed degree of polymer molecule transformation by changing sodium ion for *s-, d*-metal cation. Then the target compounds were obtained by the reaction of ligand change of Na^+ ions for the corresponding *s-, d*-metals. The target complex was precipitated with ethanol, centrifuged and dried at 40–50°C. Complexation of pectin with micro- and macroelements are established by NMR, IR and ESR methods. Solutions of the pectin polysaccharides metal complexes are investigated for the first time by the AFM method. The particle average size for the pectate complexes with calcium is established to be equal to 45 nm, with copper – 55 nm, with iron – 65 nm, cobalt – 115 nm (Fig. 1).

Among the polymetal complexes of pectin (with Fe^{2+}, Co^{2+}, Cu^{2+}) the compounds are revealed, possessing high antianemic activity, increasing hemoglobin concentration and the erythrocytes number by 23–26%. Ca^{2+} and Fe^{2+} pectin complex is shown to manifest the same efficiency by the action on restoration of hemoglobin concentration, as the well-known preparations “Actiferrin” and “Sorbipher-Durules”, what was proved by performing tests on laboratory rats after loss of blood.

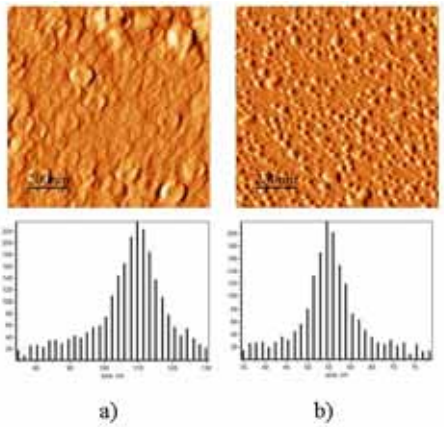

Fig. 1. AFM image of the surface of pectin complexes samples and the particle size distribution: a) NaPe, b) NaCuPe.

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PHYTOECDYSTEROIDS FROM *Polygonatum verticillatum*

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Ecdysteroids are chemically polyhydroxysteroids that contain specific structural elements such as 2,3-diol and 14α-hydroxy-Δ^7,6-ketone groups and *cis*-fused rings A and B. These features enable them to be classified as a separate group of natural compounds.

Ecdysones exhibit a specific effect on insect metamorphosis progresses. Thus, juvenile and molting hormones were discovered among this group compounds. A third generation of insecticides that had excellent selectivity and lacked harmful environmental effects could be created by using these properties against insects.

From Georgia flora it can be disguinshed genus *Polygonatum* (family *Convallariaceae*) as a rich of active compounds, which are used in traditional medicine and in homeopathic practice and characterized by wide spectrum of pharmacological activity. In total 25–30 *Polygonatum* species are described, from which only 5 are grown in Georgia.

0.5 kg air dried material of *Polygonatum verticillatum* L. was collected during the flowering phase (May–June) in the suburbs of Tbilisi, study involved the rhizomes and roots of plants. The plant material was extracted with alcohol water, after removing alcohol the solution was extracted with *n*-BuOH, and purified from ballast substance by aqueous NaOH (5%). The purified *n*-BuOH extracts were condensed; the resulting precipitates were separated by filtration and dried to afford total ecdysteroids. These were separated over columns of silica gel ($100/160_{\mu m,}$ Crech Rep.). We used solvent systems of $CHCl_3$–MeOH: 1) 15:1; 2) 9:1; 3) 4:1 and 4) $CHCl_3$–MeOH–H_2O 4:1:0.1. The purity of the fractions was monitored on Silufol plates (UV-254).

Elution of total ecdysteroids for the first time by system 1 and then by system 2 were isolated polypodine B and its acetate and benzoate derivatives. Elution by column chromatography by systems 3 and 4 were isolated ecdysteron, and produced its acetate and benzoate derivatives.

Identification of individual compounds and their derivatives, such as: polypodine B ($C_{27}H_{44}O_8$); polypodine B-22-*O*-acetate ($C_{29}H_{46}O_9$); polypodine B-22-*O*-benzoate ($C_{34}H_{48}O_9$); 20-hydroxyecdysterone ($C_{27}H_{44}O_7$); 20-hydroxyecdysterone-22-*O*-acetate ($C_{29}H_{46}O_8$); 20-hydroxyecdysterone-22-*O*-benzoate ($C_{34}H_{48}O_8$) were performed with melting point, angle rotation, the analysis of IR, UV, Mass, ^{1}H NMR spectra and comparing with literary data.

All studied ecdysteroids were isolated and characterized from plants of the *Polygonatum verticillatum* L. for the first time.

HERBAL SUBSTACE BASED ON LEAVES *Malva sylvestris* WITH ANTI-INFLAMMATORY PROPERTIES

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The *Malva sylvestris* L. attracts the attention of pharmacists, phytochemists and technologists in recent years, growing interest in which is primarily associated with high biological activity and multi-faceted.

The purpose was to study the anti-inflammatory activity of thick extract from the leaves of *Malva sylvestris* for further use as an antiexudative properties. The study of anti-inflammatory properties was perform on the formalin model of acute inflammation exudative by subplantarly injection of 0.1 mL of 2% solution of formalin into one hind limb of the animals. Reference – preparations and analyzed extract was applied to the paw, followed by applying a gauze patch afore 1 and 2 hours before the induction of inflammation. Animals were divide into 4 groups (7 rats in each group). The first members of the control animal, which in pre-production paw subplantarly received 2% formalin solution. Animals of reference groups previously was impose patch with gauze soaked in reference drugs: calendula ointment (group 2), and 1% diclofenac sodium gel (group 3).The experimental rats carried a thick application of the studied sample, extract of malva sylvestris in a similar way (group 4).

The results demonstrate that the effect of the studied pathology manifested crosses (27%) and significant increase in weight (to 38%) increase in the diameter of the paw of rats studied in the control series. This development of edema in the injection solution of formalin. It should be noted that the extract from the raw material of malva sylvestris in the modeled pathology showing expressed by anti-inflammatory properties, which are primarily implemented significant decrease inflammation index values (45%) and exudation rate (53%) in the experimental group of animals as compared to control. This suggests the ability of the test extract to adjust the inflammation process in the direction of reducing the latter. Noteworthy is the fact that the dense extract from the leaves of malva sylvestris showing a very expressed anti-inflammatory and anti-exudative properties, significantly outperforming similar action reference drugs by 30–50%.

The anti-inflammatory activity of extract from the malva sylvestris was proved, which extends the arsenal of herbal drugs for the treatment and prevention of the inflammatory dermatological diseases. The extract can be used an independent drug and as an active substance for new drugs development in various drug formulations.

THE STUDY OF THE ESSENTIAL OILS OF THE PLANTS OF THE *Apiaceae* FAMILY IN A COMPARATIVE PERSPECTIVE

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The plants of the *Apiaceae* family are classical plant, which are concentrated essential oils. The fruits of these plants have been used as an ether- oil and spicy food plant culture by long time. Standardization of fruit of *Apiaceae* family in Pharmacopoeias of various countries are conducted on the content of essential oils. Essential oils of plants in the same family are similar in components of the composition and are variable only a certain amount of substance. Therefore the study of the component composition of essential oils of the plant of the *Apiaceae* family in a comparative perspective to highlight the marker substance is of interest for pharmaceutical research.

The essential oil was obtain by steam distillation using Clevenger apparatus. Qualitative and quantitative composition of the content of essential oil components were determined by gas chromatography-mass spectrometry method. The study was performed on a gas chromatograph Agilent Technology 6890N brand with a mass selective detector 5973N. Parameters chromatography: silica capillary column HP-1 30 × 0.25; gas – helium; carrier gas velocity of 1 mL/min; sample volume – 0.1–0.5; temperature of the thermostat is 50°C and the temperature detector – 250°C.

In essential oils generally was identified 161 substance. Each essential oil is characterized by accumulation of a large amount of the basic compound, which are a marker substances. For example, in the greatest quantity in the essential oil of anise fruit contains anethole (92.01%). For the essential oil of caraway fruits are characterized by 83.54% carvone. Essential oil from celery roots differs from other oils containing predominantly derived class phthalides, namely prevail 2- and 3-metilbutilftalid (21.40% and 25.51%, respectively). Oils of fennel fruit and herbs are similar and differ carvone content as the main compound (68.38% and 62.79%, respectively). Essential oils of fennel fruits and herbs also have one thing in common marker substance - *trans* - anethole - the content is the same amount (69%). Essential oils from fruits and herbs of the coriander are very different. In the largest amount in the fruit of coriander essential oil contains linalool (78.06%), while grass coriander essential oil containing different primary aliphatic aldehydes (34.55% overall).

However, despite the rather diverse and multicomponent composition of essential oils from plants of the family *Apiaceae*, they share common presence substances – limonene, which is accumulated in an amount of from 0.69% to 17.99% , and which can be regarded as a marker compound to the group of essential oils of *Apiaceae* family.

INVESTIGATION OF THE PLANTS OF THE GENUS *Datura* IN ORDER TO DEVELOP NEW DRUGS

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The problem of treating wounds remains relevant, despite the great variety of the proposed methods and drugs. In most cases, a local medication is preferred to treat wounds. For this purpose antimicrobial agents are widely used, including ointments containing antibiotics – chloramphenicol, erythromycin, gentamicin. The disadvantages of antibiotic therapy are allergization of the body, development of resistant wound microflora, etc. One way to solve this problem is to use herbal antimicrobial drugs such as calendula ointment, kalanchoe juice, sea buckthorn oil, etc. Specified herbal medicinal products are characterized by a combination of the expressed pharmacological action with minimal negative effects on the body. However, the lack of analgesic effect is among the disadvantages of these drugs. In this connection, the plants of the genus *Datura* are especially interesting due to their antibacterial, antifungal, anti-inflammatory, and local anesthetic properties.

The aim of this study is to develop a novel medicine for the treatment of wounds in the form of a gel based on *Datura innoxia*. Using the decomposition approach, the first step is to conduct a preliminary phytochemical analysis of the leaves and seeds of *Datura innoxia* compared to *Datura stramonium*, which is officinal plant of the State Pharmacopoeia of Ukraine.

Using well-known chemical reactions and thin-layer chromatography (TLC), the comparative qualitative analysis of classes of biologically active substances (BAS) of *Datura stramonium* and *Datura innoxia* leaves and seeds was conducted. In the leaves and seeds of both *Datura* species the presence of polysaccharides, coumarins, flavonoids and alkaloids is detected; in the leaves of studied species condensed tannins are also found. By TLC the flavonoid quercetin and the alkaloids scopolamine and hyoscyamine are revealed in the leaves of both *Datura* species, as well as scopolamine and hyoscyamine – in *Datura stramonium* seeds; alkaloid scopolamine is only identified in *Datura innoxia* seeds.

Quantification of total flavonoids was done by spectrophotometry, and the total alkaloid content was determined by alkalimetric back-titration method. The results are shown in the Table.

Groups of BAS	Plant materials, %			
	Datura stramonium		*Datura innoxia*	
	leaves	seeds	leaves	seeds
Flavonoids	3.87 ± 0.17	1.15 ± 0.12	3.20 ± 0.15	1.03 ± 0.12
Alkaloids	0.28 ± 0.03	0.23 ± 0.02	0.41 ± 0.05	0.59 ± 0.03

Thus, in the work the objective is scientifically substantiated – the development of a novel medicine for the treatment of wounds in the form of a gel based on *Datura innoxia*, and its decomposition on particular tasks is held. The comparative phytochemical study of *Datura stramonium* and *Datura innoxia* was carried out, that shows the potential to use *Datura innoxia* for the development of new drugs.

THE C-ALKYLATION OF NATURAL ANTHRAQUINONES

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Creation of high-performance low-toxicity medicine preparations is one of the most important challenges for medicine, pharmacology and organic chemistry. Scientists in many countries search for biologically active compounds extracted from natural materials with synthetic methods as well as synthesized as a result of structure change in well-known biologically active compounds by inclusion of new functional groups, replacement of heteroatoms, creation of new types of chemical bonds and other processes.

Among high-performance low-toxicity medicine preparations, especially, preparations of selective action, an important place is occupied by the derivatives of anthraquinone.

This is well proven in the literature on biological activity of anthracene-containing plants, natural anthraquinones, their synthetic analogues and phytopreparations, and it should be noted that synthetic analogues have wider spectrum of biological activity.

Well known reactions with Greenyar reagents (RMgHal), where R=CH_3, C_2H_5, n- and *iso*-C_3H_7, *tret*-C_4H_9, *iso*-C_5H_{11}, C_6H_5 – result in mono- and diadduct (*cys-trans* form) of ordinary 1,2 and extraordinary 1,6 connection. Substituents in *L*-position, such as Cl, CH_3, C_6H_5 are observed not to interfere with the reaction with methyl and phenyl-magnesiumhalogenides, but no information on the influence of OH-groups in *L*-position to C=O groups has been found. C-alkylation is possible into side rings with the exchange of the movable halogen according to Fridel-Crafts and Marshalk reactions. A attempt to use known from literature information about reactions to chrysophanol and emodin showed that 8 hours heating the chemical efficiency of end products is not. Monoadduct with chemical efficiency 29.7% was observed in ether solution. When carrying out the reactions with Greenyar reactants in benzene solutions the chemical efficiency of monoadduct was observed as 35–47% depending on the radical size and composition. Diadduct with chemical efficiency 25–27% is formed with ethyl and methylmagnesiumbromides. A dioxane solution the diadduct chemical efficiency reaches 55–70% when heating it for 8 hours. Chromatographic analysis of the reaction mixture composition during the reaction showed that the spot intensity corresponding to monoadduct was decreasing gradually that may testify that diadduct storing is partly taking place from monoadduct as well. At ^{1}H NMR spectra monoadduct of emodin of the reaction with butylmagnesiumbromide in aliphatic past of spectrum there are signals of 12 protons, aromatic 1H signals displaced for 0.115 m.d., other aromatic protons – for 0.03–0.05 m.d. Monoadduct are more stable to electron blow, in mass-spectra there M^+ signals out with 12–17% intensity in comparison to M^+ diadducts 3–6%.

Thus, using multi-functionality of natural hydroxyanthraquinones, it is possible to carry out directed chemical transformations to study the role of the structure of anthraquinones, various inserted functional groups or chemical bonds.

THE EFFECT OF SOME ANTHRAQUINONES ON PHYTOPARASITIC CAULINE NEMATODES

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Agricultural production is the main method to solve industrial problems all over the world. The plants protection against blights and pests is the most important element of agricultural production. It allows not only to increase the yield but also to improve its quality, which is usually low for blight plants. The development of phytochemical methods of the pest control is one of the directions in the field of plants and environmental protection. At present the dozens of phytopreparations are made for pests bioregulation. However, phytopreparations have huge unused abilities to solve the pest control problem. The selection of the perspective plants for preparation of any biopreparation implies a series of researches on detection of the most active preparations and optimal conditions selection for their extraction. During the investigations we have obtained a series of anthraquinones having antagonistic activity concerning blights causative agents. Some of these anthraquinones are able to act witheringly on phytoparasitic nematodes at certain conditions. The information indicating the correlation of the phenols series with the germicidal, antiparasitic, and antigelmint and nematocidal properties of some plants is presented in many papers. In the correlation with it, we have conducted the experiment for anthraquinones detection from seven *Polygonum* kinds and determination of their bioactivity in respect with *Ditylenchus dipsaci* cauline nematodes.

The presence of a 3,4,5-trihydroxy-, 3,5-dimethoxy-4-hydroxy- and 4-hydroxy-3-methoxyanthraquinones were determined as a result. The water suspensions of this substance were tested in laboratory on *Ditylenchus dipsaci* nematodes at different concentrations on clock glasses. Our investigations did not indicated the withering action of extracted substances on the phytoparasitic nematodes, however there were some depressing of them, expressed in slowed down motion of nematodes in the version with 4-hydroxy-3-methoxyanthraquinone since the first day of the experiment. The effect of 3,5-dimethoxy-4-hydroxyanthraquinone at the concentration of 0.0658 mg/mL was expressed by temporary (24–48 h) catalepsy of nematodes, while in the monitoring the nematodes were moving actively during the experiment (7 days). The version with 3,4,5-trihydroxyanthraquinone has appeared at the monitoring level. Apparently, the effect of these substances results in temporary disturbances of astasia of nematodes and the further investigation will allow us to find out the mechanism of its inhibition. These facts are interesting and they should be taken into account when one uses similar compounds as the potential agents for the development of the fight strategies against nematodes. So, the inhibition of a motor activity of nematodes in the indispensable period of plants vegetation will allow to lower the damage inflicted by them to plants. It should be also mentioned, that the extracted plant anthraquinones were tested in the form of water suspensions, that is ecologically safe. It is possible, that in the case of their recombination into dissoluble substances the influence on nematodes will be improved.

THE INFLUENCE OF *P*-CRESOL ADDITIVES ON THE STABILITY OF DIESEL FUEL/WATER EMULSIONS

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P-cresol presents in plant essential oils of *Anthriscus silvestris (*L.) Hoffm., *Lilium candidum*, *Helichrysum arenarium* L., etc. along with other alkyl substituted phenols. The application field of alkyl substituted phenols is constantly expanding. Some of these substances are used as antioxidants in fuels, lubricating oils and nutrition products. One of the important properties of these compounds is their surface activity. Due to the relatively high surface activity, antioxidants based on of alkyl substituted phenols can be assumed to promote formation of dispersed systems (emulsions, microemulsions, nanodispersions) in matrices, if matrices contact with insoluble liquids.

Cresols cannot be used as emulsifiers. Nevertheless, *p*-cresol can act as co-emulsifier. The partition coefficient of *p*-cresol in the system hexane–water is 0.97 [1], i.e. the solubility of *p*-cresol in both phases is approximately the same. Thus, *p*-cresol in the presence of other emulsifiers goes from one phase of emulsion to the other. This can lead to significant decreasing of interfacial tension and nanodispersion formation. The phenomenon of nanodispersion formation has been investigated in systems containing ethanol as co-emulsifier (co-surfactant) [2].

The authors of this abstract have compared the stability of emulsions with the same pH values of water phase, containing and non-containing p-cresol. The organic emulsion phase consisted of diesel fuel. The diesel fuels of two different marks (№1 and 2) were used. The water phase contained solutions of either sodium hydroxide, or sodium sulfide, or sodium sulfite. Initially pH of the prepared solutions was 12 (solutions of sodium hydroxide or sodium sulfide) or 10.5 (solution of sodium sulfite). Then the initial solutions were being diluted by distil water (emulsions with such water phase did not contain *p*-cresol) or by *p*-cresol 0.01 M water solution (in this case emulsions contain *p*-cresol) down to the required pH value. The ranges of the solutions pH were 8.5–12.0 (for the solutions of sodium hydroxide or sodium sulfide) and 8.5–10.5 (for the sodium sulfite solutions). All emulsions were prepared by shaking for 20 seconds. The stability of the emulsion has been determined as a period of total phase separation. The obtained results indicate that *p*-cresol additives lead to the significant (by 3–8 times) stability increasing for the emulsions containing diesel fuel №1, sodium hydroxide solutions (if pH value of water phase is 8.5–10.5) or sodium sulfide solutions (pH is 10.0–11.1) and for the emulsions containing diesel fuel №2, sodium hydroxide solutions (pH 9.5) or sodium sulfite solutions (pH 8.5; pH 9.3). Thus, the introduction of *p*-cresol in diesel fuel can increase the stability of the formed emulsions if diesel fuel contacts with alkaline solutions. The explanation of these phenomena requires further investigations.

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MOLECULAR COMPLEXATION OF IVY AND LICORICE SAPONINS WITH DOXORUBICIN

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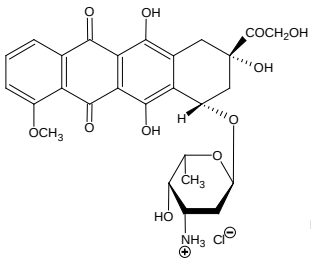
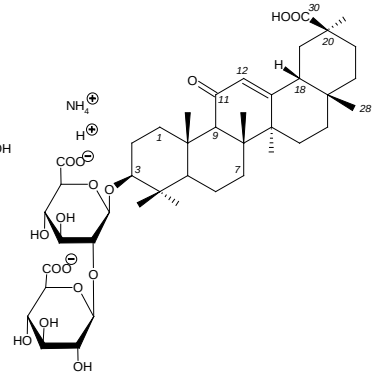
One possible method for reducing therapeutic doses of drugs, increasing their solubility, and expanding the spectrum of biological activity is to form clathrates with plant saponins.

Triterpene saponins α-hederin (hederagenin 3-*O*-α-*L*-rhamnopyranosyl-(1→2)-*O*-α-*L*-arabinopyranoside) and hederasaponin C (hederagenin 3-*O*-α-*L*-rhamnopyranosyl-(1→2)-*O*-α-*L*-arabinopyranosyl-28-*O*-α-*L*-rhamnopyranosyl-(1→4)-*O*-β-*D*-glucopyranosyl-(1→6)-*O*-β-*D*-glucopyranoside) are predominant triterpene glycosides of most species of the ivy genus *Hedera* L. Glycyrrhizic acid is the main triterpene saponin of licorice roots *Glycyrrhiza glabra* L. Monoammonium glycyrrhizate (glycyram) is used as anti-inflammatory and antiallergenic drug.

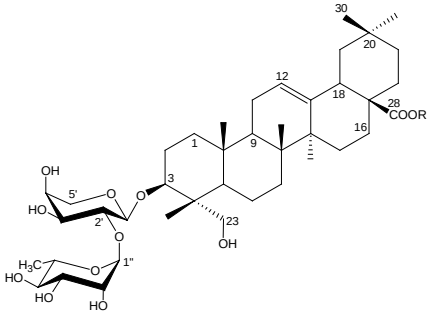
We prepared molecular complexes of ivy and licorice triterpene glycoside with doxorubicin (adriamycin). Doxorubicin is one of the most widely used and potent drugs against human cancer.



Hydrochloride of doxorubicin



Glycyram



α-Hederin (R=H) and hederasaponin C (R=←βGlc*p*-(6←1)-βGlc*p*-(4←1)-αRha*p*)

Using a method of spectrophotometry, the complexation of hydrochloride of doxorubicin with α-hederin, hederasaponin C and glycyram in aqueous solutions at pH 7.2 was investigated. Glycosides form complexes with doxorubicin in the 1:1 molar proportion. The stability constants for doxorubicin complexes with α-hederin, hederasaponin C and glycyram were determined ($K_s = 4.20 \times 10^5$, $K_s = 1.56 \times 10^7$ and $K_s = 5.63 \times 10^4$ M^{-1}, respectively).

ANALYSIS OF THE WATER′ FORM OF *Polygonum amhpibium*

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Polygonum amhpibium in national medicine in the capacity of diuretic and antineurologic means, for treatment of diabetes, hemorrhoids, and gout, rheumatism, dropsy and depletion nervous and endocrine systems is used for a long time. In a national economy this plant for skin tanning and for dye of silk and wool is used. The width of use of this plant is caused by presence of polyphenols, flavonoids, vitamins and tannins in its chemical composition.

Earlier in Kazakhstan the terricole′ form of this plant has been studied. Studying of qualitative structure of a grass and roots *Polygonum amhpibium*, prepared in flood plain of the Esentaj River was the purpose of our research. For extraction of bio-active substances of a plant we had been used 50% water ethanol and water acetone. At the analysis of the extracts prepared by maceration and thermal extraction, has been established:

- In both extracts from grass and roots of *Polygonum amhpibium*, a considerable quantity of amino acids, flavonoids, hydrolabled tannins, catechins and polyphenols has been defined.
- The smaller quantities of carbohydrates and alkaloids are present at this plant.

The comparative qualitative analysis water–acetone extracts of terricole' and water′ forms of *Polygonum amhpibium* has shown:

- In the terricole′ form of a plant contains more than polyphenols, and in the water′ form aminoacids and flavonoids is prevail.
- Aqueous-alcoholic extracts of a plant contain considerably quantity of flavonoids.

The component composition of carbohydrates, amino- and phenolic acids, phenols and flavonoids has been identified by HPLC analysis.

Researches of a chemical composition of *Polygonum amhpibium* are proceeding.

INTENSIFICATION OF F HYDRATION AND ALKALI REFINING PROCESSES OF COTTONSEED OIL IN THE MICELLA USING ELECTROMAGNETIC IMPACTS

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At the present stage of oil industry development the new technology using electro-physical impacts on the perfected process is developed and implemented.

Technology of refining of cotton micella has a number of drawbacks that determine a significant loss of neutral fat, alkali, etc.

Therefore, modernization of this technology with the using of electromagnetic impact is considered to be scientifically and practically important.

We have using the electromagnetic field with strength H = 1000–1500 oersteds for treatment of cotton micellas for 5–15 minutes and further subjected to alkali refining in concentration 150–200 g/L, with an excess of 50–100%. Refined samples of micellas were separated and cotton soapstocks of different quality obtained. The traditional method and mode of refining of cotton micella were used as a control [1].

It was founded, that use of electromagnetic impact leads to the formation of the more dense soapstocks, than in the conventional method of separation. For example, neutral fat content of 10–15% less than the conventional method of producing cotton soapstock. Also content of phosphatides and unsaponifiables is higher in the soapstock obtained using electromagnetic impact, than the control samples of soapstock.

It should be noted, that cottonseed oil obtained using electromagnetic impact is for 3–5 units lighter, than the oil obtained by conventional techniques. Consequently, soapstocks obtained using electromagnetic impact are darker, than soapstocks obtained by conventional techniques.

This effect can be explained by the fact that the electromagnetic force and the polarity of the surface tension of gossypol phosphatides and their derivatives, as well as other coloring oil components, thereby improving their coagulation and separation.

Thus, our studies show that the use of electromagnetic interference at the refining of cotton micelle allows increase the quality of the oil, and reduce the loss of neutral fat in the soapstock, which has a positive impact on improving the technical and economic efficiency of the technology.

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TECHNOLOGY OF EXTRACTION OF SAFFLOWER OIL FROM GRANULATED CAKE

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Nowadays the introduction of technological scheme "form pressing-extraction" for the production of safflower oil is hampered by lack of effective technology for stable granular cake with easily-extractable structure.

The experimentally obtained data allowed to set the absolute value of the coefficient of diffusion from its inner side and end walls, this ratio also changes depending on the value of its diameter and length. It is known, that the nucleus of safflower seed husks difficult to separation and therefore, in practice, often the pulp produced with high husk content, which negatively affects the quality of the obtained oil (taste imparting bitterness, etc.) and reduces the output of press oil extraction.

One solution to this problem is the granulation of pomace (cake) produced safflower pulp molding method in industrial pellet press.

On the basis of the study of composition, external and internal structure of the pulp and safflower oil cake we developed an effective technology for the extraction of safflower oil from granulated cake, which makes it the lowest rate of the solvent to obtain the highest yield of valuable oil.

Particularly, it was founded that the porosity of the granules on the lateral surface is for 20–25% higher than the end face. It is favorable for extraction by repeated washing with hydrocarbon solvent.

Spectral analyzes of pressed and extracted safflower oils showed, that the final content of carotinoids and chlorophyll are for 10–15% more in the extracted oil.

The optimal grain sizes of safflower oil cake, modes of extraction were developed. In particular, a rational scheme of the streams in the industrial extractor, low residual oil content in the meal (no more than 1.0% by weight of the meal) was developed.

Comparative analysis of the chemical composition of safflower oils derived by pressing and extraction methods had been carried out. It was founded, that the fatty acid composition identical, but the acid number, content of unsaponifiable matters are differ. In particular, the extraction safflower oil their contents are more approximately for 1.5 times and 1.7 times, respectively.

Were studied changes in the absolute value of the coefficient of internal diffusion of its protein wall and decreasing of straight depending on 45×10^{-7} to 30×10^{-7} cm^2/sec to granules with a diameter of 10 mm, and on the end wall in the range from 42×10^{-7} to $44 \times 10^{-7} cm^2/sec$.

The experimentally obtained data allowed to set the absolute value of the coefficient of diffusion from its inner side and front walls, this ratio also changes depending on the value of its diameter and length.

Thus, the developed technology for the extraction of safflower oil from granulated cake can significantly improve the technical and economic performance of oil and fat industry and expand its range of oils products.

THE STUDY OF THE CHEMICAL COMPOSITION OF *Polygonum amphibium*

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The genus *Polygonum* (*Polygonaceae*) consists of about 300 species, which are distributed worldwide, mostly in the Northern temperate region [1]. The diversity of the genus *Polygonum*, which comprises 49 species, is not well known in Kazakhstan [2]. *P. amphibium* L. grows in standing or slowly moving water in lakes, reservoirs, canals, ditches, large fenland drains and sluggish streams and rivers [3].

The object of study – *P. amphibium* which collected in the summer of 2012 in Almaty region, Pervomay lakes. We determined the purity of raw materials: moisture – 6.89%, ash content – 8.49%. Extractives were determined by extracting agents: water (13.05%), 50% ethanol (14.93%) and 50% acetone (15.27%). By methods of PC and TLC were identified groups of biologically active substances: triterpenoids, tannins and flavonoid, carbohydrates, polysaccharides, amino and phenolic acids.

Hydrolysis of ethanol extract 2% sulfuric acid for 3 h showed that *Polygonum amphibium* contains glycosides of quercetin and isorhamnetin.

We have defined the quantitative content the macro- and micro-elements analysis of the ash residue by gas-liquid chromatography method (Table).

TABLE. **Micro- and Macro-Element Analysis of the *Polygonum amphibium*, %**

Element	Content	Element	Content
Na	2.913	Mn	0.234
K	12.021	Zn	0.061
Mg	5.0151	**Ca**	18.943
Cu	0.0115	Cd	6.28×10^{-4}
Ni	1.56×10^{-3}	Pb	No.
Fe	0.958		

The Table shows that the *Polygonum amphibium* is dominated by K, Mg, Ca; heavy metals and radionuclides are not detected, which indicates the ecological purity of the studied species.

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SYNTHESIS OF KETOAMIDE OF PULEGONE

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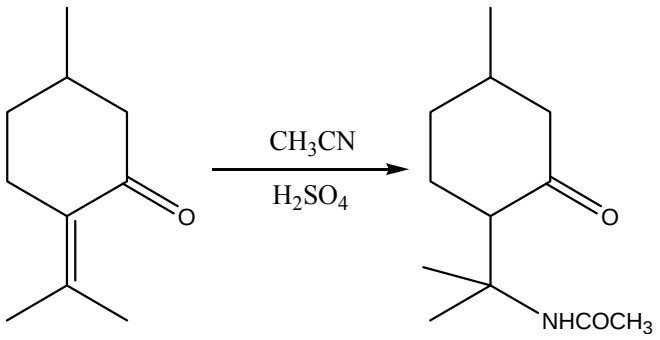
Pulegone is widespread component of essential oil of genera of *Nepeta* (*Nepeta cataria* L.) and *Mentha* (*Mentha piperita* L.*, Mentha pulegium* L.). Pulegone is used in perfumery and aromatherapy [1].

Pulegone (**1**) was isolated from the essential oil of *Ziziphora interrupta* Juz. Purpose of investigation was to obtain new nitrogen-containing derivative. Acid-catalized reaction between acetonitrile and pulegone was investigated. After neutralization of reactionary mix, new compound ketoamide – *N*-(2-(4-methyl-2-oxocyclohexyl) propan-2-il) acetamide (**2**) was obtained.



1 **2**

In IR-spectrum of (**1**) the intensive absorption bands of carbonyl group were observed at 1710 cm^{-1} and absorption band characterizing $NHCOCH_3$ group at 1560, 1643 and 3293 cm^{-1}. In ^1H NMR spectrum (δ, ppm., J/Hz) were observed signals: 7.33 (1H, s, NH), 2.06, 1.94, 1.76, 1.71 (3H, s, $NHCOCH_3$), 1.32 (3H, s, CH_3), 1.14 (3H, s, CH_3), 0.92 (3H, s, CH_3). In ^{13}C NMR spectrum (δ, ppm, J/Hz) were observed signals: 211.3 (C=O), 169.40 (NHCO), 54.24 (CH), 54.29, 51.91 (CH_2), 35.97 (CH), 34.34 (CH_2), 28.19 (CH_2), 25.31 (CH_3), 24.07 (CH_3), 24.02 (CH_3), 22.62 (CH_3). Found, % C 68.17; H 10.41; N 6.43, $C_{12}H_{21}NO_2$; calcd, %, C 68.21; H 10.02; N 6.63.

Thus, the proposed structure for (**2)** was confirmed by IR-, ^1H NMR, ^{13}C NMR spectrum.

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THE REACTION OF *N*-ALKYLATION ANABASINE

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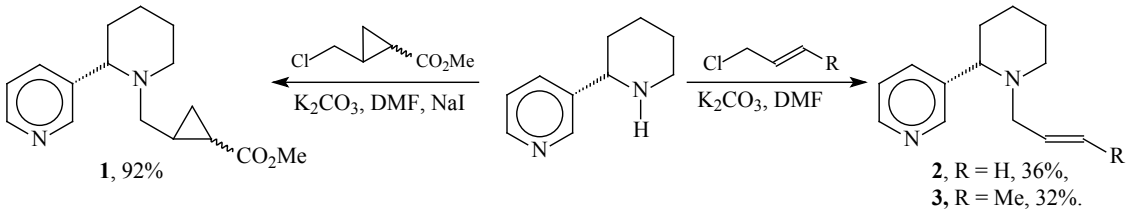
The alkaloid anabasine derivatives have been used as agonist and antagonist of neuronal nicotinic acetylcholine receptors (nAChR), relating to the group of neurotransmission receptors, targeting on the treatment of such debilitating neurological disorders as Alzheimer′s disease, Parkinson′s disease, schizophrenia and depression. The methods of introduction Boc [2], benzyl [3] substituents to N-H bond are particularly defined in the literature, however, the dates about synthesis of *N*-cyclopropyl- and *N*-alkenyl derivatives anabasine, to be interest as biological active compounds, are virtually absence.

The manner of synthesis *N*-replaced anabasines containing cyclopropylmethyl- and alkenyl groups as substituents have been proposed.

It is established, that interaction anabasine with methyl 2-(chloromethyl)cyclopropane carboxylate at 110°C in the media of DMF in the presence of 1.5 excess K_2CO_3 and 10% mol. NaI proceeds to formation methyl 2-((2-pyridin-3-yl-piperidine-1-yl)methyl)cyclopropane carboxylate (**1**) with the yield 92%. At the use of 1% mol. NaI, and also other solvents (Me_2CO, MeCN) and at more low temperatures the conversion of anabasine didn′t exceed 30%.



1, 92%

2, R = H, 36%,
3, R = Me, 32%.

The reaction of *N*-alkylation anabasine by alkenylhalogenides (allyl- and crotylchloride) on the media of DMF in the presence of K_2CO_3 proceeds at 40°C with the formation of 3-(1-allylpiperidine-2-yl)- (**2**) or 3-[1-(*trans*-but-2-en-1-yl)piperidine-2-yl]pyridine (**3**) with the yields 36 and 32% respectively. The angles of rotation *N*-allyl and *N*-crotylanabasine composed of $[\alpha]_D^{25}$ –125.2° (*c* 1.46, $CHCl_3$) and –139.5 (*c* 6.85, $CHCl_3$).

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ASARONE ISOMERS – THE MAIN COMPONENTS OF ESSENTIAL OIL FROM AERIAL PARTS OF *Valeriana transjenisensis* (*Valerianaceae*) OF SIBERIAN REGION

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Valerian zaeniseyskaya (shaded) – *Valeriana transjenisensis* Kreyer is one of the smallest species of the genus *Valeriana officinalis*, native to Siberia. The plant is found in forest and steppe zones of the Krasnoyarsk Territory, the mass does not form thickets. For medicinal purposes is harvested underground part of the plant (rhizomes and roots) – a source of essential oil, which is associated with sedation and other valerian activities. Before harvesting the rhizomes with above-ground part roots of valerian, representing 80% of the total weight of the plants, mowed and burned, ie hardly used, despite the long history of its use. Therefore, the study of biologically active substances of valerian herb will solve the problem of complex processing officinal medicinal plants. In this regard, the purpose of the study was a component of essential oil of aerial parts of *V. transjenisensis* by using the gas chromatography-mass spectrometry.

Studies were conducted in 2012 in natural populations of *V. transjenisensis* in vicinity of Krasnoyarsk. Aboveground part of *V. transjenisensis* was collected during dry weather in the phase of flowering. Essential oil from the aboveground plant parts were obtained by exhaustive water and steam distillation from air-dry raw material for 9 hours. The duration of the process water and steam distillation was established experimentally by studying the dynamics of change of the output of essential oil in time. Based on the results of three chasing away the oil yield was 0.4%. Component composition of the oil was determined by using the method of gas chromatography-mass spectrometry (Agilent Technologies 7890 A).

The sample of oil is easily movable fluid lighter than water. The oil has a light yellow colour.

Chromatography-mass spectrometric method for the study of samples of essential oil of *V. transjenisensis* provided the possibility to establish the presence of more than 40 components, 35 of them making up 94.3% of the total, they are known compounds and identified by us.

The content of other components (including monoterpenes such α-pinene, β-pinene, limonene, etc.) does not exceed 0.1%. The absence of sesquiterpenoids with pronounced sedative activity (valerenol, valerenal, valeranon) characteristic of the essential oil from the roots and rhizomes of valerian were noted In the composition of the essential oil aboveground *V. transjenisensis* compounds found phenylpropenyl group – eugenol and its methyl ester in the form of two isomers: (*Z*)-methyl isoeugenol and (*E*)-methyl isoeugenol, elemitsin and all three isomers asarone: α-asarone ((*E*)-asarone), β-asarone ((*Z*)-asarone) and γ-asarone (sekishon). The total content of the three isomers asarone is 55.7% of whole oil, with a predominance of the most toxic (*Z*)-asarone (32.7%).

Taking account the pharmacological properties of isomers Asarone, the need for further study of the essential oil of the aerial *V. transjenisensis* is quite obvious.

ELECTROCHEMICAL MODIFYING OF STARCH AS THE WAY CHANGE OF ITS PROPERTY AND STRUCTURE

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As is known starch application in many industries is demanded by modifying of its structure and properties, and methods of updating would not change feature and individuality of this natural polymer. Among numerous ways of modifying of structure and properties of polymers chemical updating takes a special place. As the way of creation of materials with the improved complex of properties will receive this way development and further. And successes in this area first of all should be connected with the physical and chemical approach to an estimation and generalization of already existing extensive experimental and theoretical material from the point of view of the polymeric nature of reacting particles.

Here some years in chair the General chemistry within the limits of the state project on working out of technologies of reception of the modified starch, for the purpose of its application in the textile industry are conducted researches. One of such directions is starch oxidation electrochemical by in the presence of sodium chloride. Natural starches subjected to electrochemical processing in process flushing to starched suspension through electrolyze. The scheme of reception of the starch modified in the electrochemical way, it is based on formation reactions of hypochlorite from the received chlorine, being a process product electrolyze and oxidations of starch by means of it hypochlorite in this solution.

Transmission a current through starched milk has led to its decrease pH. Physical and chemical properties of the starch modified in the electrochemical way, are similar with oxidized starches. The increase in quantity of the electricity spent for processing of starch, naturally led to increase of degree of oxidation. It is established, that electrochemical processing of starched suspension allows to receive the starch forming transparent, not inclined to gelatinization of paste, at drying it forms elastic films. Thanks to the charged – groups at oxidized starched reduction of propensity of paste to retro gradation is observed.

At not selective oxidation of starch occurs destruction of polysaccharide links to formation aldehyde groups which usually are oxidized faster, than hydroxyl. At initial stages trailer aldehyde groups are oxidized in carboxyl. Though aldehyde in native starch it is not enough groups, as a result of hydrolysis or rupture polysaccharide chains in the course of oxidation are formed additional aldehyde groups which can be oxidised further in carboxyl. Thus, electrochemical processing of starch is similar to not selective oxidation.

Hence, at use of an electrochemical way of updating polysaccharide it is accompanied its oxidizing destruction which results to reduction supramolecular the fragments forming structure colloidal of a solution of starch.

AMINO ACID DERIVATIVES OF 3-ARYLISOCOUMARINS

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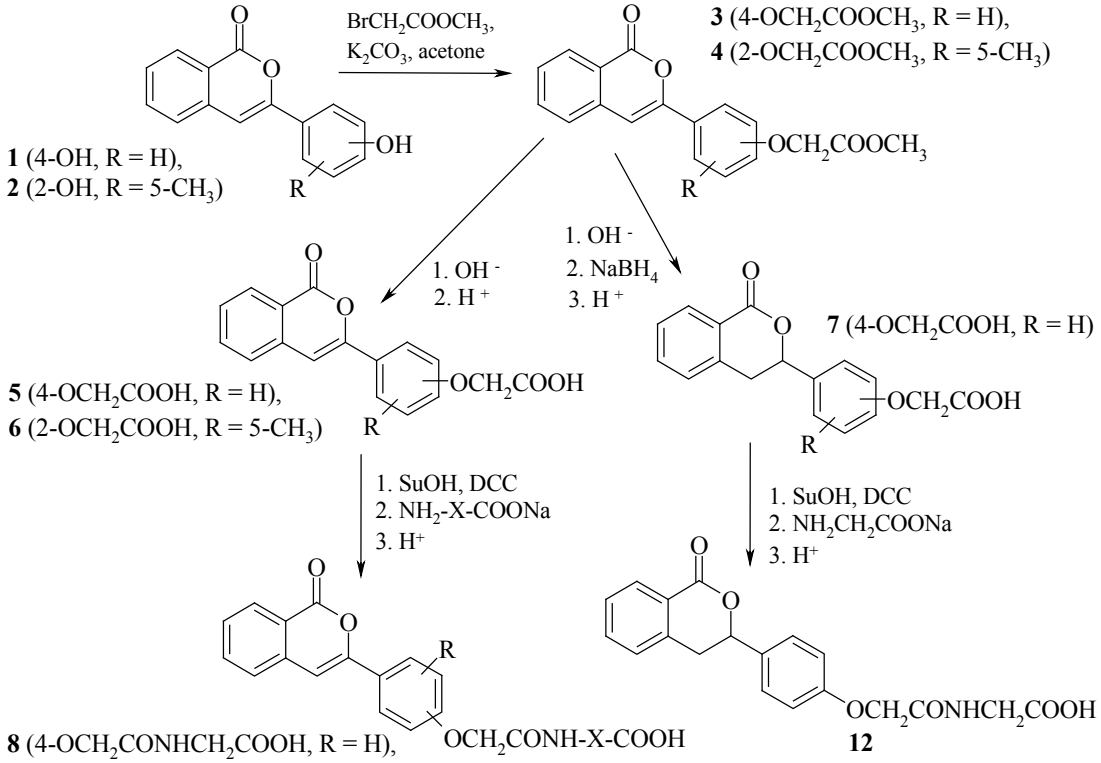
It was known that natural (homalicine, dihydrohomalicine) and synthetic 3-phenylisocoumarins and dihydroisocoumarins with hydroxyl groups in the phenyl substituent demonstrate biological activity (anticoagulant, laxative action). But untill now chemical transformation and using in organic synthesis are not insufficiently investigated for 3-(hydroxyphenyl)-isocoumarines. For example, these substances can be modified by amino acid residues. 3-(Hydroxyphenyl)isocoumarines **1**, **2** were alkilated by methylbromoacetate giving esters **3**, **4**. Based on compounds **3**, **4** 3-phenylisocoumarins **5**, **6** and 3-(phenyl)dihydroisocoumarin **7** with acetic acid fragment were synthesized [1].



Activated esters of acids **5–7** were obtained by *N*-hydroxysuccinimide (SuOH) and dicyclohexylcarbodiimide (DCC) treatment. *N*-Acetyl amino acids **8–12** with glycine, alanine, β-alanine residues were prepared via condencation of activated ester and sodium salts of the amino acids in aqueous dioxane (1:1) at room temperature with subsequent acidolysis of the resulting salts [2].

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THE INFLUENCE OF BIOCOMPLEX CO III ON THE PASSIVE ELECTRIC PARAMETERS OF BLOOD CELLS

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The study of activity of synthesized new biologic active substances in radiation lesion of the human organism doesn't loose its actuality. Synthesis and study of radioprotection property of biocomplexes of microelements assists in the development of new radioprotector drugs.

Aim of investigation was the study of influence of biocomplex Co III on the passive electric options of blood cells.

We have studied the passive electric options (dielectric loss, electric capacity) of blood cells (erythrocytes, leukocytes, lymphocytes). The blood was obtained by decapitation white rats, 180–200 g. By centrifugation from blood we isolated the blood cells and founded their passive electric parameters using bridge scheme. Radiation of animals was performed with γ-setting in dose 5 g. The biocompex was injected in dose 4 mg/kg intraperitoneally.

Experimental animals were divided on the following groups:

I – control (intact);

II – control (radiated);

III – animals received biocomplex within 20 days (4 mg/kg).

Animals were followed up during 30 days. Passive electric options were measured with bridge of alternating current (frequency 1000 Hz).

The results of research showed that passive electric options slowly become high and reach the reliable values in the top heat of radiation disease and is 50%, in comparison with control-intact animals.

The dielectric looses of erythrocytes is about 60%, leucocytes – 40% from the normal parameters.

Use of Co III after radiation in dose 4 mg/kg significantly decreased passive electric parameters of blood cells, erythrocytes and leukocytes in radiated animals during the study, especially in erythrocytes for 40% and leukocytes for 20% from the control ones.

Thus, the results of our study shown, that the biocomplex Co III had normalized violations caused by radiation and passive electric options of blood cells. This may be considered as significant pharmacologic effect of this preparation.

INFLUENCE OF THE DITERPENOID SALVIFOLIN ON THE PERMEABILITY TRANSITION PORE IN RAT LIVER MITOCHONDRIA IN STREPTOZOTOCIN-INDUCED DIABETES

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It is known, that the activity of a mitochondrial permeability transition pore (mPTP) depends on concentration of intracellular Ca^{2+} and plays the leading role in regulation of cellular processes and mechanisms of dysfunction of mitochondria at various pathologies. Besides, it is shown that the mPTP inhibition pharmacological agents lead to stabilization of membranes of mitochondria. In this regard, search of the new plant compounds interacting with mPTP and possessing tyre-tread effects at mitochondrial dysfunction are very significant.

The overall aim of this work was to study the effect of diterpenoid salvifolin, isolated from a plant *Pulicaria salviifolia*, on mPTP of rat liver under the streptozotocin (STZ)-induced diabetes.

The experiments were carried out on outbred white rats of 180–200 g. Laboratory animals were divided into 4 groups: The I group was intact; 2) The II group, animals with STZ-induced diabetes; 3) The III group with STZ-induced diabetes + insulin; 4) The IV group was of STZ-induced diabetes + salvifolin. Intact animals were injected intraperitoneally with 0.2 mL of 0.9% physiological solution after daily starvation. The animals of other groups after daily starvation were injected intraperitoneally with streptozotocin in dose of 60 mg/kg. After 11–12 days of the injection went by, when the quantity of glucose in blood reached 11 mmol/L, animals, during 8 days, were intraperitoneally injected with 0.2 mL of 0.9% of the physiological solution – II group, 0.5 u/kg insulin – III group, 3.32 mg/kg salvifolin – IV group. Ca^{2+} dependent swelling of liver mitochondria was photometrically studied in 540 nm.

The obtained data show that the speed of swelling of the mitochondria isolated from a liver of streptozotosin animals was much more comparing to mitochondria of the liver of intact animals, when 10 μM of Ca^{2+} is available. It gives evidence that, in these conditions, mPTP of mitochondria of a liver of streptozotosin rats passes more open condition. It is known that, at experimental diabetes, the mPTP function is broken. At pharmacotherapy of experimental diabetes with insulin (group III), and salvifolin (group IV), inhibition of swelling of mitochondria is observed comparing with swelling of the mitochondria isolated from a liver of control animals (group II). As our experiments show, the inhibition of swelling noted by us, result in closing of mPTP under the influence of insulin and/or salvifolin.

Thus, on the basis of the obtained results we demonstrated, that salvifolin has stabilizing effect on membranes of mitochondria of a liver of rats, inhibiting mPTP at STZ-induced diabetes.

MICROBIOLOGICAL TECHNOLOGY IN COMPLEX WITH MICRONUTRIENT SEED DRESSING

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In recent years, significant progress in the creation of artificial casings to protect the seed are reached. Among the methods of applying artificial membranes are most promising panning, and inlaying (inlay). Pelleting of seeds, that is, coating the seed of protective nutrient shell (formed spherical pellets) – One of the ways of their pre-training. In order to study the impact of complex microbial drugs and trace elements in the seed dressing are made with carrot seeds (small seeds) and tomato (medium). As a microbiological preparation was selected domestic complex microbial fertilizer "Baikal EM1", produced by SPC Ltd. "Baikal CMU" and as micronutrient supplements concentrate "Bio-bromo-iodine", produced from mineral sources Chartak district.

Solutions "Baikal EM1" taken in the ratio of 1:100 , the concentrate "Bio-bromo-iodine" in the ratio of 1:200 were moistened with seeds of carrot and tomato added to the adhesive solution of bentonite clay. The filler was applied Dried, sieved compost manure through a sieve diameter holes: for very small seeds – 0.15, for small and medium – 0.25 mm. Dosed spraying was conducted adhesive liquid (the estimated flow rate – 20 liters per 1 ton of seeds) seeds which are in constant motion in the drum at a predetermined interval of time (several minutes). Seeds thus treated until it reaches the small size of 3–5 mm and the average – 7 mm or more. Dried in an oven with IR heating seeds stored three months.

Sowing seeds held in the spring on an area of 100 m2 on 2 sites (carrot, tomato) and 3,4-D reference to the same crops. Obtained seedlings for 2–3 days before controlling for carrots and tomatoes for 3–4 days. During the growth of the disease in experimental plots were observed. Singly produced spray formulations "Baikal EM1" in the proportion of 1:800 and 1:100 concentrate trace elements. A harvest of carrots have been got 20% higher than the control and 25% for tomato. The taste of the received products are improved, the color of the leaves and a bright range of products.

The results obtained in this work showed that the use of microbiological preparation Baikal EM1 in combination with trace elements can degrade minerals, turning them into organic, to increase the survival rate of plants due to the formation of soil biocomlex. On the whole Baikal EM 1 can be effective as a biological method of land reclamation. The complex trace element iodine increases the disinfecting properties of seeds in the initial period. Disinfection prevents the spread of fungal and bacterial diseases. The combination of microbiological fertilizer "Baikal EM1" with a set of trace elements containing iodine improves the initial and consistent protection of plants.

THE α-SANTONIN TRANSESTERIFICATION AND SYNTHESIS OF EUDESMANE ACIDS ESTERS

N. Merkhatuly, S. B. Abeuova, A. N. Iskanderov, L. T. Balmagambetova

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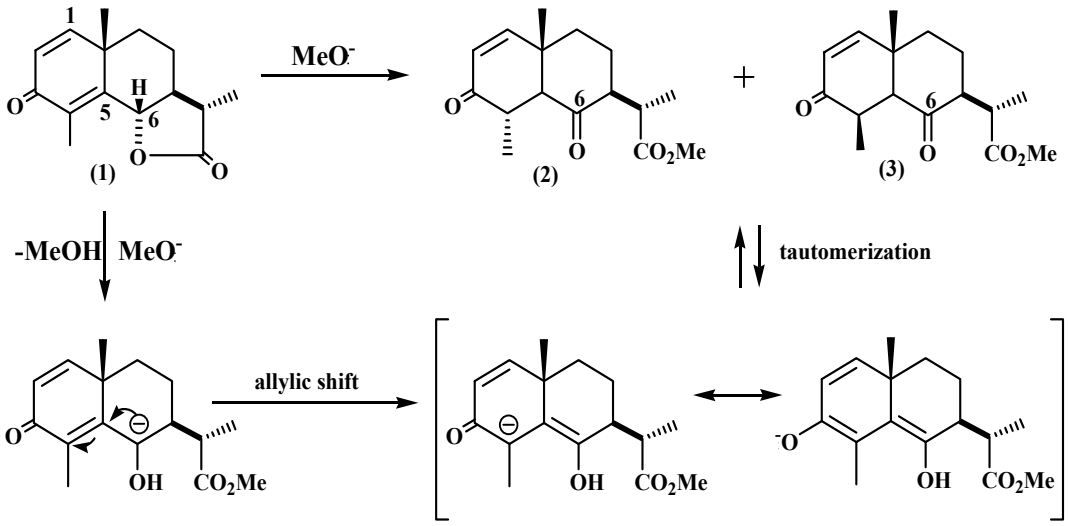
The alkaline transesterification of eudesmanolide α-santonin with methanol in the presence of sodium methoxide was investigated. The epimeric 6-keto-esters (**2**) and (**3**) in 50% and 40% yields were synthesized.



The structures of synthesized compounds (**2**) and (**3**) established using UV-, IR-, ^{1}H NMR, mass-spectroscopy.

ALLYLIC REARRANGEMENT AND SYNTHESIS OF α-SANTONIN NEW DERIVATIVES

N. Merkhatuly, A. N. Iskanderov, S. B. Abeuova, A. T. Omarova

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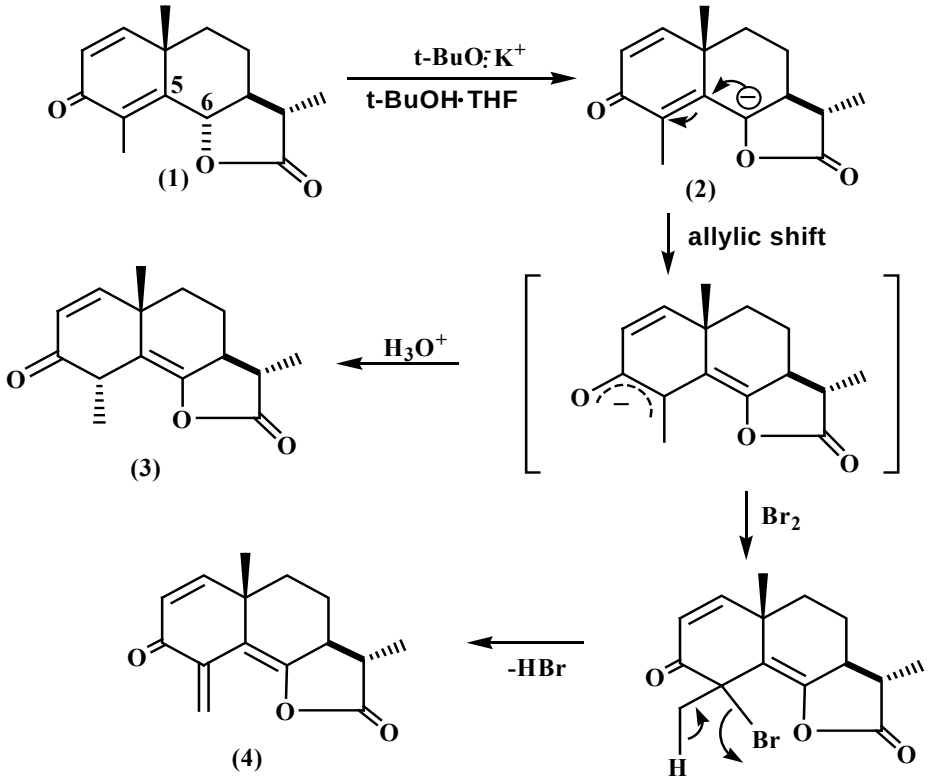
The carbanionic allylic rearrangement of eudesmanolide α-santonin (**1**) in super-basic medium was investigated. The generated enolate-anion (**2**) was then treated with acid and bromine to give the new derivatives of α-santonin, (**3**) and (**4**), in 95% and 96% yields, respectively.



The structures of synthesized compounds (**3**) and (**4**) established using UV, IR, ^{1}H NMR, mass-spectroscopy.

SYNTHESIS OF BICYCLIC SESQUITERPENOIDS BASED ON HANPHILLINE

N. Merkhatuly, S. B. Abeuova, A. N. Iskanderov, Z. S. Suleymbekova

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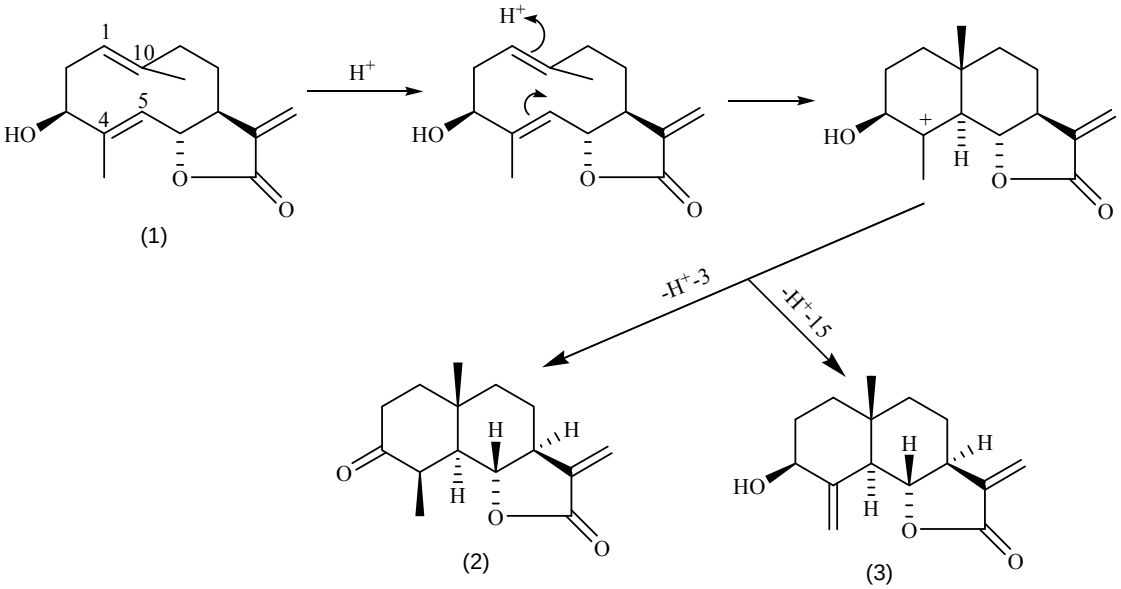
The stereocontrolled carbocyclization of *E,E*-germacranolide hanphilline (**1**) with 99%-pure formic acid was investigated. As a result the *trans*-condensed-5α(*H*),10β(Me)-eudesmanolides (**2**) and (**3**) in 65% and 30% yields were synthesized.



The structures of synthesized compounds (**2**) and (**3**) established using UV-, IR-, ^{1}H NMR, mass-spectroscopy.

THE ESSENTIAL OILS OF THE PALEOENDEMIC, RELIC AND SUBENDEMIC PLANTS FROM MONGOLIAN GOBI

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The essential oils were isolated by hydrodistillation from the aerial parts of the some paleoendemic, relic and subendemic plants from Mongolian Gobi.

The essential oils were analyzed capillary GC and GC-MS. A summary of results is as follows:

No	Plant names	Main components
1	*Asterothamnus molliusculus* Novopokr	Camphor (34.9%), β-pinene (20.9%), sabinene (9.8%), 1.8-cineol (9.2%), limonene (5.8%), α-pinene (4.9%), myrcene (3.5%), β-phyllandrene (3.7%), α-thujone (2.8%)
2	*Asterothamnus central-asiaticus*Novopokr	β-Pinene (11.6–31.4%), sabinene (9.8–22.0%), β-phyllandrene (5.3–7.6%), *Z*-β-ocimene (5.0–8.9%), *E*-β-ocimene (4.0–5.6%), terpinolene (5.1–6.2%), α-pinene (3.7–5.3%), terpinene-4-ol (1.0–7.1%)
3	*Caryopteris mongolica* Bunge	α-Thujone (18.72%), *E*-β-ocimene (11.0%), limonene (8.8%), β-pinene (8.0%), terpinene-4-ol (7.2%), α-pinene (6.3%), sabinene (5.6%), germacrene-D (2.3%), γ-terpinene (3.1%)
4	*Thymus mongolicus* Ronnig	*p*-Cymene (35.6%), thymol (29.4%), thymol acetate (11.3%), terpinene-4-ol (3.2%), borneol (2.4%), carvacrol (2.4%), camphor (1.9%), γ-terpinene (1.8%), 1.8-cineol (1.6%)
5	*Thymus gobicus* Tschern	Thymol (29.6–36.0%), myrcene (2.8–14.6%), *p*-cymene (3.2–10.0%), borneol (8.4%), carvacrol (2.6–4.8%), camphor (3.2%), terpinene-4-ol (3.2%), limonene (1.0–2.7%), linalool (2.2%)
6	*Artemisia mongolica* (Bess) Fisch. ex. Makai	*Z*-β-Ocimene (14.6%), 1.8-cineol (14.6%), camphor (7.1%), myrcene (4.3%), sabinene (2.2%), limonene (1.7%), terpinene-4-ol (1.5%)
7	*Artemisia gobica* (Krasch) Grub	Camphor (25.2%), 1.8-cineol (15.3%), α-thujone (12.8%), terpinene-4-ol (5.2%), β-tujone (3.7%), artemisia alcohol (3.4%), α-terpineol (2.5%), myrcene (1.6%), *p*-cymene (1.4%)

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DERIVATIVE HUMIC ACIDS – A UNIVERSAL PRODUCT FOR SOLVING ENVIRONMENTAL PROBLEMS OF MINING TERRITORIES

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Ecological situation in Russia is one of the most important factors determining the health of the nation. In the mining districts contaminated surface and underground water. A large area of land occupied by numerous authorized and unauthorized, industrial and household waste dumps and landfills, also adversely affects the ecological situation. A lot of previously fertile soil is in a degraded state. In a number of territories violated or no natural soil cover. In the current economic conditions unfavorable ecological situation persists.

The most important solutions to the existing problems is the development and widespread application of the effective and economically acceptable environmental technologies. Biosphere stability to intensive human impact and its ability to recover due to the presence of its soil organic component – humus, the most important of which are humic acids.

Mastered at the pilot scale technology of production of the humic sorbents, which have unique properties, functions and areas of application. One of the important properties of sorbents on the basis of humic acids, which determines its role in the environmental technologies – ability to intensify the activity of soil microorganisms, oppressed presence in the soil of various toxic pollutants. This technology has a double effect determines the speed of treatment of polluted soils.

The experiments on studying the effectiveness of the derivative of humic acids as sorbents in the flood of crude oil showed that the drug particularly effective in cases when the content of oil products in soil does not exceed 1–2%. Given the low cost of such sorbents, simplicity of use and availability of raw materials for production, as well as the speed of the generated a process of self-purification of the soil can say that this method has no analogues and its rapid implementation of the absolutely real. An important property of sorbents of organic nature is their ability to provide rapid recovery of disturbed lands in conditions of mining.

Derivative humic acids developed and tested effective technology renovation of soils and lands, contaminated inorganic and organic toxicants, technology creation of fertile techno genic soils on artificial and natural soils, technology of restoration of the natural soil, sediment disposal of urban wastewater, detoxification of the body landfills, cleaning leachate landfill and wastewater.

Technology sanation of soils and lands disturbed during the development of mineral deposits, includes the handling of sorbent surface of the polluted area with a simultaneous or subsequent plowing disking.

Humates increase the water-holding capacity of soil, prevent dusting, increase resistance to water erosion.

Derivative humic acids effectively absorb ecotoxicants and enhance the livelihoods of local micro flora. Thus they become available to the influence of microorganisms, resulting in a relatively rapid degradation of these substances and clean-up of contaminated soils and lands.

HETEROCYCLIZATION OF CARBOHYDRATES REPLACED β-OXYTIOCARBAMIDE

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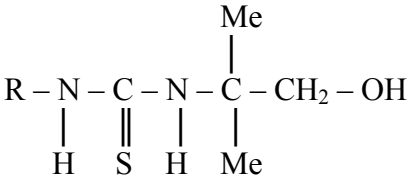
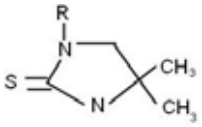
Glycosides of β-oxytiocarbamides, which formed as a result of accession 1,2-aminospirts to glycosilisotianates, have in *N*-aglicon structure some reaction centers, inside molecular interaction between which can lead to formation of a number of heterocyclic structures. Dehydration processes belong to number of the most probable ways of heterocyclization in the presence of dehydrating agents or the reagents promoting elimination of OH-groups. On the example of *N*-β-*D*-glucopyranosyl-*N*′-α-tetraacetate, α-di-methyl-β-oxyethyltiocarbamide (**I**) we studied reactions of heterocyclization of *N*-aglikon.



I

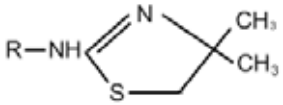
R – 2,3,4,6-tetra-*o*-acetyl-β-*D*-glucopiranosyl

It is established, that depending on the nature of initiating reagent and conditions of reaction *N*-aglicon cyclization to (**I**) can proceed with primary formation of one of three heterocyclic compounds:



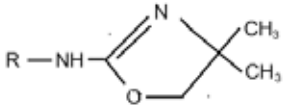
II

R – tioxo-4,4-dimethyl-1,3-diazol



III

R – amino-4,4-dimethyl-Δ^2-tiazolin-1,3



IV

R – amino-4,4-dimethyl-Δ^2-oxazolin-1,3

In the reaction mixture some some substances founded, but only one main product may be isolated as pure, thus, it will reveal the main direction of heterocyclization in the set conditions. The structures of the received compounds are identified by the spectroscopy PMR and IR-method, elemental analysis.

In spectrum PMR II, except signals of protons of a carbohydrate ring the widened signal is observed at 6.7 m corresponding to a proton H-N, and also a doublet 1.8 m.d. groups C–CH_3 and a quartet of AB groups of CH_2 group at 3.2 m d. Nature of splitting of signals C–CH_3 and CH_2 will be explained by entry into a cycle of the specified groups.

In IR spectrum of II, except an intensive strip at 1740 cm^{-1} (acetyl group) absorption is observed at 1340 cm^{-1} (val.w. C=S), 1440 and 1520 cm^{-1} (N–H, amide).

Comparing these data with spectral characteristics of initial substances, it is possible to explain the absence of characteristic for H-N poorly full widened signals in PMR, lack of a singlet IT-groups, perfect multiplicity of signals of protons in acyclic and cyclic aglicones. Besides, in IR spectrum of II there is no absorption strip IT-groups and there is an essential shift of a strip, characteristic for C=S. These data allow to consider structure of connection 2(*R*)-tiokso-4,4-dimetil-1,3-diazol of the quite probable.

PURIFICATION AND CONCENTRATION OF ANTIVENOM SERUM «ANTIVIPER»

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In TashIVS possibility of purification and concentration of the native horse serum against snake venom of the Central Asian Viper (Vipera Libetina) has been studied.

For this purpose we used the conventional in our country method "Diapherm III», which is based on the enzymic hydrolysis of native serum by pepsin; release of the active protein fraction by ammonium sulfate salt followed by isoelectric precipitation in the presence of chloroform.Determination of activity of native and concentrated serum Anti-Viper was performed by intravenous titration on white mice weighing 16–18 g by a mixture of viper venom with different antidote dilutions. As a working dose of the test – venom we took 2.5 LD_{50} poison that will kill 50% of the animals involved in experience. The processing of native serum Anti-Viper by "Diapherm III» method has brought about a significant degree of its purification and concentration. If for neutralization of venom doses of 2.5 LD_{50} it was necessary to take 0.2 mL of native serum, then for concentrated one it was required by 9 times less.Thus, the method of "Diapherm III» can be used in the production conditions for purification and concentration of native serum Anti-Viper.

TECHNOLOGY FOR PRODUCTION OF HIGH-TITER IMMUNE SERUMS AGAINST THE DONOR TRANSFERRIN WITH POLYMER CELLULOSE MATRIX

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In production of the diagnostic test-systems used for iron metabolism abnormalities diagnosis, and specifically for the iron-deficient cases preparation of the high-titre immune serums against such informative iron metabolism abnormalities′ marker as serum transferrin is really an important condition. The authors have developed technology for production of high-titer immune serums against donor transferrin using polymer cellulose matrix as an adjuvant based on the oxidized cellulose suspension. Polymer cellulose matrix has been prepared by 5 g of the finely cut cotton wool soaking in 100 mL of 25% aqua ammonia solution. Then freshly prepared copper hydroxide was added to the soaked cotton wool and mixed throughly, it was added more 50 mL of 25% ammonia and infused for 20 hours in the dark. Then mixture was added 25% ammonia solution up to the volume of 50 mL and well-stirred, following which the solution was poured out to the vessel containing 5 L of distilled water, mixed and during slowly continuously stirring strong sulphuric acid was being added until blue color solution disappearance. Laid-down cellulose suspension has been washed out by distilled water to the extent of sulfate ions negative reaction in the rinse waters. Washed cellulose suspension was rinsed by 0.1 M carbonate-bicarbonate buffer pH 9.2 and it was added by solution containing homogeneous donor transferrin. This suspension was incubated at 4°C within 24 hours by continuously stirring, thus producing conjugate-transferring-polymer cellulose matrix.

Use of such conjugates based on the polymer cellulose matrix for rabbit-producers immunization according to the immunization technological scheme providing four times subcutaneous introduction of the conjugate to the animal in two-weeks interval between each immunization it was allowed to produce immune serum with antibody titre in them against donor transferrin – 1:128 – 1:256 in the reaction of the Ouchterlony double radial immunodiffusion, that is by 2–3 times greater then by using commercial ajuvants, for example, Freund adjuvant for the rabbit-producers immunization.

AMLODIPIN BESYLATE SUBSTANCE MICROSCOPIC RESEARCHES

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Uzbekistan Government is allocating great attention to the development of the local pharmaceutical industry. Establishment medicine production is one of the most important aspects of this development.

Amlodipin besylate is digidropiridin derivative.

Amlodipine besylate is used in medicine as antianginal and hypotensive medical product. The antianginal and hypotensive effects of Amlodipine besylate assist the vasodilatation, the heart performance balance, diminish vasopressor reactions, and it also has other features affecting to the cardiovascular system.

Nowadays local pharmaceutical companies do not produce Amlodipine besylate in form of capsules.

Based on the above mentioned information, our purpose was to establish the Amlodipin production technplogy in capsules.

In this work, we provide the data of the microscopic research on the shape and the dimensions of Amlodipin substance.

We have used in our research Amlodipine Besylate, produced by RakshitDrugs PVT, LTD company in 2010, batch number 005 06 2010 AB made in India.

Amlodipine besylate substance microscopic research was carried out using the microscope produced by US Company “Bipolan” magnified 500–1000 times.

Under the optic microscope the Amlodipine besylate crystals are mainly rectangular shape and there are some amorphic crystals as well.

The average length of crystals is 38.5 μm, the average width is 15.5 μm and the calculated form factor is 2.48.

According to the data in the previous researches, it was found, that the powder of anisodiametric particle with form factor of more than 2 units possess negative technologic indices. The results of microscopic research of Amlodipin.

Besylate show, that the ancillary substances should be utilized to reach the positive results in capsule production.

The research results shown, that the substance powder is anisodiametric shape and consists of particles with crystals, which are mainly rectangular.

THE SPECIFIC ACTIVITY OF BIOLOGICALLY ACTIVE ADDITIVE VERMOL-2

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The Urgency of the Problem. Recently, for the treatment of diabetes and iron deficiency anemia medical drugs and biologically active additives (BAA) used. The drug vermol-2 developed in the laboratory of bio-regulators of the Institute of Bioorganic Chemistry, academy of Sciences of Uzbekistan, is a dry extract based on camel milk, white, contains large amounts of vitamins, proteins, minerals and soluble in water.

The aim of this study is to examine the anti-anemic and hypoglycemic action of a biological additive based on camel milk.

Materials and Methods. Experiments were conducted on 70 male rats, weighing 200 ± 20 g at 5 in each group. Hemolytic anemia induced by intramuscular injection of pfenylhydrazine sulfate at the rate of 3 mg/100 g (T. E. Belokrinitskaya, B. I. Kuznik, W. H. Havansov, 1992). Preparation began to enter adjustment hemolytic anemia (5 day) every day orally for 15 days at a dose of 500 mg/kg. Test drug Tardiferon was administered orally daily for 15 days in a dose of 6 mg/kg.

Blood samples were taken before and during treatment at 1, 3, 7, 14, 21 and 30 days. The morphological structure of the peripheral blood was determined by the following methods: the concentration of hemoglobin, red blood cells, reticulocytes, platelets, white blood cells and leukocyte formula.

Results. Hypoglycemic properties of dietary supplements vermol-2 were tested for nutritional models and adrenalic hyperglycemia. Lowering of blood sugar (glucose) was measured in 1 hour after the induction of hyperglycemia. The sugar content in blood serum was determined by glucose oxidase method, using a set Bioglucofen.

The experiments showed, that the antianemic effect of dietary supplements vermol-2 was more pronounced, than in tardiferon only during its use. Discontinuation of dietary supplements vermol-2 led to a decrease in anti-anemic action.

We observed hypoglycemic effect after a single dose of vermol-2 on both models of hyperglycemia. This hypoglycemic effect after administration of epinephrine was 28%, while the introduction of sugar – 3%.

Thus, dietary supplements vermol-2 increases the arsenal of biological additives on the basis of natural lactic acid products for the treatment of diabetes and iron deficiency anemia.

PHOSPHORORGANIC DERIVATIVES OF LUPININE, EPILUPININE AND PYPERIDINE AS CARBOXYLESTERASE INHIBITORS

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Nowadays 4–6 millions of phosphororganic compounds (POC) known that can enter into human organism with water, food and air. The excess of alien toxic compounds causes slowing down and termination of such biological processes as growth, development and multiplication. Low molecular xenobiotics come across protective barriers of the organism. Among them a special role played enzymes catalyzing the transformation of lipophylic organic substances into polar metabolites. Carboxylesterases (CBE, EC 3.1.1.1) take a part in the metabolism of xenobiotics by breaking ester bonds present in POC, piretroids and others. Inhibition of these enzymes activity slows down the processes of metabolic transformations and allows prolonging the action of medicines and overcoming the resistance of arthropods to insectoacaricides. Pancreas, small intestine, liver and kidneys of mammals are rich for CBE involved in fat, POC and piretroid metabolism. CBE of insects is involved in the synthesis of cuticular wax and the regulation of juvenile hormones level. The activity of CBE as well as that of cholinesterase slows down by phosphororganic inhibitors (POI). CBE sensitivity to POI of different structure is not thoroughly studied.

Here we report on phosphororganic devivatives of piperidine, lupinine and epilupinine inhibiting CBE activity. *O*,*O*-Dialkyl-*S*-(piperidinobut-2-ynyl)thiophosphates inhibits the activity of beet borer′s CBE more strongly, than that of greenbug′s. Ethyl derivative is almost 90 times, propyl one is 166 times and butyl one is more than 550 times potent for beet borer′s CBE, than for greenbug′s. Lupinine and epilupinine derivatives also inhibit the activity of greenbug′s CBE, but they are less potent, than *O*,*O*-dialkyl-*S*-(piperidinobut-2-ynyl)thiophosphates. The activity of lupinine and epilupinine POI against CBE of 4 arthropod species increases gradually, as the length of alkyl chain increases. Among lupinine POI *O*-pentyl derivative is the most potent, and among epilupinine derivatives is *O*-butyl derivative. The potency of the compound with *O*-pentyl fragment for greenbug is 4 times, for Tetranychidae is for 2.6 times, for Sunn pest is for 4.6 times, for durra stem borer is for 13 times larger, than that of *O*-butyl-containing compound. In case of Sunn pest the highest anti-CBE activity is exhibited by POC with *O*-butyl residue. Mice liver CBE sensitivity for *O*-hexyl derivative is for 2 times lower, than that of greenbug′s, but for 4 times higher, than that of Tatranychidae′s. Selective sensitivity revealed for different CBE motivated us to study these compounds together with 2-oxo-2-*S*-(salsolidinoethyl)-4-methyl-1,3,2-dioxathio-phoosphorinane as agents potentiating the action of carbophos, rogor, phasalone, dorsan and other insectoacaricides.

COTTON LEAF UREASE AND OTHER PR PROTEINS ACTIVITY UNDER INSECTICIDE TREATMENT

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Urease is a nickel-dependent metalloenzyme catalyzing the hydrolysis of urea to ammonia and carbon dioxide, the activity of which is assayed by measuring the quantity of ammonia production. Ureases are widespread in plants, fungi and bacteria. In plants ureases from different parts were identified and studied. Better characterized plant urease was isolated from jack bean *Canavalia ensiformis*. Besides urease from mulberry (*Morus alba*) leaves was isolated and well characterized.

Despite ureases were determined and studied in cotton plant seeds and leaves, there is no much information on their activity under the influence of pesticides. Since the enzyme is one of the key factors of cotton plant defence, studying the effects of insecticide on the enzyme is one the significant problems. Due to its enzymatic production, toxic ammonia, the involvement of urease in protection against plant pathogens is proposed. Many researches give evidence that the majority of its activity is associated with the soluble fractions of the cells. Similar leaf-tip necrosis were observed after the fertilization with urea resulting the accumulation of toxic amounts of urea rather than the less toxic amount of urea as a result of urease action, since the addition of urea acted as urease inhibitor and increased leaf-tip necrosis.

In this work we studied the effects of insecticides of three different classes: sumi-alfa (pyrethroid, Sumimoto chemicals, Japan), lannate (carbamates, Du-Pont, Switzerland) and carbophos (organophosphates). Cotton leaf samples were taken on the 10^{th} and 13^{th} days of the treatment. Insecticides were sprayed with the concentration recommended against cotton pests by the producer.

The results obtained showed that urease activity in leaf samples treated with insecticide preparations was lower than control. Carbophos twice decreased urease activity on the 10^{th} day and 30% lower activity was calculated on the 13^{th} day of the treatment. Urease activity of leaf samples treated lannate was 35 and 15% lower comparing to untreated control. Pyrethroid sumi-alfa decreased the enzyme activity that, 20 and 30% lower than the control activity was determined on the corresponding 10^{th} and 13^{th} days of the treatment. The results on sumi-alfa treatment correspond with the results obtained on the activity of other pathogenesis related proteins of cotton leaves treated with insecticides. Specifically pyrethroid sumi-alfa which is efficiently used on cotton against cotton bollworm, approximately twice decreased the activity of peroxidase, polyphenoloxidase, chitinase and β-1,3-glucanase of cotton leaves. Lannate insecticide belonging to carbamates also decreased the glucanase activity significantly. Additionally PAL activity of all cotton samples which were treated with the same above mentioned insecticides was 2–4 times lower than untreated control on the 10^{th} and 13^{th} days of treatment.

Among these insecticides mentioned sumi-alfa is most efficiently used against *Heliothis* insects causing huge losses of cotton fiber, however after treatment the activity of PR proteins was decreasing thereupon. Urease activity one of the key factors of plant defence against necrosis was also found to decrease as a result of not only pyrethroid sumi-alfa but also lannate and carbophos. Following from this, the probable side-effects of these insecticides have to be taken into consideration while they are used.

BIOLOGICAL ACTIVITY OF SODIUM CELLULOSE SULFATE ON INFECTIVITY OF TOBACCO MOSAIC VIRUS IN VARIOUS pH VALUES

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Plant viruses take significant part among plant pathogens, which have strong and negative effects to the plant biomass or crop yield. Between these viruses, the tobacco mosaic virus (TMV) infects vegetable and cucurbitaceous plants and it has forcible role according to degree of infectivity and wide distribution. TMV is a rod-shaped virus composed of single-stranded RNA encapsulated with coat protein. TMV is a unusually stable, its coat protein is resistant in acidic or alkaline medium and TMV saves its native structure in pH ranging from 2 to 10. During last twenty years, attention is concentrated to investigate of compounds with antiviral activity against TMV. Until nowadays, results of some investigations were reported in the field of study of compounds possess biological activity against TMV.

In this work, biological activity of sodium cellulose sulfate (SCS) against TMV infection in various pH numbers was investigated. The TMV was separated from systematic infected leaves of *Nicotiana clevliandi* and purified by differential centrifugation. SCS was prepared by sulfation of cellulose with pyridine-chlorosulfonic acid complex. Obtained SCS converted into acidic form with ion exchange resin. SCS samples with various pH numbers were prepared by addition of caustic soda into acidic form of cellulose sulfate. Degree of substitution (DS) of SCS samples were determined by elemental analysis method. Molecular mass parameters were determined by size exclusion liquid chromatography. Degree of polymerization of obtained SCS sample was 600 and DS was 2.90 mol/AGU. Five SCS samples having pH ranging from 2.3 to 7.5 were prepared. SCS solutions were prepared at same concentration (0.5 mg/mL) and suspension of TMV was prepared by dialyzing of solution of TMV in phosphate buffer (0.5 mg TMV/mL in 0.1 M sodium phosphate buffer, pH 7.0). Concentration of TMV was 0.5 mg/mL by spectrophotometrically and amount of necrotic lesions ranging from 80 to 100 on a leaf of *Nicotiana glutinosa*. TMV solution was mixed with SCS solution or distillated water (control) and inhibitory effect of SCS on the infectivity of TMV was assayed on *Nicotiana glutinosa* by half-leaves method.

According to inhibitory test results, SCS samples with pH gradient 7.5, 7.0, 4.85, 2.98 and 2.3 decreased TMV infectivity 28.6, 21.2, 20.6, 19.2 and 18.8% respectively on *Nicotiana glutinosa* leaves compared to control (pH 6.5). Decrease of pH value of SCS solutions showed an increase in inhibitory activity against TMV infectivity compared to the control. But non-significant difference (2.4%) was observed in inhibitory activities of acidic (pH 2.3) and neutral (pH 7.0) SCS solutions.

As a conclusion, SCS possesses biological activity against TMV in solution and biological activity mechanisms almost do not depend on pH gradient of the SCS solution. It seems that the biological activity mechanisms of SCS on the TMV infection are related with molecular parameters of SCS macromolecule.

EFFECT OF γ-IRRADIATION AND ISOFLAVONES-RICH SOY PROTEIN ON IMMUNOLOGICAL PARAMETERS OF TUMOR-BEARING ANIMALS

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A standardized combination of polypeptides from soy flour with a molecular weight of 12.5-79.0 kD enriched by isoflavones (daidzein content per a gram of protein is in average 1.50 ± 0.3 mg, genistein – 0.52 ± 0.2 mg) was obtained in the Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan. Soy protein, administered as monotherapy, shows antitumor effect on animals with sarcoma-180 transplantable tumor, and tumor growth inhibition (TGI) was 94.3% by weight and up to 94.0% by volume. At administration of soy protein at complex therapy with γ-irradiation, TGI reaches 91.2% by weight and 90.3% by volume. γ-Irradiation as monotherapy provides TGI of 85.6% by weight and 82.0% by volume.

The objective of the study was a comparative evaluation of immunological parameters of animals with transplanted sarcoma-180 tumors after exposure to γ-irradiation and soy protein at early stage of tumor development (3–13 days after tumor transplantation).

The method of immune status assessment is based on a quantitative test for lymphocyte subpopulations with receptors specific for each species – clusters of differentiation (CD) [M. Zalyalieva, 2004]. The following CD-markers were used: CD3, CD4, CD8, CD16, CD20, CD25, CD95.

The results of immunologic examination of intact animals and animals with sarcoma-180 transplanted tumor have shown that the appearance and development of tumor in animal organism leads to a proven increasing the numbers of CD3-cells – for 20%, CD8 – for 70% and CD16 – for 90% ($p < 0.05$). Also, the level of cells bearing CD95-receptor increases significantly ($p < 0.05$) – for 50%. At the same time there is a significant decrease in IRI – from 1.6 to 0.83 and reduction the number of T-helpers for% and CD20-cells for% ($p < 0.5$). Exposure to radiation therapy significantly reduced the level of CD3-cells for 36%, CD4 – for 40%, CD8 – for 20%, CD16 – for 20% and CD20 – for 20% in comparison with untreated control animals ($p < 0.05$), IRI – 0.83. An increase was also observed in such indicators as the number of CD16-cells – by 70% and CD95 – for 65%, but only when compared with control animals.

Combined effect of γ-irradiation and soy protein ($p < 0.05$) decreased the total pool of T – lymphocytes for 25%, the proven difference was observed in comparison with the tumor-bearing animals. Furthermore, there was a reduction ($p < 0.05$) in the proportion of T-killer cells (for 50%), and natural killer cells (for 40%). The number of CD95-cells also decreased (for 18%).

In addition, at combined action of γ-irradiation and soy protein the average group value of IRI significantly increased to 1.23 and the number of CD25-cells – for 20%.

Monotherapy using soy protein causes significant reductions only in three parameters – CD8-by 28%, CD16 – by 57%, and CD95-cells – by 33% ($p < 0.05$). This was accompanied by increase in CD20-cells by 17% ($p < 0.05$) and IRI increased to 1.16.

Normalizing immunological parameters by soy protein correlates with its antitumor action.

SYNTHESIS AND STRUCTURE OF NICKEL COMPLEX OF *p*-AMINO BENZOIC ACID

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p-Amino benzoic acid is considered to be biologically active compound having a significant in living organisms. This compound is effective in delayed growth and development, increased mental and physical fatigue, anemia with the deficit of folic acid etc. Literatures give evidence, plants collect minor amount of nickel which stimulates and provides normal growth.

Besides nickel promotes normal uptake process of nitrogen with leguminous plants, thus helps to supply contents of important nutritious compounds in soil. Therefore searching the structure and synthesis of new nickel complexes with *p*-amino benzoic acid is very significant.

In this work it is reported about the synthesis and structure of $n[NiL_2(H_2O)_2]nH_2O$. The crystals of this complex belong to triclinic syngony, the space group of which is P-1, Z = 2, a = 7.343(5), b = 9.103(5), c = 12.283(5) Å, α = 71.306(5)°, β = 86.712(5)°, γ = 76.852(5)°, V = 757.227 Å^3. X-ray analyses were made on CCD defractometer «Xcalibur^R» (CuKα, graphite monochromator, at room temperature).

Structure of this investigated polymeric compound $n[NiL_2(H_2O)_2]nH_20$ consists of neutral polynucleic chains, the part of which is given with the numeration of atoms in Fig. 1.

The nickel atom localized in special position is surrounded with two oxygen atoms and two nitrogen atoms of p-amino benzoic acid, in apexes of bypyramid two water molecules are localized. As X-ray analysis shown, every metal cation is bound with two water molecules and four anions of *p*-aminobenzoic acid, and every anion is bound with two nickel atoms. The remaining water molecule localized outer part of coordinating sphere participates in intermolecular hydrogen bonds which lead to the formation of 3D-network consisting of linear polynucleic associates.

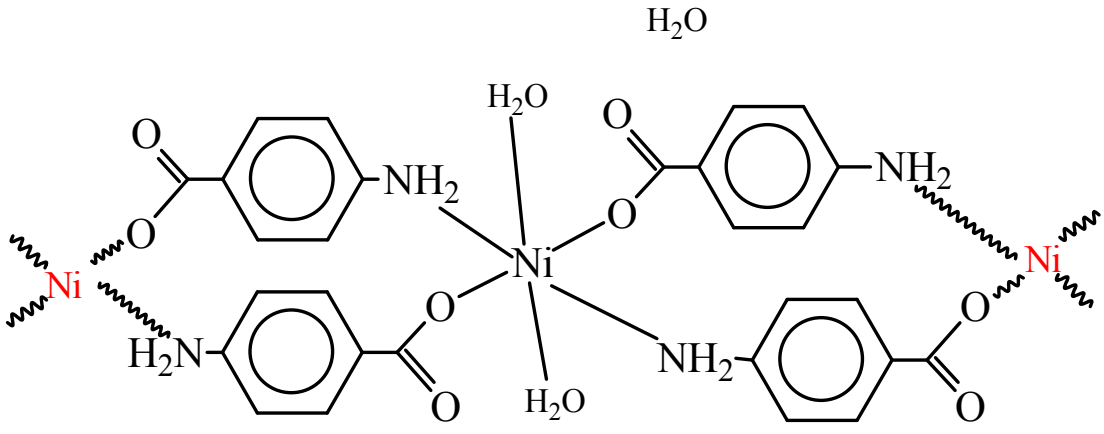

Fig. 1. Structure of $n[NiL_2(H_2O)_2]nH_2O$ complex.

Thus, new amino benzoic acid complex with nickel is characterized with polymeric structure in direction [101] and hydrogen bonding 3D-network.

SYNTHESIS OF ALKYLATED AND PHOSPHORYLATED DERIVATIVES OF 8-MERCAPTOQUINOLINE

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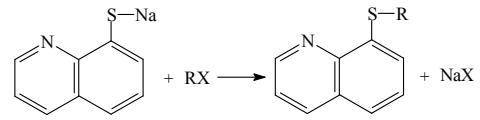
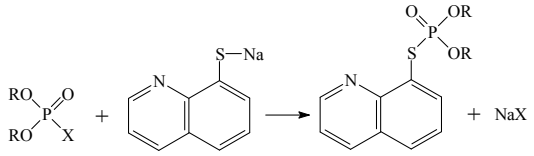
New 8-mercaptoquinoline derivatives have been synthesized to reveal effective inhibitors of agricultural insect pest esterases and extractants of precious metals.



R=CH_3 - C_9H_{19}; i-C_3H_7, i-C_4H_9, i-C_5H_{11},



R= C_4H_9, i-C_4H_9, C_5H_{11}, i-C_5H_{11}, C_6H_{13},
X= Cl, Br, J

The structure of the synthesized compounds has been confirmed using modern spectral methods.

The absorption bands of the following functional groups were observed in IR spectrum of 8-*S*-isopropylthioquinoline (ν, cm^{-1}): (C-H) 2895, (CH_3) 2880, (C-H/rings) 720.

In case of 8-*S*-octylthioquinoline there were absorption bands of the following functional groups (ν, cm^{-1}) in IR spectrum: (CH_3) 2880, (CH_2) 2870–2845, (C-H/rings) 750.

IR spectrum of *O*,*O*-dihexyl-*S*-(8-quinoline)thiophosphate revealed absorption bands of (CH_3) 2880, (CH_2) 2940–2915, (P=O) 1280, (P-OAlk) 975, and (C-H/rings) 780 (ν, cm^{-1}).

In ^{1}H NMR spectrum of 8-*S*-butylquinoline H-2 proton forms a doublet at 8.85 ppm (J = 5.6 Hz). H-4 proton is observed in the form of a doublet at 8.03 ppm (J = 8.7 Hz). H-3, H-5, H-6 and H-7 protons form multiplet in the field of 7.3–7.7 ppm. Two protons of S-CH_2 group are revealed in the form of a triplet (J = 6.5 Hz) at 2.96 ppm. Protons of two methylene groups (4H, -CH_2-CH_2-) form multiplet in the field of 1.3–1.9 ppm. A triplet at 0.93 ppm belong to the three protons of the methyl group (J = 6.6 Hz).

In ^{1}H NMR spectrum of *S*-isoamylquinoline H-2 proton (J = 5.5 Hz) is observed in the form of a doublet at 8.84 ppm. H-4 proton forms a doublet at 7.97 ppm (J = 5.5 Hz). Multiplet in the field of 7.2–7.4 ppm belongs to the protons of H-3, H-5, H-6 and H-7. Two protons of S-CH_2 group form a triplet at 2.91 ppm (J = 6.6 Hz).

In the UV spectrum of alkylated derivatives of 8-mercaptoquinoline there are two maximums at λ_{max} = 253 nm and λ_{max} = 339 nm. Introduction of alkoxyphosphate groups (phosphorylated derivatives of 8-mercapthoquinoline) instead of alkyl chains in UV spectrum of molecules the hypsochromic shift of a long-wave maximum ($\Delta\lambda_{max}$ = 11 nm) is observed. This displacement probably is caused by change displacement of π-electrons of sulfur from quinoline core aside P=O-group. The change of length of alkyl groups does not lead to significant changes in UV spectra of compounds.

THE INFLUENCE OF THE CENTRAL ASIAN TORTOISE′S EXTRACTS ON TORTOISE′S BONE MARROW CELLS PROLIFERATION

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The progressive development of modern technologies in synthetic drug production doesn′t decrease the interest of medical practice to natural product. The potential source of such biological active substances is the Central Asian tortoise well known by its very high radio resistance (50–100 times higher then mammalian′s one). In this work we tested the influence of tortoise′s embryo extract (TEE), water-alcohol shell extract (SE) and preparation Tortezin on tortoise′s bone marrow cells using developed in our laboratory method of tortoise′s haemopoietic cells culture.

The male and female tortoises of sexually mature adults (11–15 years old) were used. TEE was prepared according original patented method from 60-days embryos without using yolk sac. After decapitation of tortoises the blood was collected into heparinized tubes and was centrifuged (4000 X g for 6 min) for serum preparation. The tortoise's bone marrow was isolated from both extremity of humeral, tibial, femoral bones and pelvis by strong compression and subsequent wash of cancellous tissue with PBS. For culture RPMI-1640 was supplemented with *L*-glutamine, 0.22% Na bicarbonate, 5% autologous tortoise′s serum, 100 mkg/mL gentamycin, 1 mkg/mL fungizone. TEE, SE and Tortezin were added in final concentration 10 mkg/mL. Incubation in concentration of 100 000 cells/mL during 7 days was performed at 25°C in humidified incubator with 5% CO_2 atmosphere in centrifuge tubes with gas exchange. The quantity of bone marrow cells before and after cultivation was determined using cell counter. Differential cell counts were performed after cells fixation and Giemsa staining of specimens. Bone marrow cells were determined as haemocytoblasts, myeloblasts, heterophils, eosinophils, basophils, monocytoids cells, lymphoid cells, erythroblasts, erythrocytes, thrombocytes from 500 cells/sites.

Between tested preparations TEE was the most active: the total cellularity of sample with TEE was 1.48 ± 0.02 time higher than in control after 7 days of incubation in optimal condition, even though the single mitotic cells were detected in control specimens. Also TEE protected bone marrow cells during their incubation in the dry environment with no gas exchange, while in control the total absence of erythrocytes was determined.

Differential cell counts revealed the predominance of erythropoiesis over the other lineages during incubation with or without stimulating preparations.

The tortoise′s embryo extract as multicompound preparation contents the biologically active substances with different potencies such as stimulating and anti-apoptotic un that number.

COMPARATIVE FREE AMINO ACID ANALYSIS OF INTACT AND INFECTED BY *Fusarium oxysporum* COTTON SEEDLINGS

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Obtained results indicate, that there is dependence between amino acids and fungi pathogenesis of processes such as spore germination, prolongation of germ tube, biosynthesis and enzyme efficiency. For instance, alanine, asparagine, glycine and tryptophan completely suppress the synthesis of pectic acid lyase. Phenylalanine and leucine repress hydrolytic enzymes′ (polygalacturonase) synthesis. Leucine, cysteine and phenylalanine totally inhibit the biosynthesis of pectinmethylgalacturonase in *F. oxysporum* and *F. moniliforme*.

Aim of the work is to conduct comparative analysis of free amino acids in intact and infected with *Fusarium oxysporum* lines of varieties and cotton plant.

Seedlings were extracted with 10% acetonitrile for amino acids analysis. Phenylthiocarbamoyl derivatives were obtained by the reaction with phenylthioisocyanate. Amino acids derivatives were identified in Chromatographer Agilent Technologies 1200 equipped with DAD detector, and with column Discovery HS C_{18} 3 μm (75 × 4.6 mm).

Total Free Amino Acids in Intact and Infected by *F. oxysporum* Cotton Seedlings

Cotton varieties and lines	Amino acids (mg/g)	
	Intact	Infected
Namangan 77	41.058	12.608
(+) G	34.884	18.203
MG-02	35.948	30.766
Glandless	17.503	24.084
5541 F_6 3x C6530	24.142	12.141
5542 F_6 3xC 6524	20.572	19.041
5540 F_6 3xC-6524	39.569	32.781

Obtained results of analysis showed, that after fungi infection, free amino acids in variety Namangan 77 (69%), and lines 5543 $F_6$3xC-6530 and 5541 F_6 3xC-6530 (50%) drastically lowered, especially the contents of serine, glycine, asparagine, phenylalanine and tryptophan. In variety MG-02 and lines 5542 $F_6$3xC-6524 and 5540 $F_6$3xC-6524 the amount of amino acids practically did not change. Only in Glandless line amino acids quantity increased over 50% after the infection with fungi.

THE ROLE OF NATURAL BENZOFURANS IN REGULATION OF ESTROGEN BIOSYNTHESIS

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4) Republic Oncologic Science Center, Tashkent

Estrogens are the sex steroid hormones playing a pivotal role in the regulation of many biological processes. Estrogens are known to induce physiological responses in the reproductive tract, mammary tissue, and the pituitary gland and to affect non reproductive processes, such as bone formation and cardiovascular health. The biological actions of estrogen are mediated through nuclear and membrane estrogen receptors (ERs), which are expressed in a variety of cell types and mediate the genomic and nongenomic effects of estrogen. Numerous factors have been implicated in the increased incidence of breast cancer in humans, including the Western-style diet and environmental endocrine-disrupting chemicals, which are thought to alter the production, metabolism, and action of estrogen. In humans, estrogen biosynthesis occurs at a number of different sites, with the major sites being the granulosa cells of the ovary in premenopausal women and stromal cells of the adipose tissue in postmenopausal women.

The work aimed at studying regulation of estrogen biosynthesis and catabolism by natural benzofuran-based products.

For the purposes of the study estrogen-dependent lines of breast carcinoma MCF-7 and SK-BR-2, osteosarcoma ROS 27/2.8 and ovarian carcinoma KGN strains were used. Natural benzofurans were isolated from the raw material of *Styracaceae* plant family, such as, *Styrax japonicum, S. formosanus, S. obassia, S. macranthus* and S. *officinalis*.

The study showed, that KGN cell line possesses the highest sensitivity to the effect of natural benzofurans. In all concentrations plant benzofurans were shown to efficiently reduce amounts of estrogens in the tumor cells. Under the effect of benzofurans in the concentrations of 1 mM, 10 mM and 100 mM amount of estrogens in KGN cells was found to decrease to 0.5554, 0.5642 and 0.5149 pg/mL, respectively. The similar control parameter was 0.7143 pg/mL, upon addition of substrate (testosterone) only, amount of estrogens being 0.5644 pg/mL.

The findings showed, that benzofurans obtained from the *Styracaceae* plants, possess by high anti-tumor activity in relation to KGN tumor cells resulting from estrogen biosynthesis and catabolism inhibition. KGN line cells obtained from steroidogenic tumor of the human′s ovary possess normal properties of granulose-like cells and contain functional receptors to follicle-stimulating hormone (FSH). KGN cells have relatively high activity of aromatase stimulating FSH or cAMP. Thus, inhibiting activity of aromatase and reducing amount of estrogen activators of proliferation natural benzofurans are capable of acting as efficient natural preparations against malignant ovarian neoplasma.

LIPOSOMAL PREPARATION FOR REGULATION OF GLUCOSE TRANSPORT IN TOXIC HEPATITIS

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Liposomes, also called lipid vesicles or simply vesicles, are supramolecular assemblies of amphiphiles, surface active substances, that normally contain two hydrophobic tails and one hydrophilic head group. The origins of liposome research can be traced to the contributions by Alec Bangham and colleagues in the mid 1960s. The description of lecithin dispersions as containing ‘‘spherulites composed of concentric lamellae’’ (A. D. Bangham and R. W. Horne, *J. Mol. Biol*., 8, 660, 1964) was followed by the observation that ‘‘the diffusion of univalent cations and anions out of spontaneously formed liquid crystals of lecithin is remarkably similar to the diffusion of such ions across biological membranes (A. D. Bangham, M. M. Standish and J. C. Watkins, *J. Mol. Biol*., 13, 238, 1965). Following early studies on the biophysical characterization of multilamellar and unilamellar liposomes, investigators began to utilize liposomes as a well-defined model to understand the structure and function of biological membranes. It was also recognized by pioneers including G. Gregoriadis and D. Papahadjopoulos that liposomes could be used as drugs and drug delivery vehicles. The aim of our study was to study hexose uptake by rat hepatocytes in toxic hepatitis. The experiments were conducted *in vitro* on the liver slices of experimental and control animals. Glucose transport was studied by intracellular glucose concentration measurement after incubation of liver slices with hexose and liposomes. Liposomes were prepared from the liver of experimental normal animals. Two types of liposomes were used in the experiments. Phospholipids and cholesterol were the basic for creation of liposomes of the first type; glycosphingolipids were added to them in the second one. The findings show that upon incubation of toxic hepatic rat liver slices with liposomes there were significant alterations in hexose transport. Thus, transfer of glucose was enhanced by addition of the first and second types of liposomes by 57% and 72%, respectively. Transfer of glucose and galactose was intensified too, addition of phospholipid-cholesterol liposomes to the incubation medium resulted in fructose and galactose transfer intensification by 31.7% and 16.6%, respectively, while addition of liposomes containing glycosphingolipids resulted in the intensification of fructose and galactose transfer by 47.4% and 31%, respectively. The findings from the experiments could be explained by two suggestions. First, there was more intensive binding of liposomes containing glycosphingolipids with cell membrane. Second, correction of lipid membrane composition by the liposomes gives the better result.

MASS SPECTROMETRIC ANALYSIS OF PEPTIDE FRACTIONS FROM UZBEK LEGUME SEEDS

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Legumes are a good source of food proteins and biocide peptides. From seeds of *Cicer arietinum* two antifungal peptides cicerin and arietin [1], defensins [2], cyclic and antioxidant peptides [3] were isolated. We are isolated peptides from Uzbek legume seeds with water and 50% ethanol extraction and gradient (0–80%) HPLC. Peptide fractions were analyzed with Accurate-Mass Q-TOF LC/MC for presence of cyclotides. Results of determined molecular mass are shown in the Table. The peptides isolated by us had antimicrobial activity again *Staphylococcus aureus, Staphylococcus epidermidis, Esherichia coli, Proteus vulgaris, Klebsiella, Salmonella typhimurium* and *Shygella flezneri.*

Molecular weight of peptides from Uzbek legume seeds

Phaseolus vulgaris ethanol soluble	*Vigna radiata,* ethanol soluble	*Cicer arietinum* water soluble
1190; 1315; 1393; 1512; 1522; 1526; 1577; 1743; 1755; 1777; 1796;	1241; 1392; 1508; 1654; 1767; 1792; 1909; 1925;	1909;
2043; 2122; 2190; 2406; 2598; 2645; 2708;	2121; 2172; 2177; 2299; 2314;2404; 2472; 2526; 2591; 2669; 2706; 2771; 2876; 2888; 2895; 2904; 2985;	
3160; 3325; 3543; 3676; 3807;	3047; 3053; 3090; 3169; 3173; 3328; 3446; 3557; 3566; 3764; 3780; 3835; 3846; 3878; 3901; 3999; 4086; 4031; 4167; 4176;	3090; 3764; 3780; 3834;
4315; 4998;	4237; 4291; 4616; 4721; 4759; 4776; 4780; 4788;	
5078;	5000; 5215; 5224; 5241; 5257; 5449; 5716; 5833;	
6178;	6231; 6993;	6905;
7605;	7530; 7562; 7795; 8725;	7149

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ANGIOGENESIS INHIBITORS IDENTIFIED IN SNAKE VENOMS PROSPECTS OF USAGE

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Search for angiogenesis inhibitors was performed in venoms of lebetina viper (*Viperidae*) and copperhead snake (*Crotalidae*) on the model of chorioallantoic membrane of 7- and 11-day chicken embryos. In the venom of lebetina viper angiogenesis inhibitors were identified in II and III fractions (Sephacryl S-200), protease and LAO being found in fraction I, inhibitors of agonist-inducing platelet aggregation, phospholipase A2 and BAEE-esterase being found in fraction II and nonenzymic components being found in fractions III–V. Components with Mr = 35–45 kDa in the native conditions and Mr = 16 and < 10 kDa in the denaturant ones were found by means of active material electrophoresis. Fraction II as one containing most active inhibitors was fractionated on Q-Sepharose. The material divided into three distinct fractions; maximum suppression of angiogenesis (more than 60%) was localized in fraction 2-Q1, the one able to suppress platelet aggregation (55%), while two other fractions, 2-Q2 and Q3 were found less active (17% and 14%, respectively). In the model of ADP-induced platelet aggregation inhibitors of serine proteases and metalloproteases (FMSF 0.1 mM and EDTA 10 mM) were found inefficient (10–15% of inhibition), that is, effect of angiogenesis inhibition and platelet aggregation can be determined by joint effect of phospholipase A2 and a low-molecular (7–10 kDa) protein or peptide identified electrophoretically. In the venom of copperhead snake specific angiogenesis inhibitors were identified in fractions III–V (HW-55), IIC-4 (Sephadex G-75, DEAE-Sephadex A-50) and IIC-4 F1 (Q-Sepharose, HA-Ultrogel). In concentrations of 25–75 μg/embryo fractions V (Mr = 14–15 kDa and trace phospholipase A2 activity) and IIC-4 F1 (chromatographically pure one) were found to inhibit angiogenesis at the moment of applying. Fraction IIC-4 F1 is a glycopeptide (6–8% of sugars) with Mr = 8–9 kDa in the denaturant and 34–36 kDa in the native conditions. In the breast cancer cell culture fractions V and IIC-4-1 demonstrated dose-dependent cytotoxic effect. Thus, fraction IIC-4-1 (250 μg/6 × 10^6 cells) caused death of more than 50% of tumor cells. Fraction V turned out most active since total death of tumor cells, apoptotic ones included, was 71%. More pronounced cytotoxic effect the fraction (50 μg/6 × 10^6 cells) produced on peripheral blood lymphocytes in patients with colorectal cancer; total death of tumor cells, apoptotic included, exceeded 70%. Thus, proteins and peptides with Mr < 14 kDa identified in the venoms of lebetina viper and copperhead snake are promising modulators of angiogenesis and functions of platelets as well as antitumor agents.

CHANGE OF POTATO MICROTUBERS SUGARS COMPOSITION IN VITRO DEPENDING ON EXPLANT ORIGIN AND EXOGENIC KINETIN′S CONCENTRATION

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Development of cellular technology methods allows intensifying the processes of getting biotechnological product and also drastically changes existing ways of their producing. So, on the base of interrelation studying between explant′s physiological condition and concentration/structure dependence of exogenic cytokinins action the effective way of obtaining virus free potato micro tubers has been developed. The method includes two basic moments: a process of induction of tuber formation at a radical part of a potato plant *in vitro* and induction of tuber-formation process from apical part of plants *in vitro*. In both case as a regulator of morphogenetic processes used kinetin (6-furfurolaminopurin) in a combination with adenine. It has been experimentally established, that for an induction of tuber formation process from a radical part of a plant concentration of kinetin is 10^{-6} M, for an induction of tuber-formation process from apical parts – 10^{-4} M is most effective. In both cases formed microtubers normally develops, type a biomass up to 200 mg, have well generated integumentary tissues, well endure dormancy and easily adapt for a ground. However, till now here is no accurately established opinion about hormonal regulation of tuber formation and interrelations between exogenic factors which are control this process, and qualitative composition of tubers. In this connection the content of soluble carbohydrates, in the potato micro tubers obtained in the presence of various concentration of kinetin was studied.

Content of soluble sugars of micro tubers was analyzed by means of HPLC method using Agilent 1200 chromatograph equipped with RI detector, 0.46 × 15 cm Spherisorb-NH_2 column and 8:2 acetonitrile-water mixture as mobile phase was used.

It has been shown, that apical parts origin micro tubers (AT) induced at high concentration (10^{-4} M) of kinetin contents 3–5 times more soluble sugars than radical parts micro tubers (RT) induced at low (10^{-4} M) concentration of kinetin. Comparison of individual carbohydrates concentrations revealed more contrast differences. So, concentration of arabinose, mannose and sucrose in AT sample 10, fructose and glucose 5 time riches than in RT sample. Intrinsic change in glucose–fructose proportion also was shown. In AT sample this proportion is 1:10 and in RT sample is 1:0.5.

Thus, content of soluble sugars in the *in vitro* produced potato microtubers, change′s depending on exogenic kinetin concentration; at the same time difference in sugars content does not influence such processes as endure of dormancy period, germination and ability to ground adaptation.

ISOLATION OF PROTEIN PRODUCTION FROM WASTE SILK

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Proteins are macromolecular organic compounds consisted of amino acid residues linked together by peptide bonds and having a complex structural organization. The molecular weight of proteins is changed from 5.000 to many millions of Daltons. The protein is easily destroyed by high temperatures, a sharp rise of medium pH and other exposures. Such perturbation is called denaturation and usually accompanied by losing of biological properties. Proteins pupae are full-value: 1 kg of dry pupae by proteins is equivalent to 2.5 kg of meat of warm-blooded animals.

It is known that the yield of protein products, their structure and properties depend considerably on the degree of silk waste hydrolysis. The protein from freshly prepared solution is a mixture of high molecular weight polypeptides. Protein is obtained by alkaline treatment of waste pupae of silkworm *Bombyx mori*. When protein is selected from the silkworm pupae initially it crushed and the resulting powder is extracted in an autoclave (chloroform, ether, ethanol, benzine) to complete removal of fat and wax. The extract is transferred to an extractor for removing the solvent from the oil and centrifuged. Then powder is transferred to a reactor 0.5 m3 filled with water, and prepare a 0.2 percent solution of sodium hydroxide, thoroughly stirring of the downloaded mass for 3 hours. The completion of the deproteinization controlled by the degree of protein separation. The protein concentrate is unloaded into the filter tank and filtered, collected to the intermediate container and left to decant. Extract is centrifuged, transparent centrifugate is saturated with ammonium sulfate and left for overnight. The proteins precipitate is filtered off or centrifuged, suspended in water and dialyzed for remove salts and other low molecular weight additives. Dialysis is carried out until the complete removal of the sulfate ion (about 2 days). The precipitate is separated by centrifugation, which then washed sequentially with acetone, alcohol, ether, and dried in a vacuum oven at 50–60°C. Dry protein weighed. The yield is 45–45.7%.

Processing of second group silkworm pupae performed as described above. For deproteinization used of 0.3% caustic soda solution. Analysis of protein solutions shows that the yield is 45.7–45.8%, and as described above (0.2% solution).

Deproteinization was carried out at 0.4 and 0.5% of alkali solution after oil extraction. Oil yield was 10–12%, which is agree with laboratory data. Analysis of protein solutions shows that the yield was 45.8–45.9% and 45.9–46.0%, respectively at concentrations of 0.4 and 0.5%. Such a small difference of the protein output is revealed inappropriate use of high concentrations of caustic soda.

Thus, the developed process parameters allow separating the protein with sufficient yield: 45–46.0% from raw material, using low concentrations of alkali.

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PROPERTIES AND USE OF PROTEIN *Bombyx mori*

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Due to famine and high cost of animal origin feed, a search for most efficient food for fish, based on proteins produced from waste silk production is currently prospective, allowing to expand the range of feed and reduce cost per unit of fish growth. The prospect of the production of protein products from sericulture waste is due to their non-toxicity, and functional properties.

At processing of the silkworm *Bombyx mori* pupa the mandatory steps are demineralization, deproteinization, depigmentation and removal of residual lipids. The protein concentrate (and after protein obtained from it) is realized after chitin separation. The technology of raw materials processing determines the sequence of the steps and the conditions under which is achieved the fullness of the separation all the components. Protein is extracted from protein concentrate then amino acid composition was determined. Completeness extraction of fats and proteins was controlled by determining of the residual components in demineralised chitin.

Proteins isolated from presented samples contain of the whole set of irreplaceable amino acids, which is a good indicator of the nutritional value of the inverstigated proteins. Excess amounts of irreplaceable proteins refers to amino acids such as lysine, histidine, threonine, isoleucine and phenylalanine, as well as to partial replaceable amino acids: arginine, glycine, and tyrosine. By IR spectroscopy and chromatography were identified the structure of isolated proteins.

The use of protein in the fish feed was held at the apparatus recirculation hatchery of Syrdarya thermal power plant. Fish production reached about 20 kg/m^3, which is 150 times higher than the standard indicators. According to the standards, the fish is grown for two growing seasons (16–20 months) in fish farms. In our case, the fish grows to standard within 6 months, i.e. 3-fold faster. During one year in the same pool can hold two of the growing cycle of commercial fish.

It was done work of the use of protein for growing hutchling (Cyprinus carpio) to converse to fish farming material. In this case the object is the most mass of commercial fish. The result of the research revealed that observes: first-high density planting (on globally level), secondly – the good growth of fish (fish reaches the stage of stocking material for 1.5 months), third – a low feed conversion rate – 1.49.

Protein isolated from silkworm pupa, was tested as a 5% supplements feed for chickens on the farm "Olmazor" Vabkent district of Bukhara region. Compared with controls, there is a high efficiency: reduce of a disease – to 50%, the growth rate increased to 40%, weight – 65%.

The hens, which feeds this mixture, there was an increase in productivity of eggs to 25–28% in comparison with the control.

The results of the work show a huge prospect of the use of high protein feed on the base of *Bombyx mori* protein for the development of intensive fish farming and aviculture in Uzbekistan.

STUDY OF DIURETIC ACTIVITY OF DRY EXTRACTS FROM PLANTS EQUISETUM ARVENSE L, AERVAE IANATAE, ALHAGI PSEUDALHAGI (MB) DESV.

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Search for new diuretics based on plant raw materials is an important task of pharmaceutical science allows us create domestic, affordable medicines without long-term side effects.

The objects of the study folk medicine herbs with diuretic properties: horsetail herb, grass half floors (ervy woolly), grass false yantak were triple extracted with water in ratio 1:30 at a temperature of 70–80°C (first extraction) in 1 hour, 1:15 ratio (second extraction) for 30 minutes, 1:7 ratio (third extraction) for 30 minutes and 18–25% yield of dry extracts in form of brown to dark brown powder were obtained. The evaluation tests for tannins, flavonoids and the amount of organic acids in the dry extracts of the GF X1. So, tannin content in the dry extract of horsetail grass – 3.90%, in dry herb extract ervy woolly – 4.49%, in the dry extract false yantak – 7.8 %. The contents of flavonoids were 0.84%, 2.57% and 3.1%, respectively. The contents of organic acids were 3.5%, 3.0% and 4.8% respectively.

Diuretic activity of the resulting dry extract has been studied in 24 rats of 140–165 g of both sexes. The experiments were performed according to the method of V. V. Gatsura (Methods of the primary pharmacological studies of biologically active substances, Moscow, 1974, 144 pages). According to this technique, the day before the experiment rats did not receive food and water and then the animals were placed in a special chamber, and urine was collected daily for 6 days without water load. Then the experiment continues with a water load of the animals reached by using of distilled water to 4 mL per 100 g of weight, the animals were placed in a special chamber for a day and measure the initial amount of urine.

Dried test extracts (as 1% solution) were administered to animals at a dose of 100 mg/kg orally, while the control animals were administered the same way with distilled water.

Experiments have shown, that under the influence of dry extract (at a dose of 100 mg/kg) of horsetail grass the urine output increases for 29.8%, with the application of dry herb extract of ervy woolly – for 40.78%, with the application of dry herb extract of false yantak – for 40.6% compared with the control.

It was founded, that the resulting dry extracts have a good diuretic effect, and they need for further in-depth study.

STUDY OF *Alcea rosea* L. AS A SOURCE OF MEDICINES

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Alcea rosea L. (*Malvaceae*) is the wild perennial herb. From the flowers of pink roses stock food dye produce, and the roots infusion and dry extract having expectorant and anti-inflammatory properties, the stems are used in inflammatory diseases of the gastrointestinal tract.

Chemical studies of stems and roots of *Alcea rosea* L. showed that they contain at least two polysaccharides and 10% respectively. According to the chemical composition of the polysaccharides *Alcea rosea* L. essentially contains rhamnose, glucose, galactose, xylose and galacturonic residues and glucuronic acid.

Dry extract of the stems and roots contain 16% and 20% water-soluble polysaccharide (slime), respectively. Hemicellulose in the stems is 26.6%, in the roots 14.1%.

In dry extracts of stems rhamnose, arabinose, glucose and galactose in the ratio of 17.6:2:1:2.8, respectively, as well as galacturonic acid and glucuronic identified by GLC and BH. In the hydrolysate of mucus of roots dry extracts as rhamnose, arabinose, glucose, galactose in the ratio of 20:2:1:1 and the same uronic acid detected. It should be noted, that rhamnose predominates in mucus samples.

On the basis of the pharmacological properties of the dry extract obtained from the roots *Alcea rosea* L. (FS 42 Uz-1067-2012) found that it has expectorant and antitussive properties. On its basis a drug "Altseum", which in the form of tablets of 0.2 g is approved for medical use as an expectorant for the treatment of chronic catarrh, bronchitis, chronic obstructive pulmonary disease, bronchial asthma.

In a combination of dry extract *Alcea rosea* L. and dry licorice extract in the ratio of 2:1 we established drug "Glitsirozin", which in the form of tablets of 0.15 g allowed for medical use as anti-inflammatory and expectorant for the treatment of diseases of the upper respiratory tract. Ministry of Health of the Republic of Uzbekistan had given the permission for drug medical use.

On the basis of the dry extract of *Alcea rosea* L. stems (FS 42 Uz-1370-2012) received the drug "Gastrofit," which has anti-ulcer and anti-inflammatory properties.

And in combination with the enriched dry licorice extract (containing glycyrrhizin acid not less than 30%) drug "Glitsirofit" with a healing effect and is used for gastritis and enterocolitis established.

The Projects of the temporary pharmacopoeia clauses on drugs "Gastrofit" and "Glitsirofit", the documents on the production schedules and the laboratory production of drugs are prepared.

SCREENING OF 8 DERIVATIVES OF TROPOLONE ALKALOIDS ON THREE STRAINS OF SOLID TUMORS, SHOWN HIGH ACTIVITY *in vitro* IN NCI, USA

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A number of new derivatives of tropolone alkaloids colchicine and colchomine at research in NCI USA *in vitro* on the panel from 60 human cancer lines have shown considerable cytostatic activity. It was necessary to conduct researches of antineoplastic activity of these substances *in vivo* on animals with tumors, for selection of the most active substance.

We evaluate LD_{50} and antineoplastic activity at 10-fold introduction of a preparation on animals with tumors on the early period (in 2–4 days) after tumor inoculation.

LD_{50}, MUD_{10} and for some THD_{10} are studied at intraperitoneal 10-fold application of eight new preparations (К-1, К-21, К-23, К-26, К-30, К-50, К-60 and К-61). Antineoplastic activity was studied on tumoral strains АКАТОL, АКАТОN and the Sarcoma 180 in comparison with activity of the known antitubuline preparations taxol and etoposide.

Tumor strain	Taxol	Ethoposide	К-2	К-1	К-21	К-23	К-26	К-50	К-60	К-61	К-30
	(mg/kg dose), % of growth inhibition of tumors at 10-fold application on volume (V)/to weight (m)										
АКАТОL	(12)	(15)	(100)	(40)	(9)	(22)	(22)	(40)	(60)	(20)	(6)
	83/76	82/89	100/98	64/57	64/69	77/74	80/69	72/62	57/58	65/56	16/28
АКАТОL	(12.5	(15)	(100)	(40)	(8)	(20)	(20)	(40)	(60)	(20)	(8)
	78/42	100/97	76/75	100/95	94/91	99/97	77/67	87/77	90/92	100/100	82/69
Sarkoma 180	(12)	(15)	(120)	(40)	(9)	(20)	(20)	(40)	(70)	(18)	(8)
	95/83	93/87	99/100	40/55	99/96	99/82	98/82	99/95	97/76	98/81	88/59

The high antineoplastic activity of new preparations on studied strains of solid tumors was revealed, where all preparations have shown activity on one (К-1, К-50, К-26) or two (К-21, К-23, К-60 and К-61) tumors, exceeding 90%, testifies to necessity of their further wide studying for the subsequent introduction as possess activity (on «to Methodical instructions on studying of antineoplastic activity of pharmacological substances», Moscow, 2005), meeting the requirements: the perspective antineoplastic preparation should on 3 strains tumours show activity not below 70%, or on one strain not less 90%. К-30, which activity on two strains exceeded 80 %, further will be rechecked.

PHARMAKO-TOXICOLOGICAL INVESTIGATION OF NEW PREPARATION COLCHOMINOL (К-19)

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In NSCO of MH of RUz preclinical studying of new derivative alkaloid colchomine under the name colchominol (К-19) passes. Average lethal dose LD_{50} at mice at intraperitoneal introduction was 350 (270÷490) mg/kg. LD_{10} was 250 mg/kg. LD_{50} at intraperitoneal introduction in rats was 129 (110÷150) mg/kg. LD_{10} was 100 mg/kg. The preparation concerns to IV class of little toxic substances. К-19 was active in researches *in vitro in NCI*, it has shown the expressed efficiency at researches on tumors of animals *in vivo*. Preclinical pharmaco-toxicological researches of К-19 were the purpose of the present work.

Toxicological researches of К-19 at chronic intraperitoneal introduction to rats and rabbits within 15 days with the subsequent regenerative period within a month, have shown that preparation К-19 does not influence on behaviour and dynamics of weight of animals. К-19 does not render toxic action on function of kidneys, and also on quantitative structure and morphology of peripheral blood. In a dose of 40 mg/kg it is reversible influenced on ALT of liver, and also morphology of internal bodies of animals. К-19 at intraperitoneal introduction to rats in doses 10; and 20 mg/kg on 20–30% were accelerated fibrillation process due to acceleration of thromboplastine formation. In one month of the regenerative period all these indicators changed within physiological norm. By pathomorphological research of internal bodies of animals it was established: animals tolerate to introduction of a dose of 10 mg/kg, this dose practically non toxic and has no effects on vital systems. At application of a dose of 20 mg/kg it has weak destructive influence on internal parenchymatous bodies of animals (basically on a liver and kidneys). Preparation application in a dose of 40 mg/kg causes a number of negative effects, that is expressed in the form of deep dystrophic changes of parenchymatous bodies, as a liver, a spleen and kidneys, in which inflammatory reaction in the form of hypostases and apobiosis accompanies not sharply expressed. The general toxic action of the preparation is shown on reduction of lymphoid fabrics in a spleen. Research of cumulative property of the preparation has shown that it possesses by weak cumulative action (coeff. of cumulation = 0.75). Studying of allergenic activity of preparation К-19 have allowed to draw a conclusion that the preparation doesn′t cause anaphylactic shock, and contact dermatitis, i.e. preparation is not allergenic. The medicinal form of preparation К-19 essentially does not influence on cardiovascular system, breath, the central and peripheral nervous systems, reflex excitability and convulsive readiness were absent completely. The preparation possesses by sedative action.

However, К-19 in a dose of 5 mg/kg at i/p introduction possessed with pressor action. Probably, application of К-19 will be combined with muscular weakness. The above data shown, that the preparation in a therapeutic doses does not render the expressed toxic action on an organism of animals.

INVESTIGATION OF ANTINEOPLASTIC ACTIVITY OF THE NEW PREPARATION FROM COLCHAMINE OBTAINED FROM LOCAL PLANT RAW MATERIALS

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Expressed total toxic effect of a considerable quantity of the applied antineoplastic preparations, quickly developing resistance, absence of sensitivity of some tumors to available medical products dictates necessity of creation of new more effective antineoplastic preparations. New preparation К-19 investigated in NCI (USA) *in vitro* on the panel from 60 human cancer lines has shown considerable cytostatic activity. It was necessary to conduct researches of antineoplastic activity of this preparation *in vivo* on animals with tumors.

LD_{50} and antineoplastic activity defined at 10-fold introduction of a preparation on animals with tumors on the early and late periods after tumors inoculation.

Acute toxicity of К-19 is studied at intraperitoneal and peroral introduction on mice and rats. Antineoplastic activity of К-19 is revealed at intraperitoneal 10-fold introduction in the early and late period (in 12–15 days when the tumor is not less 1 cm^3) after transplantation: on АКАТОN at early introduction – 77/91%, (on volume/weight) at late introduction of 70/77%, on the Sarcoma 180 at early introduction - 100/91%, at late introduction of 96/92%, i.e. high activity which remains at influence on the developed tumors is observed.

Antineoplastic activity К-19 is defined by different ways of introduction (10-fold in a dose 40 mg/to) in the late period after subinoculation of tumor Sarcoma 180: at intraperitoneal (100/100%), at hypodermic – 99/98%, intramuscular – 100/100%, intravenous – 96/92% г, peroral – 97/93% – at dose 200 mg/kg.

Comparison of activity К-19 with known preparations similar tubulineinteractives actions taxol and etoposide has shown that on АКАТОL К-19 is more active (100/100%), than taxol (85/76%) and etoposide (82/89%), on АКАТОН activity К-19 (100/100%), higher, than at taxol (78/42%) and etoposide (100/97%), on a sarcoma 180 activity К-19 (100/91) also was above, than at taxol (95/83) and etoposide (93/87). The positive characteristics of the new preparation received by us specify in the big prospects of this substance for treatment of internal bodies tumors, and, in particular, colon cancer, sarcoma of soft tissues, probably, a cancer of prostate gland, and for external contact application.

Good solubility of the new preparation in water and its physical and chemical characteristics causing its stability, will allow develop its different medicinal forms, such as injection, salve (for external application), suppositories and others.

Probably, that preparation can be applied in peroral medicinal forms.

COMPLEXFORMATION OF CARBOXYMETHYLCHITOSAN *Bombyx mori* WITH IONS METALS

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Ability of polymeric chain, especially ionic groups to interactions with environment elements (molecules, atoms, ions, electrons, etc.) with change of configuration in solutions can form basis for formation of various complexes, including polymermetalcomplex (PMC) [1]. The Great value has polymer choice, and also ions of metals (Cu^{2+}; Co^{2+}) within the limits of the given work the basic emphasis becomes on natural polysaccharides-carboxymethylchitosan (CMC), received by updating chitosan dolls of silkworm [2].

At interaction CMC with ions of metals, 2 cases are possibly observed: Internal molecular and intramolecular complexformation. If complexformation. occurs in one macromolecule linkage of ions of metal of functional groups belonging to various sites of polymeric chain is possible.

As polymermetallcomplexes find wide in various areas, reaction complexformation CMC is spent at various parity polymer–metall (1:2; 1:12) for the comparative characteristic of the received salts. According to the spent researches it was revealed, that at substantial growth of the maintenance of metal in solution CMC the increase in exit PMC was observed.

Research conformations characteristic of a ball of a macromolecule at its interaction with ions of metals allows to understand more deeply law of formation polymermetalcomplexes, can be explain and predict their behaviour in solutions. In communications stated, have been spent viscosity measurements of samples.

Researches carrying out, that in process of increase in the maintenance of metal, reduction of values of viscosity of solutions that testifies to presence of processes of compression of ball of macromolecule though the size of molecular weight is constant was observed.

Thus, on the basis of the spent researches reception conditions polymermetalcomplexes carboxymethilated chitosan was revealed. It was established, that change degree viscosity characteristics of solutions essentially depends by nature metals ion – complexformating. Process complexformation of CMC is accompanied by processes of compression of ball of macromolecule, because of intramolecular interaction of ions of metals with functional groups.

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OBTAINING OF NATURAL POLYMERS NANOFIBER BY THE ELECTROSPINNING METHOD

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Recently research on working out of technology of obtaining of nanofiber polymeric materials by the electrospinning method intensively develops. In this aspect the big interest represents obtaining of nanofiber on the basis of local natural polymers which can find wide application in various areas of the industries, medicine, agriculture, etc.

Original installation of an electrospinning for formation nanofiber from solutions of polymers is collected. In this work results of comparative research on obtaining of nanofiber from solutions and mixes of local natural polymers are presented (Table 1).

TABLE 1. **Molecular Mass, Solvents and Concentration of Local Natural Polymers for the Obtaining of Nanofiber by the Electrospinning Method**

Polymer	Mol. mass.	Solvent	C, %	Thickness, nm
Chitosan *Bombyx mori*	120000	85 % CH_3COOH	5	100–500
Chitosan *Bombyx mori*	120000	Trifluoroacetic acid–methylencloride (70:30)	4	50–300
Cotton cellulose	170000	Cuprammonia complex	4	100–1000
Cotton cellulose	176000	$ZnCl_2$ (52%)	4	150–800
Cotton cellulose	176000	Trifluoroacetic acid	4	100–400
Three acetate cellulose	142000	Methylen cloride–ethyl alcohol (90:10)	6	50–300
Silk fibroin	127000	Trifluoroacetic acid	10	100–300
Silk fibroin	127000	2,5 M LiCl-DMFA	10	100–300
Cellulose–collagen (1:1)		Trifluoroacetic acid	2	50–500
Chitosan–cellulose (1:1)		Trifluoroacetic acid	4	50–500

The electrospinning of nanofiber is carried out on distance of 150–200 mm from the anode (needle with a diameter 0.5 mm) to a collector (the screen with the area 10^5 mm^2) under the influence of constant voltage 15 kV. Optimum conditions of formation of nanofiber are defined by selection of solvent, concentration (C) and molecular weight of polymers. The thickness, obtained nanofiber, is defined by methods of electronic microscopy (TEM) and atom forced microscopy (AFM).

It is revealed, that formation of nanofiber is possible at a certain range of concentration and molecular weight of polymers, and also a choice of the solvent, characterising thermodynamic quality is closer θ-solvent. It is detected, that the accretion distance from the needle to a screen arranged to decrease of nanofiber′s thickness. It is defined, that the obtained samples represent a kind of nanofiber nonwoven nanoporous material of natural polymers.

EFFECTS OF QUERCETIN AND MIRICETIN ON THE FLUORESCENCE OF ERITC LABEL IN ACTIVE SITE OF THE Na, K-ATPase

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Sodium and potassium ion activated adenosinetriphosphate (Na, K-ATPase) is a plasma membrane transport system which is essential for normal cell function in all mammalian cells. Plant flavonoids, quercetin and miricetin, are high-effective inhibitors of the Na, K-ATPase of pig kidney (90% pure protein), that inhibition constants (1.56 μM and 1.44 μM, respectively) approach to cardiac glycoside ouabain (1.04 μM). Like the specific inhibitors – cardiac glycosides, these flavonoids neither affect the apparent Michaeles constant for ATP, nor bind with active site of enzyme.

Na, K-ATPase preparation has been covalently bounds to fluorescent label erythrosinisothiocyanate (ERITC) in the active site of enzyme. Fluorescent labels allow study the intramolecular processes in the membrane enzymes. In our work the reducing of the ERITC fluorescence under affect of flavonoids in the presence of the ATP-Mg substrate complex has recorded. According to our experimental data, quercetin and miricetin in concentration $1 \cdot 10^{-6}$–$7 \cdot 10^{-6}$ mol/L reduced the fluorescence intensity of ERITC for 15–40% in labeling enzyme. Addition of ATP-Mg substrate in reaction environment after flavonoids leads to additional double reduction of fluorescence intensities. However when ATP-Mg complex was introduced in labeling enzyme before flavonoids, fluorescence decreases only for 8%. Absence of Mg ions in the reaction mixture practically doesn't reduce the fluorescence of the label.

The reversal reaction sequence of the Na, K-ATPase is depicted as cycles between two major conformational states-phosphorylated (E1-P) form in the presence of Na and Mg ions and dephosphorylated (E2-P) form in the presence of K ion. As studied flavonoids belong to the slowly-reversibly inhibitors, probably, they are bound with the enzyme before its phosphorylation with ATP, that has shown in the experiment, where fluorescence change only for a few percent. It should be note, that double reduction of fluorescence intensities indicates that quercetin and miricetin influence on phosphorylated stages of enzyme by substrate. The process of hydrolysis ATP and conformational arrangement is carried out in presence of Mg ions in membrane enzyme.

The present results are co-ordinate with early obtained data for investigation of quercetin and Na, K-ATPase (in the review of E. Middleton et al., Pharmacol. Reviews, v. 52, 2000), which show that flavonoids inhibite the transition from (E1-P) form to (E2-P), as well as the hydrolysis of the phosphoenzyme. At that time ouabain is binding to any states of enzyme, but blockades (E2-P) forms, i.e. process of Na, K-ATPase dephosphorylation.

Thus, the process the binding of flavonoids to Na, K-ATPase, as well as their inhibition mechanism is differ from the action of both cardiac glycosides and another inhibitors of enzyme.

INCREASE OF THE STORAGE PERIOD OF TUBERS BY APPLICATION OF MICROELEMENTS AND USEFUL MICROFLORA

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Loss of agricultural products during storage may be occur due to phytopathogenic microflora, rodents, shrinkage, pests. Any reason may cause a huge loss being neglected. Researches of scientists and experts provided a set of results, monographs and recommendations, which are successfully applied using modern technologies – gas environments, drying, spraying by chemicals, microbiological preparations are written. In this field the positive results were obtained by scientists of AS RUz, institutes of the Ministry of Agriculture and Water Management RUz, universities and institutes of Ministry of the higher and secondary education RUz as for separate kinds of vegetables or fruit, as in general for application on many kinds of tubers are obtained. Works in searching of new means and storage methods proceed also the present message is devoted to research of microelements and useful microflora application at storage of tubers, in particular, potato and topinambur.

Concentrates of mineral salts "Bio-iodine-magnesium" (I 350 mg/L) and "Iodine-shifo" (I 250 mg/L) diluted in 1:20 ratio have been sprayed on potato and topinambur tubers before storage, tubers are aired before a bookmark, on a storage place. Aerobic breath of roots is minimized. Other pilot series has been sprayed by a microbiological preparation Baikal EM-1 in ratio 1:100, aired before a bookmark in same temperature and humidity modes. The third series is processed twice: by mineral salts with iodine and a microbiological preparation. The treatment was not applied to the control series. Relative humidity was within 80–90%. The storage temperature is constant and close to +5°C (mountain underground storehouse). The underground storehouse before a bookmark has been neutralized by a microbiological preparation. Tubers were stored by a continuous embankment.

On the basis of the spent researches it has been revealed that processing potato by microelements and bacteria – antagonists does not cause essential changes of the maintenance of the basic chemical components of tubers, reduces the expense of spare substances on breath processes, reduces damage at the expense of rotting, intensifies disintegration of nitrates. Damage has decreased at processing by microelements for 1.8 times, by preparation Baikal EM-1 – for 2.5 times, in a combination (the third party) – in 3.5 times.

Biological product action is caused apparently by that at processing of tubers the microorganisms containing in the sprayed environment, occupy a surface of tubers and provide their protection at storage. The expense of a preparation of a concentrate of microcells with iodine has made 100 mg on 100 kg, the expense of Baikal EM-1 has made 80 mL on 100 kg of tubers. In autumn 2013 these expenses make 6000 sum on a concentrate and 10000 sum on a preparation Baikal EM-1 for processing of 1 ton of tubers.

MEDICAL PLANT SYSTEMS OF GLYCOCONJUGATE-BINDING COMPONENTS AND OXIDASES AS MEMBRANE BOUND PURIFIED SEPARATED ACTIVE FORMS

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Lectins (L) (proteins/peptides and their complexes discriminating glycoconjugates) and oxidases (O) in natural sources are spread as systems (LS and OS, respectively) possessing varying activities (antimicrobial, cytokine-like, etc.). Medical plants of local origin are used as biologically active additives (www.fitokor.ru). The aim was simultaneous identification of plant OS and LS using simple step-by-step procedure.

Protein markers were: Concanavalin A (ConA, Sigma) and erythrostim (Microgen). Linear soluble pseudopolysaccharides on the basis of polyacrylamide core biotinylated or not (Sugar-PAA-b; www.lectinity.com) and chemiluminescent substrate of increased sensitivity (BioWest, UVP) were used. Plant crude extracts as NaCl-fractionated component concentrates (> 27 kD) in PBS pH 7 were prepared and used [1]: PG-II from mixture of 7 plants for "PhytoGoR"; IT-I, II, III from leaves of "Ivan-Tea"; PC2-I, II from plant roots and birch fungus for "Phytocomposition No 2"; CV-II from birch fungus for "ChagoVit". Samples (3–7 mkL in 1% Tween-80) were applied on paper applicators on the gel at approx. pH 4. Separated by horizontal isoelectric focusing (IEF) in the gradient of pH 2–6 (equal volume mixture of Servalyts 2.5–4 and 4–6; Serva) in semipreparative block of PAA gel (non-linear gradient of power: up to 3.5 kV, up to 5 h, at 10°C; the distance between electrodes – 22–23 cm, MR – methyl red pI 3.75 had end position of 56–60% of the distance) in the presence of 7 M urea and 5% (w/v) saccharose [2]. Separated components were electroblotted on sandwich of hydrophilic Durapore and hydrophobic Immobillon-P membranes. Durapore pictures were used for tracks position control and evaluation of current purification of L and O on the Immobillon. Firstly OS chemiluminescence on Immobillon was initiated with BioWest and then LS were detected with Sugar-PAA-b in PBS (5 mkg/mL): Man-PAA-b (2 h, 25–27°C) followed by additional staining with Man-6-P-PAA-b (a night, 5°C) and then Gal-PAA-b (2 h, 25–27°C). The bound glycoconjugate was visualized with Streptavidin-Peroxidase (R&D; 1 h, 37–41°C) followed by adding BioWest. Kinetic chemiluminescence was registered as photos using succession of increased expositions within 40 sec – 20 min in the Dark Room of BioChemi System (UVP) in regime of live imagination.

OS within pI 3.2–3.7 (especially in fractions P2-II,CV-II) were identified. Synergistic action of Man-PAA-b and Man-6-P-PAA-b in detection of extended LS was observed. (Phospho)mannan-binding LS (ConA and P2-II in the region of pI 5–6 were distributed in similar manner (ConA revealed increased number of forms). Additional staining with galactan did not extend SL regions. IEF in PAA gel and electroblotting resulted in significant visual purification and separation of LS and OS from color highly negative charge admixtures and non-color background admixtures.

Approaches developed indicate usefulness of procedures for detection of L, O, LS and OS in plants of medical significance.

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THE ANALYSIS OF CORRELATION BETWEEN BIOLOGICAL ACTIVITY OF ISOXAZOLE AND ISOTHIAZOLE DERIVATIVES AND ODOR OF INITIAL SUBSTANCES

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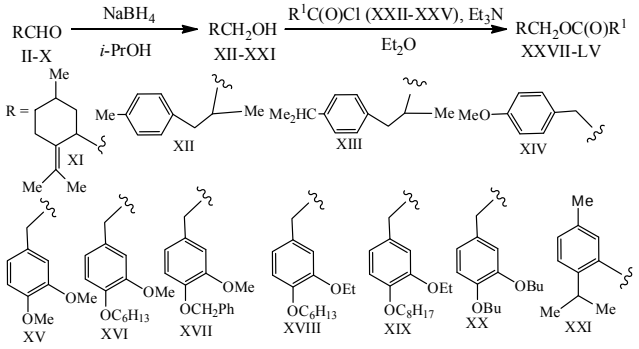
The cycloaliphatic and substituted aromatic ketone and aldehydes, such as (*R*)-(+)-pulegone [(*R*)-5-*p*-menth-4(8)-en-3-one] (**I**), jasmorange [2-methyl-3-(4-methylphenyl)propanal] (**II**), cyclamen aldehyde [2-(4-isopropylbenzyl)propanal] (**III**), anisaldehyde (4-methoxybenzaldehyde) (**IV**), veratraldehyde (3,4-dimethoxybenzaldehyde) (**V**), 4-hexyloxy-3-methoxybenzaldehyde (**VI**), 4-benzyloxy-3-methoxybenzaldehyde (**VII**), 3-ethoxy-4-hexyloxybenzaldehyde (**VIII**), 3-ethoxy-4-octyloxybenzaldehyde (**IX**), 3,4-dibutoxybenzaldehyde (**X**) are presented in the essential oils of some plants. They are widely used in the perfumery industry as fragrant substances, and also can serve as available building blocks for the purpose of biologically active substances synthesis.

A range of esters (**XXVI–LVI**) of benzoic, 5-phenyl-, 5-*p*-tolylisoxazole-3-carboxylic and 4,5-dichloroisothiazole-3-carboxylic acids (**XXII–XXV**) and a number of the cycloaliphatic and substituted aromatic alcohols (**XI–XX**), obtained by reduction of available ketone (**I**) and aldehydes (**II–X**), was synthesized.

Reduction of ketone (**I**) and aldehydes (**II–X**) to alcohols (**XI–XXI**) was carried out with the sodium borohydride in the solution of propane-2-ol. The yields of alcohols (**XI–XX**) were 68–84%. The esterification of the aliphatic and substituted aromatic alcohols (**XI–XX**) and thymol (**XXI**) with chlorides of benzoic, 5-phenyl-, 5-*p*-tolylisoxazole-3-carboxylic and 4,5-dichloroisothiazole-3-carboxylic acids (**XXII–XXV**) was carried out in the solution of anhydrous ethyl ether in the presence of triethylamine with yields of esters (**XXVI–LVI**) 88–92%.



Esters (**XXVI–LVI**) appears to be interesting for biological activity screening, caused by presence at their molecules both aromatic and heterocyclic fragments. Biological activity might also correlate with odor of initial substances. The approach on the basis of organoleptic analysis (odor) of initial substances appears to be perspective in effective design of different substances for agricultural and pharmaceutical purposes.

DEVELOPMENT OF HEAT-STABLE FOOD COMPLEX FROM TWO HYDROCOLLOIDS: STARCH AND GELLAN GUM

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Nowadays interest in changing thermo-stable properties of a fruit-stuff is very wide developed since it ranges from purely theoretical aspects, others directly applicable to food processing and manufacturing, such as physicochemical and sensory degradation of fruit fillings as well as bakery products prepared with them under applied heat.

The main goal of this research was to create a novel heat-stable complex containing two different polymeric compounds – low acyl gellan gum and amylopectin potato starch for further application in bakery fruit filling compositions.

Although gellan gum may be effectively used by itself in heat-stable fruit fillings manufacturing, it was established that′s better to utilize this food polymer in combination with other thickeners or gelling agents in order to reduce syneresis in prepared fruit compositions. Thus, amylopectin potato starch type Eliane BC-160 from AVEBE was selected to be used in combination with gellan gum for the development of heat-stable food complex to stabilize fruit fillings during baking process due to its excellent ability to bind water without moisture loss.

The starch/gellan gum heat-stable complex was prepared by solving low acyl gellan gum Kelcogel F in hot distilled water at 90°C during high-speed mixing for 30 minutes and adding amylopectin potato starch type Eliane BC-160 in the obtained clear solution and further mixing up to complete dissolution of the hydrocolloids. Electron microscope images of starch/gellan gum complexes showed that starch granules penetrated into gellan gum structure and formed a novel resistant complex.

Experimental fruit fillings′ samples prepared locally from apple puree (12 Brix), sugar, citric acid and elaborated blends of low acyl gellan gum Kelcogel F and amylopectin potato starch type Eliane BC-160 were compared to the control samples of the fruit fillings prepared without any food stabilizers in terms of physicochemical (soluble solids, water activity, pH, phenolic compounds and antioxidant activity) and sensory analysis before and after baking process. All fruit fillingsў samples were also put through a standard bakery test to evaluate their thermal stability by determining bakery index (BI) through measuring the diameter of a fruit filling before and after baking at a temperature of 220°C for 20 minutes.

Results of conducted analyses showed a significant difference in heat-stability, rheological and sensory attributes between test and control samples of fruit fillings analyzed after baking.

Although amylopectin starch/gellan gum blends offer numerous advantages in heat-stable fruit filling development, this investigation demonstrated that their synergetic effect could manifest itself differently depending mostly on manufacturing conditions, raw materials and soluble solids of the finished product.

ALKALOIDS OF THE LEAVES OF *Annona muricuta* AND *A. senegalensis*

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The plants *Annona muricata* L. and *A. senegalensis* Pers (*Annonaceae*) are widely distributed over the Republic of Guinea [1] and are used in folk medicine to treat various inflammatory diseases, dysentery, diarrhea and skin diseases [2].

We studied for the first time the alkaloid composition of leaves of *Annona muricata* L. and *A. senegalensis* Pers, which are groves in the Republic of Guinea.

The usual $CHCl_3$ extraction of leaves of *Annona muricata* L. afforded 0.125% total alkaloids that were separated into phenolic and non – phenolic parts. Separation over a column of silica gel (C_6H_6–EtOH eluents, 99:1; 98:2; 95:5 and 90:10) isolated from the non phenolic part of the alkaloid mixture five pure compound; from the phenotic part, three. Comparison of the chromatographic mobility, physicochemical properties, and lack of melting-point depression with authentic samples identified the isolated alkaloids as the following bases: anonaine (**1**), remerine (**2**), asimilobine (**3**), isolaureline (**4**), ksilopine (**5**), isoboldine (**6**), coclaurine (**7**), and liriodenine (**8**) which was isolated earlier from *Liriodendron tulipifera* L. (*Magnoliaceae*) [3] and *Cocculus laurifolius* DC (*Menispermaceae*) [4].

Extraction of leaves of *A. senegalensis* Pers by $CHCl_3$ produced 0.085% total alkaloids from the air-dried raw material. Separation of resulting mixture of bases isolated and identified six alkaloids, of which anonaine (**1**), remerine (**2**), isoboldine (**6**) and nornuciferine (**9**) were aporphine bases; the benzyltetrahydroisoquinoline alkaloid – coclaurine (**7**) and liriodenine (**8**) – oxoaporphine alkaloid.

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BIOTECHNOLOGY OF BIOLOGICALLY ACTIVE EXTRACTS OF GEORGIAN MOUNTAIN BILBERRY

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Among medicinal plant raw materials in phytotherapy stands out the bilberry. In this respect, Georgian mountain bilberry looks to us the most promising.

There experiment uses Georgian mountain bilberry (*Vaccinium Myrtillus* L.) fruit (*Fructus Myrtilli*). The samples will be dehydrated until the water content no more than 8–10%.

Dispersing of dehydrated bilberry is carried out by two stages: at first, in hammer mill (TP2 Hammer Mill), and then until nano-particles - in АГО-2 class planetary activator equipped with variable speed unit.

As an extraction agent we will use the complex hydrophilic- hydrophobic solvent. As hydrophilic component we will take 40% solution of ethanol from Borjomi-Utsera type drinking acid mineral water with mineralization at 5–15 g/L and pH 3.5–6.5. The chloroform will be taken as hydrophobic component. The optimal weight ratio of nano-dispersed raw materials, and hydrophilic and hydrophobic solvents, as well as the extraction parameters: temperature, duration and pulsing mode of the extraction mass (vibration frequency, amplitude) have been determined experimentally.

The obtained extract undergoes filtration, at first by depositing, then by centrifugation, and at the end – by using membrane filtering method. Thus, the prepared solution is concentrated in vacuum-evaporator installation at temperature no higher than 55–60°C.

The analysis of extracts previously prepared in laboratory conditions has shown that they contain considerably larger amount of anthcyanin pigments and other bioflavonoids (10–12%), than currently existing in the world market bilberry preparations such as “Fokus” (Russia 6–7%) and “Strix” (Denmark 2.8–3.0%).

There is developed the rational process flow of producing of extracts containing biologically active mixtures and quality standards of product. The technology is modern and simple, the target product is affordable.

The wide-range new medicated product with high antioxidant activity is intended for improving functional status of visual organs, and preventing the senilism processes. High antioxidant activity conditions an increased effect of preparation during overloads of visual apparatus, especially, during regular computer use. The extract is not toxic during long hours of use, it is of wide spectrum. The urgency of its production is increasingly growing against background of mass computerization and environmental tenseness, and it represents a social order of public health.

BIOTECHNOLOGY OF GRAPE-STONE EXTRACTIVE OIL

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The main way to increase the grape-stone oil production effectiveness is to use traditional organic solvents. However, there is available very little information about research works carried out in this area, and the recommendations are mutually exclusive.

Thus and so, we consider the development of the main aspects of the industrial production of grape-stone extractive oil a pressing and promising issue, especially because in case of rational selection of organic solvent and production regime, the output of oil in the grape-stone can exceed 90–95%.

In consequence of above mentioned, the proposed work is aimed at process-apparatus development of the extractive oil industrial production on the basis of results of studies of the extraction process with organic solvents of various sorts of grape-stones.

There have been established the optimization parameters of direct extraction of oil from grape-stone plural shavings, major influencing factors, their levels and variability intervals. There is implemented the four-way matrix of the industrial experiment central composite rotatable design. For the analysis of the extraction process and interpretation of its results, there have been obtained the equations of appropriate adequate regression. There is carried out the graphical analysis of one-dimensional sections and double effects of optimization parameters, and determined the process optimization strategy. By using the classical Lagrange′s method of infinite multipliers, there are established the optimal regimes of the extraction of grape-stone plural shavings with organic solvent.

By using modern physical-chemical and chromatographic methods,, there are studied the physical-chemical characteristics and fatty acid content of grape-stone oil.

There is developed the process flow of producing of oil from grape stone with its implementation. Checkout of the obtained optimal parameters of grape-stone plural shavings extraction process under factory conditions enabled us to obtain the experiment-compliant results. The determination error between them does not exceed 2–3%. There are developed the optimal regimes of the remained extracting agent distillation from the grape-stone cake, and established reference performance of the grape-stone extractive oil production.

There is shown that the grape-stone oils from white and red varieties are not very different from each other, and they correspond with high-grade vegetable oils using in traditional foods. All this enable us to use the grape-stone extractive oils for making cosmetics and functional-purpose foods.

BIOTECHNOLOGY OF TEA LEAF OIL

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Despite centuries-old history of tea culture, the tea fat-dissolving lipophilic substances have practically remained beyond the vision of scientists, the analysis of which shows that they contain considerably higher amount of valuable for human organism biologically active substances than so-called "classical" extracts of tea.

The proposed work is aimed at developing technological foundations for factory production of a completely new medical-pharmaceutical tea leaf extractive oil such as lipid complex.

It has been experimentally established that tea leaf lipid complex is interesting as a rich natural source of chlorophylls, carotinoids and tocopherols. Among fatty acids there are prevailed linolic and linoleic fatty acids. In this regard, tea leaf lipid complex considerably exceeds sea – buckthorn and wild-rose oils.

There has been determined chemical composition of tea leaf oil lipid complex, and its variability in tea extractive raw material, by impact of tender fraction share. There is established non-linear correlation between the contents of lipids and caffeine in raw material that enabled us to develop a simple and reliable indirect method of determining amount of caffeine in tea and in its lipid complex.

By implementing the four-way matrix of the industrial experiment central composite rotatable design, there are obtained the adequate regression equations characteristic of tea extractive oil production processes, and by using the classical Lagrange′s method of infinite multipliers, there are obtained the optimal production regimes. Also, there are determined the quantitative indicators of physical-chemical and quality characteristics of tea extractive oil – lipid complex.

There are developed, scientifically justified and implemented the production scheme, optimal regimes and suitable processing line of tea extractive oil – lipid complex. The 5% solution of tea extractive oil in sunflower oil (preparation "TIOL") has been undergone the clinical trials in leading clinics of Kutaisi. The results of clinical trials give us reason to recommend this preparation, as an effective remedy for skin wounds of various aetiology, as well as for treatment of stomach and duodenal ulcers.

For the first time in world practice is developed scientifically approved and practically implemented biotech regulations and technological lines of producing a new pharmacological product from the tea leaf lipid fraction (oil).

ANTI-AGES ALGERIAN VEGETAL EXTRACTS. PHYTOCHEMICAL STUDY OF *Daucus aureus*

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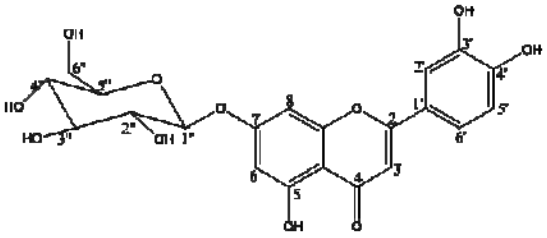
In a large project on Algerian plants, we are interested in their phytochemistry and biological properties (PHC franco-algerien Tassili, 2012-2016). Particularly, in diabetes, a chronic hyperglycaemia occurs which is responsible for complications of diabetes through advanced glycation end-products (AGEs) formation [1]. SONAS lab recently developed an automated HTS assay, suitable for compounds and extracts, to evaluate their anti-AGEs potential [2]. This assay was used to select potent anti-AGEs extract from a selection of plant species traditionally used for the treatment of diabetes in Algeria [3]. Among them, EtOAc and BuOH extracts from *Daucus aureus* Desf. (*Apiaceae*) were selected and their phytochemistry studied. Moreover, MeOH extract led to the isolation of flavonoid *O*-glucosides **1** and **2**, which structures were elucidated by spectroscopic methods, including UV, 1D and 2D NMR, MS.



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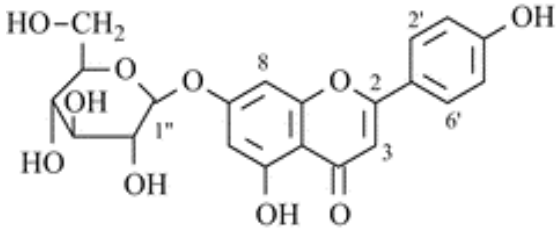

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3. See Amel Achouri poster.

CARBOHYDRATE-CONTAINING DERIVATIVES OF ALKALOID ANABASINE

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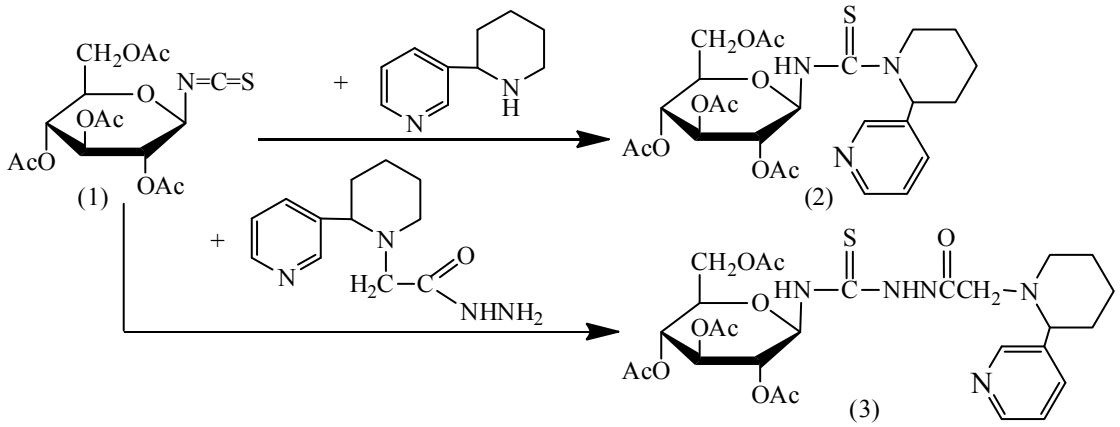
The introduction of carbohydrate residues in the structure of biologically active compounds leads to a sharp decrease in toxicity that allows to recommend the method of glycosylation of physiologically active compounds as one of the possible ways to get low-toxic, water-soluble biologically active substances [1]. In this regard, with the purpose of reception of carbohydrate-containing derivatives of natural compounds we carried out the reaction of interaction of alkaloid anabasine and hydrazide *N*-anabasinylacetate acids with 1-dezoxy-2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopiranozyl isothiocyanates (**1**). It is shown that glycosyl isothiocyanates easily reacts with nucleophiles reagents and with good outputs (75 and 82% of theor.) formed *N*-substituted as etylglycosylthiourea (**2**, **3**). The reaction was carried out at room temperature, and as solvents were used anhydrous benzene and ethanol.



The composition and structure of compounds (**2**, **3**) confirmed by the facts of elementary analysis, IR, ^{1}H NMR, and mass spectroscopy. In IR spectra of the synthesized compounds (**2**, **3**) are observed absorption bands of the acetate groups of the carbohydrate ring at 1750 (C=O) and 1240 cm^{-1} (O–C). Piranozes ring in the compounds (**2**, **3**) is characterized by an absorption band at 912–928 cm^{-1}. Deformation vibration links C1-N the field of 887–892 cm^{-1} are caused by the β-configuration of aglycone.

In the ^{1}H NMR spectrum of the compound (**2**) all protons match the expected values of the chemical shifts. In the area of a strong field, about 2 ppm, manifested four singlet methyl protons of the acetate groups. Four protons of piranozes ring identified in the field of 4.91, 5.14, 5.37 and 6.12 ppm clear triplets indicative of the equivalence of the resonant proton with neighboring piranozes ring. In ^{1}H NMR spectrum of the compound (**3**); methylene protons-*N*-CH_2-C(O)-fragment resonate with 3.1 ppm, protons N-H group – in the area of 9.3–9.8 ppm in the form of broad singlet.

CHEMICAL COMPOSITION OF THE ESSENTIAL OIL OF *Tanacetum hololeucum* FROM IRAN

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The genus *Tanacetum* L. (*Asteraceae – Anthemideae*) comprising around 160 species worldwide and according to the recent findings the number of species in Flora of Iran is increased to 36. In this research, the essential oil composition of *Tanacetum hololeucum* collected from north of Iran was investigated for the first time. The essential oil was isolated by hydrodistillation from the aerial flowering parts and analyzed by GC and GC-MS. Thirty-five constituents were identified representing 99.9% of the total oil. Oxygenated monoterpenes (76.0%) were characterized as the major compounds followed by oxygenated sesquiterpenoids (14.6%). The major compounds were artemisia alcohol (22.8%), yomogi alcohol (19.4%), artemisyl acetate (12.9%), γ-eudesmol (12.1%) and camphor (10.5%).

NEW RHAMNOGLUCOSIDES OF QUERCETIN AND ISORHAMNETIN FROM *Calendula officinalis* FLOWERS

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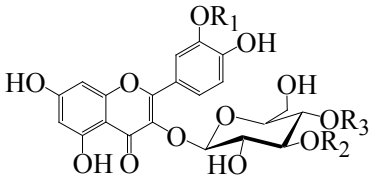
The *Compositae* annual herbaceous plant, *Calendula officinalis* L. (marigold, pot marigold) is widely cultivated as ornamental, culinary and valuable medicinal herb due to different pharmacological properties. The studies of *C. officinalis* cultivated in Buryatia resulted to isolation more than 40 compounds, derivatives of phenolic acids, flavonoids, anthocyanins, and phenylpropanoids (Olennikov, Kashchenko, 2013). In *n*-butanol fraction of *C. officinalis* flowers, using the HPLC-ESI-MS, eight flavonol biosides were detected including four compounds giving molecular peak 609 $[M - H]^-$ ($C_{27}H_{30}O_{16}$) which are derivatives of quercetin (Q; aglycone peak 301 $[M - \text{carbohydrate moiety}]^-$), and four compounds with molecular peak 623 $[M - H]^-$ ($C_{28}H_{32}O_{16}$) which are derivatives of isorhamnetin (Ir; aglycone peak 315 $[M - \text{carbohydrate moiety}]^-$). Using the complex of chromatographic procedures (CC, GPC, pTLC, pHPLC) these compounds were isolated and identified by chemical and spectroscopic methods (UV, IR, MS, NMR). The studies found that the carbohydrate moieties in all glycosides are the biosides consist of glucose (Glc) and rhamnose (Rha). Four of them are known and were previously detected in *C. officinalis*; there are Q-3-*O*-(6″-Rha)-Glc (Q-3-*O*-rutinoside, rutin), Q-3-*O*-(2″-Rha)-Glc (Q-3-*O*-neohesperidoside, calendoflavobioside), Ir-3-*O*-(6″-Rha)-Glc (Ir-3-*O*-rutinoside, narcissin), Q-3-*O*-(2″-Rha)-Glc (Ir-3-*O*-neohesperidoside, calendoflavoside). Two glycosides comprised the (4″-α-*L*-rhamnosyl)-β-*D*-glucose in glycosyl moiety, and two of them the (3″-α-*L*-rhamnosyl)-β-*D*-glucose (rungiose). These compounds a new and the following names were given for them: calendoside I [Q-3-*O*-(4″-Rha)-Glc], II [Q-3-*O*-(3″-Rha)-Glc], III [Ir-3-*O*-(4″-Rha)-Glc] and IV [Ir-3-*O*-(3″-Rha)-Glc]. There is one known (3″-α-*L*-rhamnosyl)-β-*D*-glucose containing flavonoid – kaempferol-3-*O*-rungioside (*rungioside*). Flavonoids containing the residue of (4″-α-*L*-rhamnosyl)-β-*D*-glucose are unknown.



I: R_1,R_2=H; R_3=L-Rha*p*
II: R_1,R_3=H; R_2=L-Rha*p*
III: R_1=CH_3; R_2=H; R_3=L-Rha*p*
IV: R_1=CH_3; R_3=H; R_2=L-Rha*p*

The study of the biological activity of the isolated compounds showed that the site of rhamnose attachment to glucose does not influence on the severity of antioxidant, anticholinesterase and antityrosinase activities of the rhamnoglycosides. However, it should be noted that the neohesperidosides and rutinosides of quercetin and isorhamnetin are the most effective inhibitors of amylase and α-glucosidase.

The authors acknowledge the financial support provided by the Presidium of Siberian Division of Russian Academy of Science under Program “New Medical Technologies Centers”.

NEW *O*- AND *C*-GLYCOSIDES FROM *Scutellaria galericulata* GROWING IN YAKUTIA

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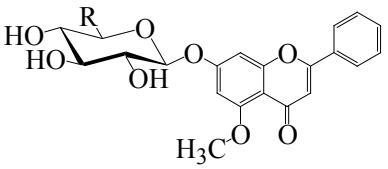
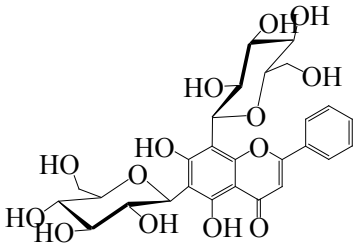
Yakutia is the largest territorial subdivision in the world. More than forty percents of the territory is located behind of the Arctic Circle. Yakutia is characterized by a variety of natural environments and resources, due to physical and geographical location of its territory. Despite the uniqueness and diversity of the Yakutian Flora, the scale of trial of its plant raw material is extremely low. As a part of the scientific programm of plant diversity investigation, we are carrying out comprehensive studies of the chemical composition of Yakutian plants. In this paper we present the results of the phytochemical investigation of *Scutellaria galericulata* collected in Central Yakutia. Thirty five compounds were isolated from *S. galericulata* herb including three new components. Two of them (**1**, **2**) were derivatives of 5-methoxychrysin, rare flavone previously detected only as trace phenolic of the Serbian origin honey (Milojkoviж-Opsenica, 2012). Both flavones are *O*-glucosides, 5-methoxychrysin-7-*O*-glucoside (**1**) and 7-*O*-glucuronide (**2**). Using HPLC technique it was found that **1** and **2** were not discovered in plant material from south regions of Russian Federation (Baikal region, Chita, Far East) that shows selective accumulation of this compounds for Yakutian territory. Third compound isolated was identified as a *C*-glucoside – chrysin-6,8-di-*C*-glucoside (**3**). In early phytochemical study of *Scutellaria* genus two *C*-glycosides of chrysin were isolated including 6-*C*-glycoside from *S. baicalensis* (Miyaichi, 1994) and *S. amoena* (Zhou, 2000) and 8-*C*-glycoside from *S. baicalensis* (Zhang, 1997). Compound **3** is the third known *C*-glycoside of chrysin. The known 6,8-di-*C*-glucosides of the flavonoids previously described in plant sources are derivatives of apigenin (vicenin II; different plants), luteolin (leucenin II; *Montanoa bipinnatifida*), diosmetin, eriodyctiol (*Passiflora tripartita*), acacetin (*Trigonella corniculata*) and other.



1: R=CH_2OH
2: R=COOH



3

Comparative analysis of individual compounds shown that 5-methoxychrysin and tectochrysin characterized by presence of methoxy-group are most effective acetylcholinesterase inhibitors than chrysin. These structural features are probably the key to increasing of activity of flavones.

The authors acknowledge the financial support provided by the Federal Objective Programm, Grant No. 14.A18.21.0217, and Russian Foundation of Fundamental Research, Grant No 12-03-31547.

SELECTIVE ANTIAGGREGATING ACTIVITY OF THIOTERPENOIDS OF PINANE SERIES

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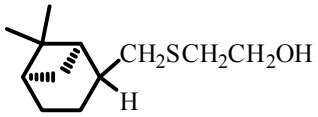
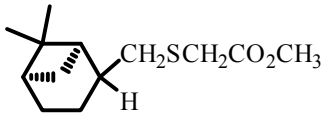
It is well-known that monoterpenes, including β-pinene, have a wide range of biological activity. On the other hand, sulfur refers to biogenic element, and sulfides, sulfoxides and sulfones often possess the pharmacological activity. Therefore, integration of these pharmacophoric fragments — terpene skeleton and sulfur-containing function – in one molecule is a precondition for obtaining new biologically active low-toxic compounds.

A number of thioterpenoids (**1–5**) have been synthesized by us based on (–)-β-pinene [1].



1



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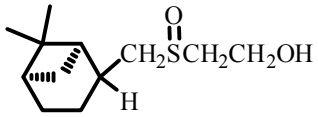

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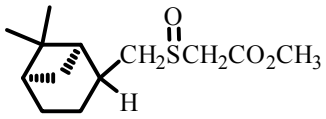

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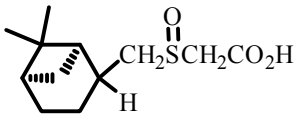

5

The possibility of using the substances obtained for correction of hemostasis was determined on human blood plasma *in vitro*. For evaluation of hemostasis system the rate determination of platelets aggregation and surface-dependent standard coagulating tests were applied: activated partial thromboplastin time, prothrombin and thrombin time with international normalized ratio. Aggregating activity of platelets were determined by means of analyser «Chrono-Log Corporation» (USA) using the method of G. Born. For determination of spontaneous aggregation of platelets and coagulating activity of plasma the venous blood of patients with ischemic heart disease (IHD) and those with evident changes in the hemostasis system. The induced platelets aggregation was studied on plasma obtained from healthy donors.

The results obtained have shown, that the basic substance (β-pinene) does not influence the state of hemostasis system of patients with IHD. The compounds synthesized on its basis have shown high hemocoagulating (antiaggregating) activity. All compounds obtained possess the antiaggregating and anticoagulating activity. The most water-soluble sulfoxide (**5**) inhibits completely the spontaneous and induced by collagen and arachidonic acid aggregation of platelets; it also reduces the coagulating activity of human blood plasma. Considering the low toxicity of thioterpenoids the compounds obtained can be considered as potential medicinal agents for treatment and prevention of trombophilia, and as a stabilizer of blood specimen in transfusiology.

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ELECTROPHILIC ADDITION OF DITHIOLS TO (+)-CAMPHENE

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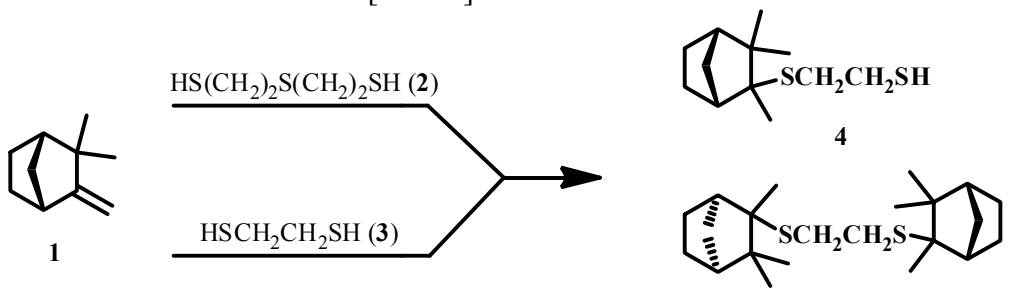
The peculiar feature of the chemical behavior of bicyclic monoterpenes in the reactions with electrophilic reagents is their tendency to various rearrangements. The most famous of them are camphene rearrangements. As a rule, the electrophilic addition to camphene is accompanied by the Wagner-Meerwein rearrangement to give the products of bornane structure. The reactions of electrophilic addition to camphene without isomerization of the original structure of the molecule are very seldom [1, 2].

In this work we studied $ZnCl_2$-catalyzed addition of 2,2′-thiodiethanethiol (**2**) and 1,2-ethanedithiol (**3**) to (+)-camphene (**1**) (terpene-thiol ratio is 1:1 or 2:1).

In the case of camphene excess bis-adduct **5** of camphene structure with *m/z* 366 has been obtained in both reactions. If in the reaction of **1** with ethanedithiol **3** formation of this product is quite trivial whereas in the reaction with sulfide **2** the most expected product was the compound with *m/z* 426. A minor product of both reactions under camphene-thiol ratio of 1:1 was monoadduct **4** with *m/z* 231 $[M + H]^+$.



1 **4** **5**

Reaction conditions: $ZnCl_2/CH_2Cl_2$, overnight, r.t.

The Products Ratio According to GC/MS

Camphene + thiol	The ratio of reactants	Products (ratio)
1+**2**	1:1	**4**+**5** (1:3)
	2:1	**5**
1+**3**	1:1	**4**+**5** (1:2)
	2:1	**5**

The structures of compounds obtained were established from ^1H and ^{13}C NMR spectra, elemental compositions were confirmed by mass spectra. For bis-adduct **5** X-ray data are available.

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CRYSTALLIZATION-INDUCED DIASTEREOMERIZATION OF CHIRAL β-HYDROXYSULFONE OF PINANE SERIES

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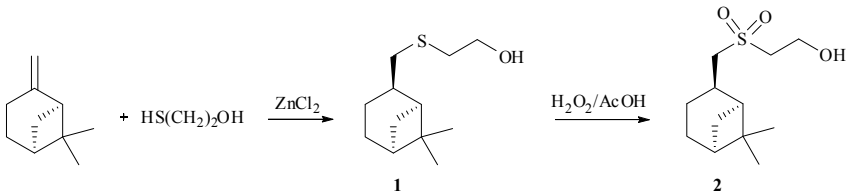
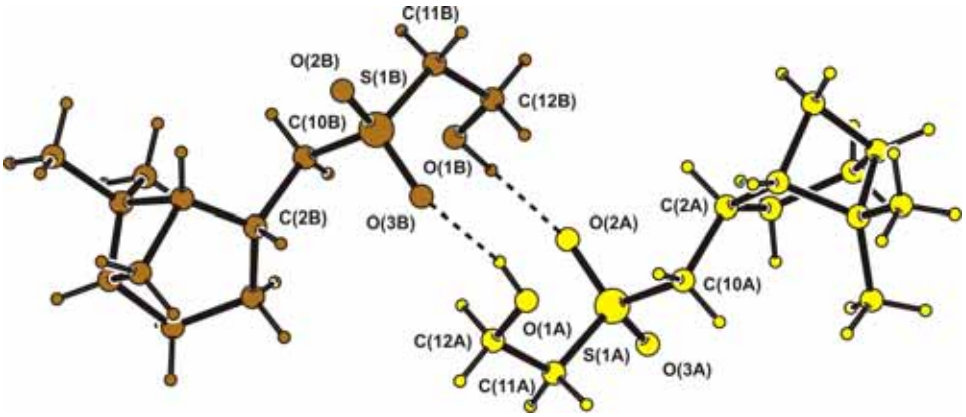
Pinanyl sulfone **2** has been prepared by oxidation of (−)-β-pinene-based sulfide **1** using hydrogen peroxide in combination with acetic acid.



1 **2**

According to XRD homochiral pinanyl sulfone **2** crystallizes as an asymmetric H-bonded dimer formed by stereochemically different oxygen atoms of sulfonyl groups of molecules A and B. Thus O^{2A} *pro-R* atom is invoked for construction of relevant H-bond in A molecule, but in the case of the molecule B only *pro-S* O^{3B} atom is involved. Newly formed chiral sulfur atoms take opposite chirality in molecules A and B, while the configuration of the pinene skeleton remains unchanged. Such stereochemical transformation is called "crystallization-induced diastereomerization".



The stability of the asymmetric dimer found in the crystal, evaluated within the framework of density functional theory (DFT, 6-31G(*d*,*p*)), as well as studied by IR spectroscopy in solution.

Acknowledgment. The study was financially supported by Russian Foundation for Basic Research (Grant No. 12-03-00898-a).

FATTY ACID COMPOSITION OF ROOTS KAZAKHSTAN *Haloxylon* SPECIES

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Fatty acid composition of following roots *Haloxylon* species Flora of Kazakhstan: *H. persicum* Bge. (white saxsaul), *H. aphyllum Iljin.* (black saxsaul) and *H. ammodendron* Bge. (zaisan saxsaul) explored [1].

The analysis of fatty acid was investigated on gas chromatograph "Chrom 42" (Czechia), adsorbent – celite 545 on hromasorb WAW. Carrier gas – helium, detector – flame ionization, the speed of carrier gas 30 mL/minutes, temperature of detector 188°C, temperature of oven 230°C. Methylation of lipids were investigated with methylate natrium in temperature 60–70°C [2, 3].

For given *Haloxylon* species was determined 8 fatty acids. From saturated fatty acids are myristic, palmitic, stearic, and from unsaturated fatty acids are myristoleic, palmitoleic, oleic, linoleic, linolenic. The most quantities of fatty acid consist of palmitic, oleic, linoleic acids. The most quantities of fatty acids in *H. aphyllum Iljin* (1.993%).

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ALKALOIDS OF *Nitraria sibirica* STRUCTURE OF SHOBERICINE

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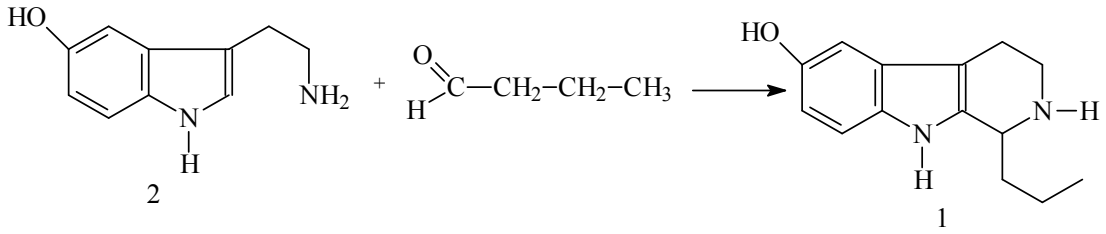
We continued study alkaloids of the aerial parts of plant *Nitraria shoberi* L. [1] collected in the vicinity of the Derbent village of Surkhandarya region of Uzbekistan during the flowering period. From the phenol-chloroform sum the bases were isolated by serotonin column chromatography as the hydrochloride [2] and the new base mp. 193–195°C called shobericine (**1**).

Shobericine $C_{14}H_{18}N_2O$, in its mass spectrum shows a molecular ion peak with M^+ 230, in the UV spectrum, the following absorption maximal: at 232, 278, 292 (lgε 4.35, 3.81, 3.80), typical for a non-conjugated indole chromophore [3]. In the IR spectrum of **1** were the following absorption bands: 745 (*o*-disubstituted benzene ring), 1452, 1468, 1580 and 1620 (indole nucleus), 2845 and 2930 (saturated C-H), 3057 (Ar-H), 3300–3400 (-NH and-OH). Mass **1**, showing the molecular ion peak M + 230, fragments characterized by fragmentary indicating release propyl group $(M - 15)^+$, $(M - 29)^+$ and $(M - 43)^+$.

PMR spectrum reveals two two-proton triplet at 2.65 and 3.08 ppm from neighboring methylene groups. There signals 0.97 (3H, t), 1.63 (2H, m), 1.75 (2H, m) and 3.52 (1H, m). Aromatic protons (3H) appear in the 7.0–7.75 ppm.



On the basis of physico-chemical data, we assumed that shobericine refers to alkaloids of tetrahydro-β-carboline range and is the most likely structure is **1**. The compound with the determined structure is synthesized by condensation of serotonin (**2**) with butyraldehyde by Pictet–Spengler′s method [4].

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TECHNOLOGY OF SUBSTANCE ISOLATION FROM *Hipophae rhamnoioles* PLANT SPECIES AND THEIR ANTIOXIDANT PROPERTIES

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It is known that fruits of the sea-buckthorn (*Hipophae rhamnoides*) possess antibacterial, granulating, pain killing, epithelizing properties, while leaves are a source of tannins, and displaying antiviral activity [1]. This species is widely represented in flora of Kazakhstan, but almost unstudied.

While developing the technological scheme of substances isolation from the leaves and stems of *Hipophae rhamnoides* as a parameter for optimization was its maximum extraction by adjusting the degree of fineness of raw material (1–3 mm), the extractant (ethanol, acetone and aqueous solutions of various concentrations), raw material to extractant ratio, ranging from 1:4 to 1:10, time (2–48 h), temperature (22–50°C) and a multiplicity (one to three times) of extractions. Crushed raw material (3 mm) was extracted twice with 50% ethanol or 50% acetone in a ratio of raw material to extractant of 1:8 and at a temperature of 23–25°C. The extract was filtered and concentrated until obtaining substance in the form of dry extracts.

To study their antioxidant activity hepatocyte membranes were obtained by method [2]. Accumulation of lipid peroxidation (LPO) products in liver microsomes was evaluated by reaction with 2-thiobarbituric acid and determined by the intensity of staining, using method, developed by Ohkawa H.O. [3]. LPO in membranes was induced with Fe^{2+} /ascorbate system, by incubating test samples at 37°C in medium, containing 0.85% NaCl, 50 mM KH_2PO_4, pH 7.4. Absorbance was measured at 532 nm.

Comparative study of the antioxidant properties of substances, isolated from leaves and stems, by their extraction with 50% aqueous ethanol, showed that substance exhibited significant antioxidant effect, reducing the dose-dependent formation of LPO products.

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CHEMICAL COMPOSITION OF THE VOLATILE COMPOUNDS OBTAINED FROM THE AERIAL PART OF *Limonium myrianthum*

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Limonium is a genus of 120 flower species in *Plumbagenaceae* family. Literature search showed that nothing had been done on the chemistry and pharmacology of the plant *Limonium myrianthum*, and encouraged us to carry out detailed phytochemical and biological studies on the aerial parts of this plant species. This is the first report on the composition of essential oils in *L. myrianthum.*

Chemical composition of essential oil, obtained by steam distillation from the flower, leaf and stem of *L. myrianthum*, was studied by GC/FID and GC/MS. The percentage of essential oil in the air-dried plant material was 0.015% (w/w). Aerial part, including flowers of the plant *L. myrianthum*, was collected during the flowering period in summer, 2010 from Almaty region. The plant material was initially air dried, then grounded to a particle size in the range 2.0–3.0 mm, according to regulatory documents.

The components of the oil were identified by comparing their retention time and mass fragmentation patterns with those of the available references and / or with published data as well as through GCMS library search. Essential oil from the aerial parts of the plant *L. myrianthum* was obtained by hydrodistillation. The oil was light yellow in color with unpleasant smell, indicating that the oil composition was different than that of regular volatile oils. For GCMS analysis essential oil was dissolved in methanol at a concentration of 10 mg/mL.

GCMS analysis of the oil resulted in the identification of 17 components. Four acids were identified in the oil (nonanoic, decanoic, palmetic and linoleic). They constitute 12.41% of the oil.

Four alcohols were identified in the oil (1-octen-3-ol, hexanol, cedran-8,13-diol, drimenol), which together constitute 10.84% of the oil. The major constituents in the oil are: hydrocarbon heneicosane (14.52%) and hexahydrofarnesyl acetone (17.28%).

PRODUCTION OF TABLETS BASED ON MEDICINAL HERBAL SUBSTANCES

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Isolation of substances from the roots and aerial parts of *L. gmelinii* medicinal plants was conducted using a simple, economically feasible and environmentally friendly method with a high yield (30–35% of the dried raw material weight). The aqueous solution of ethyl alcohol, which is generated during the process of production, was used as an excipient. Isolated substances are characterized by considerable amount of polyphenols, including hydrolyzable and condensed tannins, glycosides of oxidized forms of flavonoids, as well as sterols, amino acids and polyenoic acids acting synergistically with them [1].

Vegetable substances extracted from the test plants in the form of dry extracts are characterized by hygroscopicity; their complex with β-cyclodextrin was obtained in order to reduce this hygroscopicity. The molecular complexation of β-cyclodextrin with the substance was studied using 2 methods: a) method of paste-forming; b) method of briquetting (passing through a roller compactor under 20 tons of pressure). The method of paste-forming gives the yield of less than 50%, while the method of briquetting allows producing an inclusion complex with nearly quantitative yield. The process of nano-encapsulation was monitored by observation of changes in shape and size of the particles. The resulting complex of the Limonidin substance with cyclodextrin is a light-brown powder with the patches of darker particles with faint odor, moisture content of not more than 3%, soluble in water, 0.1 N HC1 solution and aqueous solutions of ethyl alcohol (30, 50%). Bulk density before shrinkage is 0.707 g/cm, after the shrinkage – 0.809 g/cm. The study of the complex was carried out using the methods of IR and UV spectroscopy and diffractometry. The biopharmaceutical properties of the complex were studied: release of the active substance in the amount of not less than 46.0%, in various environments, Quality specification was designed. On the basis of this complex of the substance and β-cyclodextrin, two sets of granulates were developed. The tablets produced on their basis meet the requirements of pharmacopoeia on the following indicators of quality: compressibility profiles, hardness, friability, friability, disintegration, quantification of the active substance and its release.

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OBTAINING OF MODIFIED GOSSYPOL RESIN AND ITS APPLICATIONS

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Gossypol resin is a viscous homogeneous mass of dark brown to black in color, which is a by-product of the vacuum distillation of fatty acids in the cottonseed oil processing. This product contains 52–64% of raw fatty acids and their derivatives, and the rest are products of polymerization and condensation of gossypol and its conversions in the oil recovery process. The presence of a significant amount of valuable organic components makes the above-mentioned by-product a promising raw material for commercial products obtaining.

By saponification of gossypol resin via treatment by NaOH solution at 100–110°C and separation of the residue from the unsaponifiable part we received the so-called «modified gossypol resin». This product consists mainly from the salts of high fatty acids, and it is readily soluble in water. The formed surfactant reduces the surface tension and facilitates the formation of dispersions, in particular, emulsions. This surfactant is well adsorbed on hydrophobic surfaces.

The obtained product was tested by us as a drilling fluid additives by way of alternative to expensive surfactants which conventionally used in oil production. The drilling fluid is complex multicomponent liquid dispersion system used for cleaning wells during drilling. The drilling fluid includes surfactant as one of the major component. The following model drilling fluid has been studied (%): bentonite clay (3–4); chalk (6–8); uniflok (0.1–0.2); carboxymethylcellulose (0.8–1.0); condensed sulfate-alcohol mixture (0.1–0.3); Na_2CO_3 (0.1) + tributyl phosphate (0.014); modified gossypol resin (2–14); water – the rest.

We have determined that the optimum concentration of modified gossypol resin in drilling fluid lies in the range of 8–10%. At such concentrations of modified gossypol resin the drilling fluid has the following properties: density (kg/m^3) 1800; viscosity (c) 60–62; static shear stress ($SSS_{1/10}$, Pa) 5-6/6-8; filtration (F, cm i/30 min) 4–5.

The modified gossypol resin as a component of the drilling fluid acts as a filtration reducer, viscosity controller, and lubricity additives.

SYNTHESIS, CHARACTERIZATION AND ANTIOXIDANT ACTIVITY OF NEW COUMARINS

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The antioxidant activity of new synthesized coumarin derivatives were studied with the DPPH method and compared with the known antioxidant ascorbic acid. Structures for the synthesized coumarins are proposed on the basis of spectroscopic evidence. Density Functional Theory calculations of the synthesized coumarins were performed using molecular structures with optimized geometries. Molecular orbital calculations have provided detail description of the orbitals, including spatial characteristics, nodal patterns, and the contributions of individual atoms.

CONSTITUENTS OF *Curcuma aromatica*

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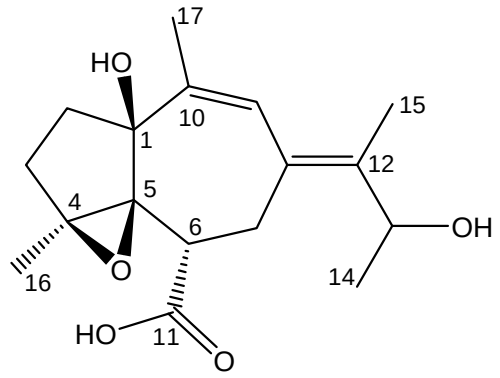
Curcuma aromatica Salisb. (*Zingiberaceae*) is also known as Jungle Haldi and found through out in India though cultivated in West Bengal and Travancore [1]. The plant is known for the use in oriental medicine and has hemagglutinating activity [2]. Aqueous extract of *C. aromatica* induces apoptosis and G2/M arrest in human colon carcinoma LS-174-T cells independent of p53 [3]. Polyxyloses extracted from the rhizomes *C. aromatica* have cell proliferative effect [4].

Naturally occurring C17 compound dihomosesquiterpene isolated (**1**) along with two known compounds curdione (**2**) and β-sitosterol (**3**) from ethanolic extract of *Curcuma aromatica* rhizomes. Compound **1** was isolated as an off white amorphous powder. The HR-MS and ^{13}C NMR data established the molecular formula as $C_{17}H_{24}O_5$ indicating six degrees of unsaturation. In HMBC, proton signal at δ_H 2.5 (H-2β) correlated with the carbon signal of C-1 (δ_C 75.5) suggesting the bicyclic structure of the compound **1**. The relative stereochemistry at C-1, C-4, C-5, and C-6 centers were assigned on the basis of specific rotation value, chemical shifts of protons and NOESY interactions as *S* at C-1, C-4, *R* at C-5 and *S* at C-6. On the basis detailed spectroscopic data the compound **1** identified as "Termioic acid A″ ((1*S*,4*S*,5*R*,6*S*,8*E*,10*Z*)-1,13-dihydroxy-4-epoxy-8(12),9(10)-diene-termi-11-oic acid) and was found new from nature.



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5β-*H*/5α-*H*-EPIMERIZATION AND 9α-HYDROXYLATION OF ECDYSTEROIDS UNDER ALKALINE CONDITIONS

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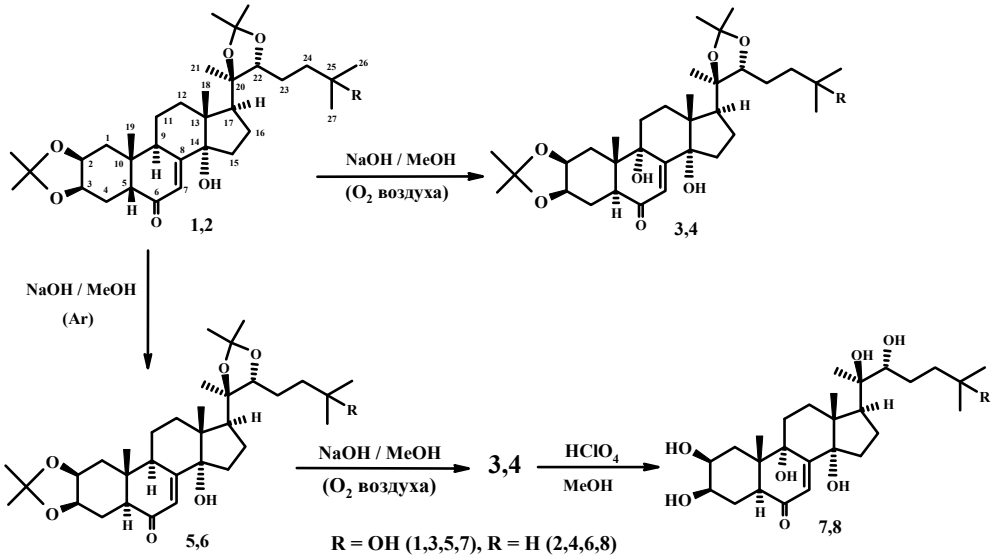
It is known that in an aqueous alcoholic medium under the action of sodium or potassium carbonate the 20-hydroxyecdysone is occurring of epimerization at the C (5)-chiral atom to form a mixture of the 5α-*H* and 5β-*H* epimers [1, 2].

We established that by exposing at the 10% solution of NaOH in methanol (room temperature, 24 h) 20-hydroxyecdysone (**1**) and ponasterone A (**2**) diacetonide entirely converted into the 9α,20-dihydroxy-5α-ecdysone (**3**) and 9α-hydroxyponasteron A (**4**) diacetonide (yield 68 and 70% accordingly), i.e. the 5β/5α-epimerization proceeds with the process of oxidation by air oxygen (autoxidation). In an inert atmosphere the epimerization is going with the formation of a mixture of the corresponding 5β- and 5α-epimers (**1**, **5**) and (**2**, **6**), that oxidized at the air and converted into the compound (**3**) and (**4**) accordingly.



The hydrolysis ($HClO_4$/NaOH) of the diacetonide (**3**) and (**4**) give to the corresponding 9α-hydroxy-5α-ecdysteroids (**7**) and (**8**). The structure of compounds (**3**, **4**, **7**, **8**) was confirmed by 1D and 2D methods of ^{1}H and ^{13}C NMR spectroscopy and the mass spectra MALDI TOF.

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CHOLINESTERASE INHIBITING POLY HYDROXYSTEROIDS FROM THE GENUS *Haloxylon*

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Chenopodiaceae is a medicinally important genus which comprises 100 genera and 1200 species. In Pakistan 35 genera of this family are present. Out of these 35 genera, *Haloxylon* is one of the important genera and in Pakistan 5 species of *Haloxylon* are present which are widely distributed from latitude to attitude. These species are *Haloxylon recurvum*, *Haloxylon griffithii*, *Haloxylon persicum*, *Haloxylon salicornicum*, and *Haloxylon stocksii.*

There is not enough knowledge in literature for the medicinal use of these plants. Local practitioners used these plants for the treatment of insect bites, internal ulcers and wound healings. In our research on these plants we have found that these plants are the rich source of poly-hydroxy steroids.

The chemotaxonomic importance of these plants prompted us to carry phytochemical investigations. We have isolated a variety of phytochemicals from these plants but found that these plants are the rich source of poly-hydroxy steroids. Later on we have evaluated these steroids randomly for their biological importance and found that these are the potent inhibitors against the cholinesterase enzymes.

ISOLATION, STRUCTURE ELUCIDATION AND BIOACTIVITY OF THE CONSTITUENTS FROM *Indigofera oblongifolia*

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Indigofera oblongifolia belongs to the family fabaceae or *Leguminoseae* which is commonly called as legume, pea family. *Fabaceae* covers 730 genera and 1900 species. *Indigofera* is one of the important genus and in Pakistan it is represented by 24 species. Local practitioner′s uses for the urinary tract infections cough and skin diseases. *I. oblongifolia* is a small shrub with pinnate leaves while the flowers are red, white and yellow coloured. Fruits are legume pods which are different size and shape. The chemotaxonomic and ethano-pharmacological importance of *I. oblongifolia* prompted us to investigate the bioactive constituents from it. From the ethylacetate soluble fraction of the whole plant of *I. oblongifolia* we have isolated several polyhydroxy coumarins, dimeric coumarins and polyhydroxy xanthones. The structure elucidation of these isolated compounds was done by the use of 1D (^{1}H and ^{13}C NMR) and 2D NMR (HMBC, HMQC, COSY, and NOESY) spectroscopic techniques. Later on the isolated compounds were evaluated randomly for their inhibitory potential against several enzymes such as cholienesterases, lipoxygenase, and tyrosinase. The isolated phenolic compounds also possess moderate to potent anti-oxidant activity.

STUDY OF THE TERPENOID COMPOSITION OF A PINE *Pinus sibirica*

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Common pine (*Pinus sylvestris* L.) is widely distributed in all forested regions of Siberia and comprises the principal mass of Siberian forests. Pine oils are widely used as fragrances in cosmetics, flavoring additives for food and beverages, scenting agents in a variety of household products, and intermediates in the synthesis of perfume chemicals. The wood greens coniferous contains a plenty of biologically active substances, including essential oil valuable in the medical attitude. Influence of climatic and ecological factors on a content of the essential oil and its composition is marked. In this context was of interest a method of chromato-mass-spectrometry to study composition of essential oil of a pine cedar Siberian [Pinus sibirica (Rupr.) Mair.], growing on territory of Khanty-Mansi autonomous region of Russia. Fresh needles crushed and was hydrodistilled using a Clevenger type apparatus. The oil was collected for 3 hours after the first drop of the distillate eluted from a cold finger. Oil yields are reported on a moisture-free basis.

A chemical composition of essential oil established by methods of a gas-liquid chromatography and chromato-mass-spectrometry. In composition of essential oil of a pine cedar Siberian it is revealed about 25 components. It was established, that the basic components of essential oil are *epi*-bicyclosesqvifellandren (23.67%), δ-cadinene (12.05), α-muurolene (7.48%), δ-cadinol (7.7%), α-cadinol (6.77%), α-limonene (4.90%), γ-cadinene (4.58%). The content of other components (β-myrcene, *cys*-β-ocimene, α-terpineol, β-terpineol, β-pinene, camphene, bornyl acetate, β-cadinene, α-copaene, aomadendrine, spathulenol, globulinol, α-borubonene, α-longipinene, undecanone-2) makes less than 1%. In *P. sylvestris* needle oils bicyclic sesquiterpene types cadinene and muurolene are dominating. From monocyclic monoterpens the greatest content (4.90%) is noted for α-limonene. And the qualitative and quantitative structure of components of radio oil differs from the structure described in the literature. Possibly, variability of composition of essential oil is influenced with the period of vegetation of a plant, region of growth, climatic, ecological factors, structure of ground, light exposure and other natural factors. This circumstance should be considered at preparation of raw material for reception of radio oils and at standardization of a ready product.

We studied also EtOH extract of needles with objective of reception of biologically active connections. The combined extract was evaporated in vacuo, diluted with H_2O, and extracted successively with hexane, $CHCl_3$, EtOAc, and *n*-BuOH. Chromatography of the hexane fraction over a column of silica gel have received two substances which are identified with lambertinic acid and its methyl ether.

RECEIVING CHITOSAN STABILIZATION NANOPARTICLES OF COBALT AND COPPER

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Keen interest in the basic and applied researches connected with synthesis of nanoparticles (NP) of biogenic metals, by studying of their properties and practical application in various branches is in the last decade observed.

Now of chemical and physical methods of obtaining NP is known. Recently special interest represents receiving nanostructural systems polymer: metal on a basis chitosan and its derivatives as, comparative experiences show that nanodimensional systems of this class of polysaccharides are characterized by the expressed biological activity. Nanostructures can be received by chemical synthesis or modifications of polymeric samples by ions of metals.

Certainly, modification is one of simple and perspective methods who is based on introduction or formation of nanoparticles of metals in structure of the polymer which is carrying out function of a matrix. Thus, receive biologically active nanostructural polymeric materials possessing unique properties.

Chitosan possesses unique properties, such as bacterial action, not toxicity, a decompose microorganisms and biological compatibility. These properties are connected with presence amino-and hydroxyl groups in links chitosan. Other important feature consists that electron donor functional groups ($-NH_2$, -OH, $-NHCOCH_3$) chitosan are capable to form chelates. It provides possibility of use chitosan as stabilizer of nanoparticles.

Earlier we synthesized nanosystems polymer: metal on a basis chitosan *Bombyx mori* (CS) with ions of d-elements of a transitional row. Data on receiving and structural research NP of cobalt and the nanostructured systems are provided in this work chitosan with cobalt and copper ions. Nanostructured systems CS:Me are received by formation of metal NP in volume of a polymeric matrix. Ratio CS:Me^{2+} in reactionary system has considerable impact on the size and distribution of metal NP in a polymeric matrix. The increase in ratio CS:Me leads to natural decrease in the NP average size of metal and narrowing of distribution of NP by the sizes.

For an assessment of the size and distribution of NP of metal used microscopic methods.

Researches of structural morphology of the received nanostructured systems chitosan testify that for synthesized samples CS:Co=1:2 nanoparticles (NP) of a spherical form of 5–36 nanometers are characteristic. The histogram of distribution shows that the greatest percent of metal nanoparticles lies in the range from 15 nanometers to 28 nanometers. Probably, it is connected with conditions of receiving nanoparticles. It should be noted that polymer stabilization metal nanoparticles are thus formed.

At synthesis of CS:Cu systems as nanoparticles in the range of sizes of 5–25 nanometers are formed. The histogram of distribution of nanoparticles in a polymeric matrix shows that the greatest part of particles have dimensions in the range of 10–25 nanometers.

Thus, the obtained data confirm stabilizing role of macromolecules chitosan. The increase in its concentration in reactionary system leads to formation of rather small particles with narrow distribution. UV-spectroscopic researches of initial reagents and the received samples which testify are also conducted that in the chosen conditions of synthesis are formed microencapsulated by a molecule CS metal nanoparticles.

Thus, polymer stabilization NP of cobalt and copper by restoration with alcohol at presence chitosan *Bombyx mori* are received. The conducted structural researches show that in system the molecule chitosan plays a stabilizer role that is prevents agglomeration and oxidation of metal particles. It is established that CS is the nanoreactor that is its concentration influences the size and NP distribution in a polymeric matrix.

ADVANCED PURIFICATION METHOD OF TECHNICAL CARBOXYMETHYL CELLULOSE

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Polymers, such as cellulose derivatives, biopolymers and guar gum were introduced in the water based drilling fluids for their rheological performance and for ecological considerations. In comparison with other natural polymers, the cellulose derivative is the most used due to their biodegradable and compatible with other materials. Carboxymethylcellulose (CMC) is produced by reacting cellulose obtained from wood pulp or cotton fibers with chloroacetic acid and NaOH. The presence of polar carboxyl groups makes the cellulose soluble, chemically reactive and strongly hydrophilic. CMC is a white to almost white powder, non-toxic and biodegradable, odorless and does not ferment under normal conditions of use. It is also a low-cost commercial soluble and it can be dissolved in hot or cold water. It is largely used in industry, due to its exceptional rheological properties in aqueous solutions. The purified carboxymethyl cellulose, soluble in water, is widely applied in several industrial fields, such as textile, drug, pharmacology, food and cosmetics etc. [1].

It is known that the technical CMC consists of organic and inorganic salts mixtures. In order to use the purified CMC in the above mentioned fields, samples must be purified from mixtures [2]. The purification process is mainly performed by the washing with alcohol [3]. In this paper the specific, effective and express purification method of technical Na-CMC was shown.

Purified CMC is received by treating of technical carboxymethylcellulose with inorganic acid aiming to convert the sodium carboxymethyl (Na-CMC) groups to the insoluble acid form (H-CMC).

The obtained insoluble H-CMC is washed from organic and inorganic salts by distilled water. In the next step, the taken pure H-CMC is converted to soluble Na-CMC form by treatment with alkaline solution in alcohol. As a result high purified and water soluble Na-CMC has been obtained. In order to estimate the quality of obtained purified Na-CMC samples we have studied its properties by analytical and physical-chemical methods.

This method includes great deal of advantageous, for instance the experiments are quite easy and the purification period is for 2–2.5 time shorter in compare to other methods. In addition, lack of energy, low cost of unit cost and so on. Moreover, the degree of purification was gotten in maximum (value).

Obtained high purified CMC samples can be use in pharmaceutical, medical, food and other industries.

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BIODEGRADABLE BACTERICIDAL HYDROGELS BASED ON SODIUM CARBOXYMETHYLCELLULOSE CONTAINING SILVER NANOPARTICLES

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Nowadays, to form the silver clusters and nanoparticles in the polymer matrix is one of the most prestigious research fields. In fact, metal nanoparticles of silver have been the focus of specific interest due to its unique properties such as physic-chemical and biological properties.

In this work the forming of silver clusters and nanoparticles in the sodium carboxymethylcellulose (Na-CMC) hydrogels and their bactericidal properties were studied.

Experiment results showed that by increasing amount of Ag^+ ions from 0.1 mol% till 0.4 mol% in the CMC solution degree polymerization (DP-600) and degree substitution (DS-0.85), the relative viscosity of CMC raised from 2.128 until 4.576. Hydrogel form were observed in the solution when the amount of Ag^+ ions increased up to 0.5 mol%. This can be explained by the forming of CMC^-Ag^+ complex when CMC`s carboxyl groups bonded with Ag^+ ions and Ag^+ holds the CMC macromolecules.

The silver nanoparticles were formed in complex CMC^-Ag^+ by photo-chemical reduction.

The experimental results have shown that CMC carboxyl groups play as a main role as a nanoreactor for the formation of silver nanoparticles and also participate as reducing and stabilizing agent.

With changing the ratio of CMC and $AgNO_3$ and reaction condition the forming possibility of 2–30 nm spherical and 40–80 nm length, 5–10 nm thickness needle-like stable silver nanoparticles in hydrogel CMC was studied.

The bactericidal activity of hydrogel samples, contained silver nanoparticles tested on *Staphylococcus epidermidis* and *Candida albicans*.

High bactericidal activity of CMC hydrogels, containing 2–30 nm spherical silver nanoparticles against *Staphylococcus epidermidis* and *Candida albicans* was found.

Actually, the high bactericidal activity of this sample can be explained by small size of silver nanoparticle, high surface and can entering easily of in nucleus of microbe.

Antibactericidal affectivity of CMC hydrogel containing 40–80 nm length, 5–10 nm thickness needle-like, compared to CMC hidrogel containing silver ions can be expounded with bonding Ag^+ ions with functional groups on the surface strain will decrease activity of silver ions.

Obtained hydrogel containing silver nanoparticle can be utilized in medicine as a bactericidal drug to cure the burns.

ESTABLISHMENT OF THE MERENDERIN OXYMETHYLATE STRUCTURE

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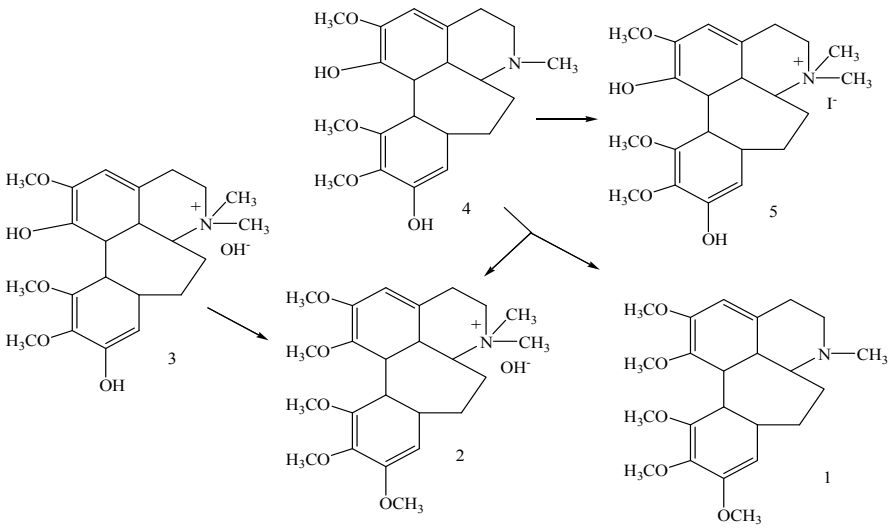
Merenderin oxymethylate (**3**) of $C_{22}H_{28}O_5N^+OH$ has in the UV absorption spectrum the maxima at 260 and 294 nm. The IR spectrum of its absorption band presented by benzene ring and hydroxyl groups (1460, 1600, 3460–3600 cm^{-1}). Its PMR spectrum two signals of aromatic protons – H-3 and H-9 (1H × 2, ss, 6.70 and 6.65 ppm), a hydroxyl group (6.16 ppm) metoxyl three groups (6H, s, 3.88 and 3H, s, 3.67 ppm) and two *N*-methyl groups (3H × 2, ss, 3.30 and 3.43 ppm) are shown.

The spectral data of the substance has been attributed to the group of homoaporphine bases. Substitution of two amino methyl groups, which signals are shifted downfield, allowed conclude that the nitrogen atom in quaternary it has in nature. Comparison of the chromatographic mobility and PMR spectra of the base and merenderin iodmethylate revealed the identity of the data for both compounds. However, the first of them showed a negative reaction to the content of halogen. Therefore, by the reaction of diazomethane as a compound and merenderin their dimethyl esters received, which were identical. Thus, isolated from the plant the structure corresponds to the base merenderin oxymethylate. Merenderin iodmetilate (**5**) prepared by heating for 2 h of 3 mL methanol solution of 0.10 g merenderin with excess of methyl iodide. R_f 0.65 (merenderin with R_f 0.75 in the system I).

Merenderin Oxymethylate. Merenderin iodmethylate 0.07 g in 3 mL of methanol was treated with freshly precipitated silver oxide obtained from 0.10 g of silver nitrate and 0.040 g of potassium hydroxide.

Merenderin methylation with diazomethane in methanol solution is implemented by adding a hexane solution of diazomethane. Isolation of *O*-methylkreusigine oxymethylate (**4**) and implemented the method described above, as in the case of merobustin. Methylation of merenderin oxymethylate in *O*-methylkreusigine oxymethylate carried out in methanol, diazomethane solution in *n*-hexane, on the above-described manner. The compound that is identical in meaning with R_f to *O*-methylkreusigine oxymethylate obtained by the action of diazomethane to merenderin have identified.



The work was supported by the fundamental Grant F7-OT-1-95320 of KKRNT CM RUz.

ESSENTIAL OIL COMPOSITION OF *Tanacetum uniflorum* (*Asteraceae*) FROM NORTHWEST OF IRAN

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Tanacetum L. belongs to the family *Asteraceae* and tribe *Anthemideae*. Within the tribe, *Tanacetum* is the third largest genus after *Artemisia* and *Anthemis*, comprising around 160 species worldwide. In Flora Iranica area, this genus was considered to have 54 species and in Iran, comprised 25 species and altogether 34 taxa. In this research, the essential oil composition of *Tanacetum uniflorum* collected from West Azerbaijan Province of Iran was investigated for the first time. The essential oil was isolated by hydrodistillation from the aerial flowering parts and analyzed by GC and GC-MS. Twenty-eight compounds were characterized accounting for 99.2% of the total oil. Oxygenated monoterpenes (68.5%) were found to be the principal compounds group, of which 1,8-cineole (48.0%) and camphor (15.0%) identified as the main constituents. Oxygenated sesquiterpenoids comprised 17.3% of the total oil with spathulenol (8.4%) as the major component.

CHEMICAL VARIABILITY IN THE ESSENTIAL OIL COMPOSITION OF *Tanacetum kotschyi* FROM IRAN

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The essential oils compositions are highly affected by the geographical location of plant species. The present work is aimed to provide more information on the variation of essential oil composition in *T. kotschyi* Boiss. populations growing wild in Iran. Hydro-distillated essential oils of *T. kotschyi* from three different provinces of Iran (Zanjan, Isfahan and West Azerbaijan) were analyzed by GC and GC-MS for determining intraspecific chemical variability. A total of 49 compounds accounting for 94.5 to 98.9% of the total oil, were identified and a relatively high variation in their contents was observed. The main constituents of the essential oils at species level were camphor (15.5–25.8%), 1,8-cineole (1.8–16.3%), caryophyllene oxide (5.4–7.9%), α-pinene (3.1–6.2%), and spathulenol (0.4–8.4%). Based on major compounds, the populations were represented by (camphor/lavandulyl isovalerate/spathulenol/1,8-cineole), (camphor/santolina triene/δ-cadinen/caryophyllene oxide), and (camphor/1,8-cineole/caryophyllene oxide/camphene) chemotypes.

THE INFLUENCE FRACTIONS OF POLICSHAHARIDES, CHOSEN FROM EXTRACTBIDENS TRIPARITAE, ON TISSUE OF THYMUS TO EXPERIMENT

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Use biologically active material in their natural combination provides the broad spectrum of the pharmacological influence and excludes xenobiotic load on organism at treatment of pathology. Fit drugs, containing complex biologically active material, act on different systems of the organism. Amongst biologically active material important place occupy polysaccharides, stimulating e of immune system of the organism, intensify the process of fagosytisis, enlarge the amount antibody-producing cellular and product them antibody, raise the amount an lymphocytes of blood , lymphoid organs.

To date is not studied action to fractions of polysaccharides, chosen from extract Bidens tripartite, on tissue of thymus.

The Purpose of the study: Experimental study of the influence upon tissue of thymus fкactions of polysaccharides, chosen from extract of Bidens tripartite.

The material and methods of the study: Experiences were conducted on 12 non-breed mouse 2–3 month age both flap by mass of the body 18–22 g, which were divided into 2 equal groups on 6 in each. I checking group animal entered distilled water on 0.5 mL, II group – a faction polysaccharides, chosen from extract of Bidens tripartite in dose 7.2 mg/kg. The Preparation to fractions of polysaccharides dissolved distilled water and itragastrical entered on 0.5 mL 1 once at day during 4 h days, as from day of the immunizations and up to kill. For study influence to fractions of polysaccharides on tissue of thymus, beside mouse extracted thymus, homogenized and prepared the bleedings of the hutches in 3% solution of the acetic acid, counted in Goryaev camera and defined the general contents of the hutches in weight. Fraction of polysaccharides, chosen from Bidens tripartite was chosen in Institute of the Chemistries plants material AS RUz method dispersation drying.

The results of the studies have shown that beside animal of the checking group amount tissue of thymus has formed 29.1 ± 0.68 mln. Beside animal II groups, which was entered fraction of polysaccharides of Bidens tripartite, tissue of thymus has formed 41.9 ± 2.08 mln. ($P < 0.001$).

As it is seen that fractions of polysaccharides, has chosen from extract Bidens tripartite realistically stimulated tissue of thymus immunized animal in comparison with control group.

Thereby, fraction of polysaccharides, chosen from herb, possesses stimulation action on tissue of thymus.

INSERTION OF BIOLOGICALLY ACTIVE SUBSTANCES IN FOOD SYSTEMS USING NANOBASED NATURAL PHOSPHOLIPIDS

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In accordance with the Government of the Russian Federation, the Strategy of development of food processing industry in Russia up to 2020, in which the task was rised "to introduce new technologies in the industry and food processing industry, including bio – and nano technology...", urgent task today not only in Russia, but all over the world, is a development of technology of fortification of foods with nutraceuticals and biologically active substances. These technologies should allow to expand the production of next-generation products with desired characteristics, health – care, specialized and other products.

To preserve the biologically active properties of nutraceuticals while the storage or processing of the product, as well as increasing the bioavailability of biologically active substances, inserted into the food system, reliable food transportation system is required.

One of the main requirements for such delivery systems is that they can only be created from components permitted for use in food industry. Among natural compounds which meet this requirement, as well as capable of forming a closed system are phospholipids [1].

Phospholipids have shown important biological functions and health benefits, and are currently used at several food products. These compounds play an important role in biological functions such as maintaining cell membranes integrity, prevention of neurological diseases and regulation of basic biological processes such as cell to cell signaling [2].

Besides, phospholipids display amphipathic character, as components of bilayers or micelles and liposomes and have been applied in food, cosmetic and pharmaceutical products [3].

This is because, the next step in the study of phospholipids is a development of delivery system for biologically active substances in the food industry, based on phospholipids. Phospholipids have long been used in the industry as emulsifiers, and are an essential component of fat and oil, dairy, meat, bakery, confectionery and other products. However, the number of dietary supplements, in which the biologically active substance is enclosed in microcapsules, based on PL, is small among domestic food additives. Therefore the development of technologies for efficient and controlled food enrichment with biologically active substances, using the PL, is a promising direction in the food industry.

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STUDY OF INTERACTION HYDROCOLLOIDS WITH FAT- AND WATER-SOLUBLE VITAMINS IN ENRICHED FOOD PRODUCTS

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Investigation and assessment of the degree of interaction between the components of food systems is an urgent problem, the solution of which depends on the quality and safety of fortified foods. Quite often, in the formulation of complex food products have to face the unintended consequences of interaction of ingredients. Given that in recent years has increased the volume of applications in the food industry as to achieve technical efficiency, so to make the functional orientation of hydrocolloids as pectin, inulin, and chitosan, etc., creating food is of better understanding of approaches and solutions to vitamin-enriched foods based on their properties, structure and interactions in the food system.

Investigation of the interaction of hydrocolloids with fat- and water-soluble vitamins in fortified food products was carried out in several stages:

• Identification of interaction of the main and most commonly used in the food hydrocolloids with vitamins in model systems to the construction activity series of hydrocolloids;

• laboratory production of industrial prototypes fortified foods containing in its composition hydrocolloids (concentrates sweet dishes – jelly, jelly, marmalade products; fat emulsion), with a preliminary justification of the prescription and the study of physical and chemical parameters of the raw materials used to produce them;

• determination of the stability of hydrocolloids and water soluble vitamins in the models enriched product to hydrolysis in the gastro-intestinal tract of humans and evaluating safety – soluble vitamins complex with hydrocolloids;

• determination of the oxidation stability of enriched fat emulsion product.

The results show that when determining the vitamin content in model systems, while significant amounts containing hydrocolloids sorption vitamins may occur, which in turn contributes to an underestimation obtained analytical data. The differences in sorption capacity due to several factors: the difference in the linear dimensions of macromolecules, some features of the spatial structure, the presence on the surface of macromolecules of different functional groups. Therefore, when designing fortified foods should be considered quantitative and qualitative interaction of the components of the product.

STUDY OF INTERACTION MCC, PECTIN, INULIN, AGAR, XANTHAN GUM, CHITOSAN, GELATIN WITH TOCOPHEROL

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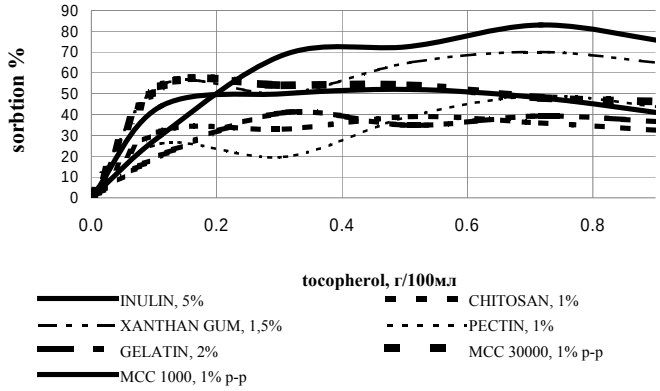
The ability of pectins to form strong gels depends on molecular weight and degree of esterification, significantly affects the properties of pectin. The highest degree of esterification, which can be achieved by extracting the natural material is 75%. We used pectin with the degree of esterification at least 70%. Sorption capacity 1% pectin solution 30% in low concentrations of tocopherol and with increasing concentration reached 45%.



With increasing content of tocopherol emulsion sorption vitamins MCC 1000/30000 increased and reached a maximum 50% at low concentrations of 0.15 g/100 mL tocopherol, which is probably due to the high porosity of the MCC and excellent properties of absorption and retention of water, oil and other substances and the presence of carboxymethyl groups that is able to bind tocopherol.

Sorption 5% solution of inulin the greatest, compared with all the previously prepared solutions hydrocolloids at high concentrations of tocopherol 0.6 g/100 mL to 0.8 g/100 mL, and is 70%.

The sorption capacity of 0.5% solution of xanthan gum in emulsion compared with the other peaks hydrocolloids 55% at low concentrations of tocopherol 0.1–0.2 g/100 mL forming a peak saturation followed by sorption not decline below 45% at medium and high concentrations.

In the model experiment, identifying interactions tocopherol with a 2% solution of gelatin in a fat emulsion, the sorption capacity increases at low concentrations of tocopherol, and reaches a limit equal to 40% of sorption at a concentration of 0.3 g/100 mL introduced tocopherol.

Sorption capacity of 1% solution of chitosan yield of 0.5% xanthan gum solution, the maximum sorption of 32% can be observed in the whole gradation tocopherol concentration of 0.1 to 0.9 /100 mL. In contrast to the plant fiber and other natural absorber, chitosan comprises an amino group which is much more efficient attracts fat cells and lipids.

THE ADSORPTION CAPACITY OF THE STRUCTURAL COMPONENTS OF VEGETABLES

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Sorption isotherms of water vapor cell walls isolated from tissue fresh vegetables with moisture forms of communication analysis shows that the primary form of communication in the cell walls of moisture are adsorbed monomolecular (8%) and capillary adsorption (16%). As the cell walls are the capillary – porous systems, the small amount of moisture retained by the capillaries, can be explained by their limited scope.

Sorption isotherms of water vapor components of the cell walls of sugar beet and pumpkin shows that the qualitative differences in sorption activity of hemicellulose beets and pumpkin is not available. When the water activity aw = 0.75 monolayer adsorption of moisture beet pulp and pumpkin is 5.6%, 5.8% hemicellulose, pectin 6.5% beet, pumpkin 4.8%. Moisture multilayer adsorption beet pulp 1.3%, 2.6%, pumpkin, beets hemicellulose 4%, 6% pumpkin, beet pectin 2%, 1.2% pumpkin. Moisture capillary – osmotic communication beet pulp 12.2%, 13% pumpkin, beets hemicellulose 22.6%, 28.0% pumpkin, beet pectin 13.7%, 15% pumpkin.

TABLE 1. **The Content and the Adsorption Capacity of the Structural Components of Beet and Pumpkin**

Name	Beet		Pumpkin	
	Content, %	Adsorption capacity, %	Content, %	Adsorption capacity, %
a_w = 0,40				
Solids	16.94	8.66	12.23	7.5
Cell wall	3.84	8.86	2.31	7.8
Pectin	1.0	8.5	1.32	6.0
Hemicellulose	1.09	9.8	0.46	11.0
Cellulose	0.38	6.9	0.68	9.0

Data on the adsorption capacity of the structural components of sugar beet and pumpkin at different relative humidity confirm that most of the moisture in vegetables is associated capillary – osmotic forces.

Individual tissue components vegetables proportion of their contribution to the water-holding capacity may be arranged in the following order: pectin > hemicellulose > cellulose

THE PROBLEMS OF CHEMISTRY OF NATURAL COMPOUNDS, BIOORGANIC AND BIOMOLECULAR CHEMISTRY, AND MEDICINAL CHEMISTRY IN RUSSIAN CHEMICAL BULLETIN

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Russian Chemical Bulletin is International Edition of a prominent Russian Journal *Izvestiya Akademii Nauk. Seriya Khimicheskaya*. It was founded in 1936 and has been published in English since 1952. The year 2013 marks the 77th anniversary of the Journal. During these years, the Journal has become one of the leading Russian periodicals in chemistry. Russian-language version is published by the Russian Academy of Sciences, while the English-language version is published by Springer. The Editorial Board of the journal includes prominent chemical scientists, in particular, thirteen full members and ten corresponding members of the RAS. The foundation in 1995 of the International Advisory Board with participation of renowned chemical scientists from various countries including three Nobel Prize winners in chemistry also contributed to the high scientific level and international prestige of the journal.

Since 1993, the journal has published papers presenting the results of original studies as full papers, brief communications, and letters to the Editor, but also analytical reviews, in particular, authors′ reviews and predictive analytical papers on topical issues of the chemical science. During this period, the volume of the journal increased more than 1.5-fold, which considerably shortened the publication time and made it possible to extend the journal coverage, first of all, by including papers in Chemistry of Natural Compounds, Bioorganic and Biomolecular Chemistry, Medicinal Chemistry, Supramolecular Chemistry, Polymer Chemistry, Nanochemistry, Materials Chemistry, and interdisciplinary articles. Besides ordinary issues, containing materials on different areas of chemical science, specialised issues are regularly published (for example, see issues 7, 2002, 1, 12 2010 and 4 2011, containing materials on Bioorganic and Biomolecular Chemistry, and Medicinal Chemistry). In 2012, more than 350 papers from 100 scientific centres of the Russian Federation and 30 scientific centres from the former USSR and other foreign countries were published.

In recent years, the Journal has become widely known in Russia and abroad. The journal is abstracted and indexed in the following base dates: RZhKhimiya, Chemical Abstracts, Chemical Titles, Current Contents/Physical, Chemical and Earth Sciences, Reaction Citation Index, Science Citation Index, Science Citation Index Expanded, The ISI Alerting Services, Chemistry Citation Index, and Energy Research Abstracts. Information about the Journal and the publications is available at the websites of the Journal (www.russchembull.ru) and Springer (www.springerlink.com). The electronic versions of the journal are available online for subscribers. Since 2005, all papers published in English starting with the first journal issue, which appeared in 1952, are available in the electronic library of Springer. In terms of the number of downloads of the full texts of online articles, *Russian Chemical Bulletin* has the highest score among Russian journals, markedly exceeding the average level (more than 1000 downloads per day on average, Information about the journal is available at www.springer.com/11172), which attests to the high need for the Journal. In addition, subscription for the online version markedly increased. Several hundreds of both individual institutions and large consortia combining many institutions have subscribed for the Journal, which made the access to the Journal global.

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CONTENTS

ALLAPININE

Composition Allapinine is the antiarrhythmic preparation that presents itself alkaloid lappaconitine hydrobromide derived from plants *Aconitum leucostomum* and *Aconitum septentrionale*.

Propers: As antiarrhythmic drug allapinine acts by depression of fast inner current of Na^+ ions. Antiarrythmic activity of preparation is revealed on auricular and ventricular disrythmias of different mechanisms. Allapinine in therapeutic doses prolongs P-Q and enlarges QRS intervals, but doesn't influence on interval QT. Preparation depress the conductivity of impulses across auricular and ventricular myocardium, atrioventricular node and His-Pourkine system. Allapinine belongs to ID group of antiarrhythmic drugs. Preparation moderately accelerates impulse production of sinus node. In patients with syndrome of sinonodal weakness allapinine practically don't depressed function of sinus node. Allapinine doesn't influence on contractility of myocardium, and reveals a weak vasodilating effect.

Indications to use: Allapinine indicated in cases of supraventricular and ventricular extrasystolias; paroxismal flutter of auricles, paroxismal supraventricular tachicardia; Wolf-Parkinson-White syndrome, paroxismal ventricular tachicardia, different forms of arrythmias, that concomitant a myocardial infarction. By method of double blind control it was shown, that therapeutic effect discovered for 70-80% of patients and effectivness of allapinine is more notable than the one of quinidine, disopiramide and aethmosine. Allapinine was high effective in cases of dangerous ventricular tachiarrythmias and reveals low degree of arythmogenity. Preparation is high effective for prolonged prophylaxis of supraventricular tachicardias.

Preferences Allapinine has benefits compared with other antiarrhythmic drugs, so as reveals high intensity, duration of action and width of therapeutic effect. Prolonged using is not concomitant by tachiphylaxia, arrythmogenity and other cardiotoxic effects; don't revealed toxic effect on internal organs, hematopoietic system, sensory organs. Allapinine is more effective than quinidine, disopiramide, cordarone and ethazysine.

Dosage and application Allapinine may be used by intravenous, intramuscular and per os administrations. It is indicated in dose 1 tablet 3-6 times per a day, i.e. 75-100 mg per a day. Intravenous administration is 30 mg (average dose) dissolved in 10 ml of saline. Slow administration in 3-5 min period is indicated. Taking of drug on empty stomach is undesirable.

Commercial product Tablets (0.025 mg) or 0.5-2.0 % solution in ampoules.

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances

***Manufacturer of dosage form*:** OJSC «Uzchemfarm» (RUz), CJSC «Pharmcenter VILAR» (Russia)

GALANTAMINI HYDROBROMIDUM

Composition: Galantamine hydrobromide is bromhydrate salt of the alkaloid galantamine derived from the snowdrop plant (*Galantus Voronovi, Galantus Nivalis*) and *Ungernia Victoris*.

Pharmacological activity Galantamine hydrobromide is strong inhibitor of cholinestherases. Drug potentiates the cholinomimetic effects of acethylcholine on cholinoreceptors, facilitates neuromuscular conductance, that blocked by antidepolarising myorelaxants; increases the tone of smooth musculature and secretion of digestive glands. Preparation easy penetrates across hematoencephalic barrier and facilitates conductance of impulses in cholinergic synapses of CNS.

Indications Galantamine hydrobromide indicated for motor and sensitive disturbances, binded with neuritis, polineuritis, radiculitis; for residual manifestation, called by disturbances of brain circulation; for psychogenic impotency and pathology of nervous conductance. At the recovery period after acute poliomyelitis and in cases of children's cerebral palsy galantamine restores the motor activity.

Doses *and aplication* Galantamine is indicated for subcutaneous injections in aqueous solution. A single dose for adults is from 0.0025 to 0.01 g, i.e. 0.25%, 0.5 and 1% and 1.0 ml. For children galantamine is used dependently from age, effectiveness and tolerance.

Side effects Salivation, bradicardia, dizziness, diarrhea and painful spasms of intestine, witches of skeletal musculature.

Contraindications Galantamine hydrobromide contraindicated in cases of epilepsia, hyperkinesia, bronchial astma, bradicardia, ulcers of stomach and duodenum.

Commercial product Preparation is produced in ampoules of 1.0 ml of 0.25; 0.5 and 1.0% solutions. List A.

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances

***Manufacturer of dosage form*:** Company “Radiks”

OLYGVON

Composition: Natural compound, derived from the *Artemisia leucodes*

Action: the original preparation possessing by the combining angioprotective and hypolypidemic action. In antiatherosclerotic activity it prevails over anginine (Japan), prodectine (Hungary), misclerone (Hungary), lypontine (Hungary).

Recommendations: recommended for treatment of different atherosclerotic plaque localizations as well as for their prophylaxis.

***Dosage*:** Per os. The course of treatment is for 3 months. The therapeutic dose is 0.03 g. The preparation is packed in tablets (0.03 gs).

***Side effects*:** no side or any other effects during oligvon application have been observed.

Contradictions: - No contradictions

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances

ECDISTEN

Composition: Natural compound derived from the *Leuzea*.

Pharmacological activity: Ecdisten is the drug of tonic action.

***Indications*:** Drug used for patients with astenic and astenodepressive status connected with the insufficiency of protein production processes in the organism; for patients with latent intoxications, somatic and infectious diseases, neurastenia, neurosis, hypotonia, tiredness. Ecdisten indicated also as tonic agent for persons having extreme mental and physical loading.

Doses and application: Drug is indicated before meal in doses of 0.005-0.01 g (1-2 tablets) 3 times per a day. Daily dose is 0.015-0.03. Course of treatment is 15-20 days. On necessity the course of treatment may be repeated after 1-2 week interval.

***Advantages*:** Ecdisten by its activity surpass the known preparations "Saparal" and "Extract of Eleuterococci".

Side effects: Patients with labile nervous system may show insomnia and hypertensia. In this case the dose should be decreased or evening dose removed.

Contraindications: Using of ecdisten is contraindicated in cases of nervous excitation, insomnia, hypertension, epilepsy and hyperkinesia.

Packing: Tablets contains 0.005 g of drug substance.

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances

***Manufacturer of dosage form*:** Company “Radiks”

ALBENDAZOL

Composition Albendazol (2-methoxycarbonylamino-5-propylthio-1H-benzimidazol) in medical practice is used in the tablets of white color or tinged with creamy or pinkish.

Properties Helminthicide of wide spectrum action. It is effective against intestinal nematodosis (ascariasis, trichocephaliasis, ankylostomiasis and enterobiasis).

Indications Albendazol differs by simple prescription, good endurance and high antiparasitic action against intestinal nematodoses (ascariasis, trichocephaliasis, ankylostomiasis and enterobiasis).

Dosage and application Albendazol is prescribed per os for adults and children immediately after meals in dose 20 mg/kg of body mass per a day. Daily dose is divided on 1-3 portions in dependence of disease nature and form.

Advantages The advantages in comparison with the preparations of similar action are in its prescription against trichocephaliasis, ankylostomiasis for one attendance only and more high antiparasitic action. The preparation possesses of high effectivity against polyinfection. Albendazol doesn't surpass to such drugs as decaris, vermox and pivantel in effectiveness.

Contraindications Application of albendazol is contraindicated at the pregnancy.

Side effects Albendazol is well endured by patients. Side reactions as a rule are weak expressed and don't require of special treatment. Sometimes the nausea and slight weakness are observed. Retrograde migration of ascarides is possible at intensive infestation.

Pharmaceutical precautionary measures List B. Keep at dry and cool place.

Package Tablets of 0.25 g. Storage period is 3 years.

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances

***Manufacturer of dosage form*:** Company "Nobel Pharmsanoat"

TEFESTROL

***Composition*:** Tefestrol is the mixture of two sesquiterpene esters ferutinin and tenuferidin derived from *Ferula*.

Properties: Tefestrol displays the estrogen like action; its activity is like to synthetic estrogens. Administration of tefestrol calls enhancement of vaginal and endometrial mucus layers proliferation; stimulates underdeveloped secondary feminine sex signs. The drug improves common disturbances called by deficit of sex glands activity. Preparation activates the synthesis and secretion of luteinizing and follicle stimulating hormones of hypophysis and stimulates ovulation process.

Indications: Preparation used for eradication of sexual maturation retardation, disturbances of menstrual cycle, dysfunctional menorragias, feminine climax, interruption of pregnancy, infertility of endocrine genesis; for preparation to child birth, pathologic tendency of birth. Low toxicity of drug and soft therapeutic effect permit its prolonged using, possible with hestagens, as a substitute therapy in many gynaecologic diseases.

Advantages: Tefestrol is the preparation of herbal origin, that don't influence on arterial pressure, practically don't influences on secretion of endogenous estrogens, in therapeutic doses not embryotoxic, cancerogenic and mutagenic. On view of low toxicity of drug there is guarantee of its safely using in child gynaecology and of pregnant women on any periods of pregnancy.

Administration and doses: Drug should be taken per os independent of meal. Doses and period of treatment course would be determined individually dependency from character of disease and effectiveness of treatment. Therapeutic dose is 0.005 g. Highest single dose is 0.02 g. Highest daily dose is 0.05 g. Preparation is produced in tablets 0.005 g.

Commercial product: Preparation is produced in tablets containing 0.005 g of tefestrol.

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances

***Manufacturer of dosage form*:** OJSC «Uzchemfarm» (RUz)

ECSUMID

Dry extract as biologically active supplement for sports medicine

***Pharmacologically active substance*:** Sum of phytoecdysteroids from endemic herb *Ajuga turkestanica.*

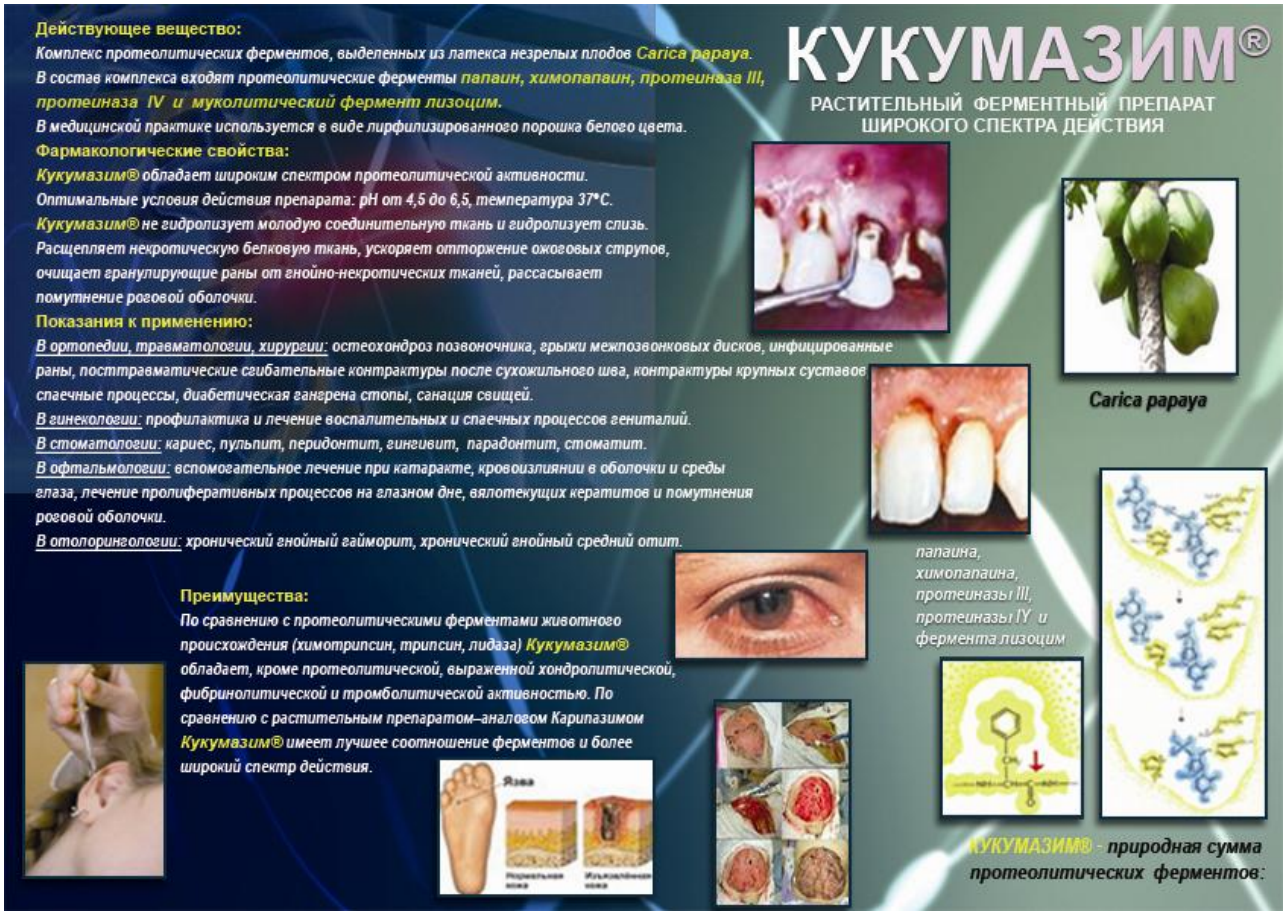
***Pharmacological properties*:**

- Enhances protein biosynthesis
- Has expressed a tonic, and anabolic effect
- Unlike anabolic steroid does not act as a male hormone
- Do not reduce the function of sexual glands
- Do not have harmful side effects
- It is not a doping

***Recommended for*:**

- Excessive mental and physical tension
- Intensive sporting loads
- Asthenic and asthenic depressive states
- Lasting intoxication
- Somatic and infectious diseases
- Neurasthenia
- Neuroses
- Hypotension
- Fatigue

***Manufacturer of substance*:** Experimental production of Institute of the chemistry of plant substances.



CUCUMAZIM

Composition: Cucumazim is lyophylic diyed sterile powder, derived from latex of Melon tree (*Carica papaya*).

Pharmacological activities: Cucumazim has proteolytic activity of wide spectrum of activity. Active principles presented by ferments papain, chymopapain, proteinase III, proteinase IV and lyzocum related to sulfohydril group of proteases. Optimal conditions for cucumazim activity: pH within 4.5-6.5, t° - 37°C. Cucumazim 50 PU hydrolyses a young connective tissue and hydrolyses a mucus. Therefore, preparation is effective at osteochondrosis of backbone, posttraumatic flexor contractures, called by tendon seam, commissure process, infected wounds; for depuration of ulcers, and acceleration of scab seizures and for depuration of granulating wounds from remains of suppurative and necrotic tissues.

Indications: Preparation is used in orthopaedia, traumatology, surgery for treatment of backbone osteochondrosis, hernia of intervertebrate disks; infections wounds - for acceleration of burn scab seizure, purity of granulating wounds from rot-necrotic tissues. In gynecology for prophylaxy and treatment of inflammatory and commissure processes of genital organs. On stomatology drug is used for treatment of caries, pulpitis, periodontites gingivites stomatites. At ophthalmology as auxiliary preparation for treatment of cataract, of haemorrhage in slices and surroundings of eye, for treatment of proliferative processes on eye bottom, sluggish processing keratitis and cornea clouding.

Methods of application and doses: Cucumazim is used as external, so by injection methods: galvanisation, electrophoresis, phonophoresis, as powder, in composition of oinment and pasts. Accuracy of dosage is necessary. pH-of solutions - within 4.5-6.5. It can be reached by dissolving of cucumazim powder in 2 ml of water for injection or procaine, lidocaine solutions. Mentioned solvents may be used for dilution of preparation.

Advantages: Cucumazim by it activity in some degree related to proteolythic ferments of animal origin (chemotrypsin, trypsin, lydasa) and differ from its by his chondrolythic and fibrinolythic activity.

Form of product: One ampule contains 50 PU and bottle contains 350 PU of proteolytic ferments complex