Lecture 1

Topic: State principles and regulations governing the quality of medicines. The relationship of biomedical requirements (efficacy and safety) with the quality of drugs. Terminology: quality, level of quality.

Purpose of the lesson: Basic principles of pharmaceutical analysis

Pharmaceutical analysis is the science of the chemical characterization and measurement of biologically active substances at all stages of production: from controlling the raw materials to assessing the quality of the resulting drug substance, studying its stability, establishing expiration dates and standardizing the finished dosage form. Pharmaceutical analysis has its own specific features that distinguish it from other types of analysis. These features consist in the fact that substances of various chemical nature are subjected to analysis: inorganic, elementorganic, radioactive, organic compounds from simple aliphatic to complex natural biologically active substances. Extremely wide range of concentrations of analytes. The objects of pharmaceutical analysis are not only individual medicinal substances, but also mixtures containing a different number of components. The number of medicines is increasing every year. This necessitates the development of new methods of analysis.

An integral part of pharmaceutical analysis is pharmacopoeial analysis. It is a set of methods for the study of drugs and dosage forms set forth in the State Pharmacopoeia or other regulatory and technical documentation (VFS, FS). Based on the results obtained during the pharmacopoeial analysis, a conclusion is made on the compliance of the drug with the requirements of the Global Fund or other regulatory and technical documentation. If you deviate from these requirements, the medicine is not allowed to be used.

The conclusion about the quality of the drug can be made only on the basis of the analysis of the sample (sample). The procedure for its selection is indicated either in a private article or in a general article of GF XI (issue 2). Sampling is carried out only from intact packaging units that are sealed and packaged in accordance with the requirements of the technical documentation. At the same time, the requirements for precautionary measures for working with toxic and narcotic drugs, as well as for toxicity, flammability, explosiveness, hygroscopicity and other properties of drugs, must be strictly observed. To test compliance with the requirements of scientific and technical standards, multistage sampling is carried out. The number of steps is determined by the type of packaging. At the last stage (after control in appearance), a sample is taken in the quantity necessary for four complete physico-chemical analyzes (if the sample is taken for regulatory organizations, then six such analyzes).

Lecture 2

Subject: Standardization of medicines, normative documentation (ND): State Pharmacopoeia, General Pharmacopoeia Articles (OFS), Pharmacopoeia Articles (FS), Pharmacopoeia Articles of Enterprises (FSP).

Purpose of the lesson: Basic principles of pharmaceutical analysis

Standardization and certification of products - the activity of setting the rules, norms, and requirements for services and goods in order to protect the interests of consumers and the state regarding the quality of services and products, ensuring their safety for human health and life, as well as preserving the environment. The task of standardization and certification of products is: creating conditions for mutual understanding between manufacturers, developers, sellers and consumers. Establishment of the optimal quality requirements for manufactured products.

Creating an order of normative documentation, which includes such documents as technical specifications, standards, guidelines, rules, regulations and other materials.

GOST R and GOST include:

- Product quality requirements that ensure the safety of human health and life, protect the environment;

- Requirements for labeling, packaging and transportation of products, their storage, as well as disposal;

- Compliance with safety and sanitation;

- The requirements of interchangeability and product compatibility, ensuring its quality.

- Standards for the preparation of technical documentation, definition and designation of terminology, metrological and other general technical provisions.

OST- Industry Standards- are developed and approved by line ministries.

Lecture 3

Topic: Analytical quality assurance of medicines in accordance with the requirements of international standards. Good Manufacturing Practice (GMP). Basic elements, principles and requirements. Introduction to pharmaceutical practice.

The purpose of the lesson:

GMP standard (Good Manufacturing Practic) is a system of norms, rules and guidelines regarding the production of medicines, medical devices, diagnostic products, food, food additives and active ingredients. In contrast to the quality control procedure by examining sample samples of such products, which ensures the suitability for use only of these samples themselves (and, possibly, batches made in the near future to this batch), the GMP standard reflects a holistic approach and regulates and evaluates the actual production parameters and laboratory testing.

In other words, we can say that the essence of GMP is to ensure the production of a drug in accordance with the requirements established during the development of this drug and in accordance with the requirements of the authority registering this drug.

In conjunction with the standards of GLP (Good Laboratory Practice) and GCP (Good Clinical Practice), it aims to standardize some aspects of the quality of medical care for the population.

Lecture 4

Subject: Evaluation of the benefit-risk ratio associated with the use of drugs.

An assessment of the potential benefits of pharmacotherapy and its associated risks must be carried out at all stages of the drug's life cycle. This article provides an overview of some of the currently existing quantitative, semi-quantitative and qualitative methods for analyzing the benefit-risk ratio, as well as an attempt to find a universal method that could be successfully

applied by both regulatory authorities of different countries and pharmaceutical companies and organizations conducting clinical trials of drugs.

Lecture 5

Topic: Modern instrumental methods for controlling the quality of medicines and their importance in pharmaceutical analysis.

Purpose of the lesson: to give a concept of all the methods

Qualitative express analysis in a pharmacy is carried out not only by chemical, but also by physical or physico-chemical methods.

Polarimetry makes it possible to draw a conclusion about the authenticity of a medicinal substance in a solution by the value of specific rotation, and refractometry - by the refractive index of a solution of a certain concentration.

Available for use in pharmacy control is the method of fluorimetry. By the nature of the fluorescence of crystals or solutions, it is possible, for example, to identify preparations of certain alkaloids, vitamins, etc. To excite fluorescence, the solutions of the tested substances are exposed to ultraviolet radiation with a wavelength of 365-366 nm. Some medicinal substances themselves do not fluoresce, but when interacting with a number of reagents, they form fluorescent products.

Chromatography is used to isolate an analyte drug from a multicomponent dosage form. Particularly promising is the use for rapid analysis of distribution chromatography on paper and thin layer chromatography. After isolation of the drug substance from the dosage form, chemical reactions to ions or functional groups are performed, and these reactions can be performed directly on the chromatogram.

For high-quality express analysis of tinctures, extracts, infusions and decoctions, a combination of adsorption chromatography and luminescent analysis can be applied. Initially, using the difference in adsorption capacity, the components of the dosage forms are divided into separate zones in alumina columns. The obtained chromatograms are identified in ultraviolet radiation or by group reactions to alkaloids, glycosides, saponins, tannins and other substances.

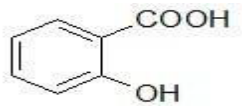
Lecture 6

Subject: Pharmaceutical analysis of drugs - derivatives of phenolic acids

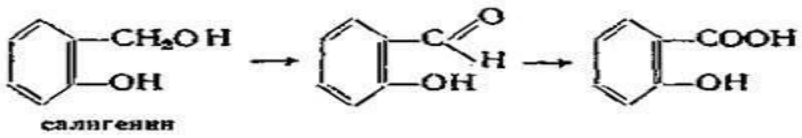
The purpose of the lesson:
- To study the methods of pharmacopoeial analysis of drugs phenolic acids and their derivatives.
- Consider modern medicines related to this group and analysis by example

Salicylic acid

Of the three possible isomers of phenolic acids, only salicylic or o-hydroxybenzoic acid exhibits the highest physiological activity.



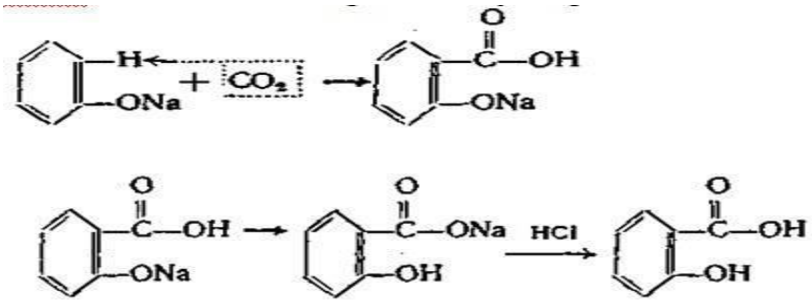
Salicylic acid itself is currently of little use, but its derivatives are one of the most large-tonnage drugs. Salicylic acid itself is needle crystals or fine crystalline powder. It can sublimate when heated - this fact is used to purify salicylic acid in the production of acetylsalicylic acid. When heated above 160 ° C, it is dexarboxylated to form phenol.
For the first time, salicylic acid was obtained by oxidation of saligenin phenol-alcohol, which was obtained by hydrolysis of salicin glycoside contained in willow bark. From the Latin name for willow - Salix - the name "salicylic acid" came from:



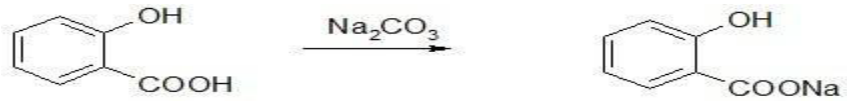
The essential oil of the Gaulteria procumbens plant contains salicylic acid methyl ester, by the saponification of which salicylic acid can also be obtained.

However, the natural sources of salicylic acid cannot satisfy the needs for its preparations and therefore the acid and its derivatives are obtained exclusively by synthetic means.

Of greatest interest and industrial importance is the method of obtaining salicylic acid from sodium phenolate. This method was first applied by Kolbe and improved by R. Schmidt. Dry sodium phenolate is exposed to carbon dioxide under a pressure of 4.5-5 atm. at a temperature of 120-135 °. Under these conditions, CO2 is introduced into the phenolate molecule in the o-position with respect to phenolic hydroxyl:



Salicylic acid exhibits both phenol and acid properties. As phenol, it gives a reaction typical of phenol with a solution of ferric chloride. Unlike phenols, salicylic acid can dissolve not only in alkalis, but also in carbonate solutions. When dissolved in carbonates, it gives an average salt - sodium salicylate - used in medicine:



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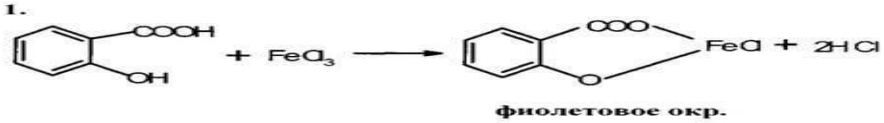

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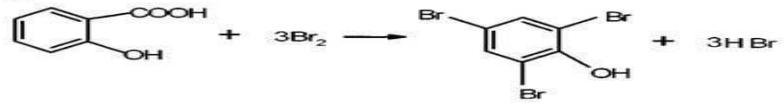


Lecture 7

Topic: Pharmaceutical analysis of drugs - derivatives of para-aminophenol.

Purpose of the lesson: acquaintance with para-aminophenol drugs and methods for determining their quality

Para-aminophenol - the compound has an antipyretic effect, is a metabolite in the conversion of aniline in the human body; very toxic metabolite, with toxicity increasing with increasing amino groups

Drugs: Phenacetin, Paracetamol / analgesic, antipyretic.4-ethoxy-acetaminobenzene

There are a large number of complex preparations containing phenacetin. Phenacetin has a nephrotoxic effect. This is due to the fact that in the body it undergoes a series of transformations with the formation of nephrotoxic substances. In particular, phenacetin forms p-phenatidine, which oxidizes further to the hydroxylamine derivative and then to the nitroso derivative (forms methemaglobin)

Lecture 8

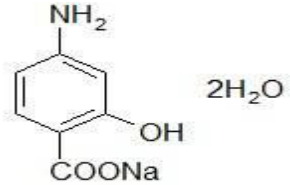
Subject: Pharmaceutical analysis of drugs derived from p-aminobenzoic acid

Purpose of the lesson: study of the principle of analysis of drugs - aniline derivatives

Derivatives of para-aminosalicylic acid.

Para-aminosalicylic acid (PASK) was first described in 1902, but its pharmacological effect was established much later (only in the 40s). P-aminosalicylic acid and its derivatives have bacteriostatic activity against tuberculosis mycobacteria. Derivatives of l-aminosalicylic acid PASK and BePASK are used in the treatment of tuberculosis. The mechanism of the antibacterial action of these drugs is similar to that of sulfanilamides (erroneous inclusion of a drug substance by a pathogenic bacterium into the structure of folic acid, a growth factor. Although the bioactivity of the compounds is high, pathogenic mycobacteria quickly develop resistance to them.

In medicine, two drugs PASK (sodium salt PASK) and BePASK are used.



Lecture 9

Topic: Pharmaceutical analysis of drugs - pyrimidine derivatives.

Purpose of the lesson: the study of methods for the analysis of pyrimidine derivatives

Pyrimidine (1, 3 - diazine) is a planar heterocyclic aromatic compound with two nitrogen atoms in the m-position. Pyrimidine Pyrimidinium ion (r.KVN + = 1, 2) • Neurotropic drugs (hypnotics, narcotic, antiepileptic, anticonvulsants) - derivatives of pyrimidine-2, 4, 6 -trione (babiturates) and pyrimidin-4, 6-dione (hexamidine); • Regenerants and reparants, hematopoiesis stimulants, anabolics - pyrimidin-2, 4-dione derivatives (uracil derivatives); • Antiviral agents, including those active against HIV strains (zidovudine, lamivudine) • Vitamins - thiamine and its

1. Derivatives of pyrimidine 2, 4 - dione The dihydroxy derivative of pyrimidine - Uracil - is found in all living organisms as part of uridyl nucleotides, RNA. It was first discovered in 1900 in the products of the breakdown of yeast nucleic acids. Lactim forms. Lactam form. Lactam form in equilibria prevail.

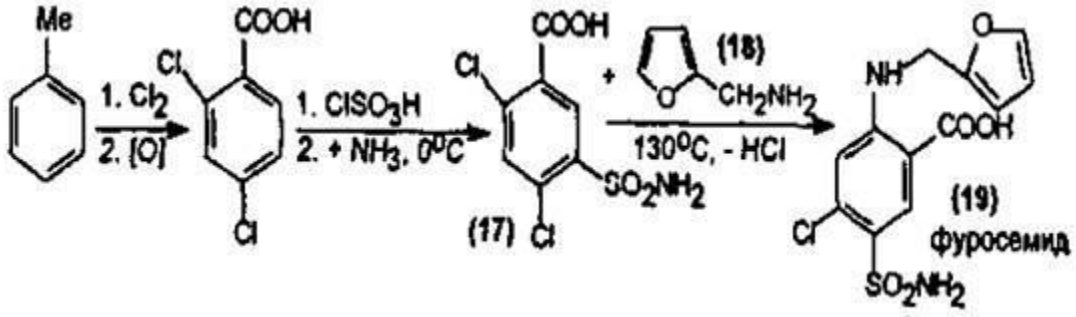
Pharmacological action: anabolic, hematopoietic (Greek póiesis - creation), leukopoietic, regenerating, wound healing, anti-inflammatory drugs • LF: methyluracil ointment 10% (for wounds, burns, trophic ulcers) • Candles with methyluracil, 5, colitis) • Tablets 0, 5 g - leukopenia, bone fractures, gastrointestinal diseases Anabolic drugs - drugs whose action is aimed at enhancing anabolic processes in the body, that is, accelerating the formation and updating of the structural parts of cells, tissues and muscle tour.

Lecture 10

Subject: Analysis of the quality of medicines and dosage forms - derivatives of sulfonic acids

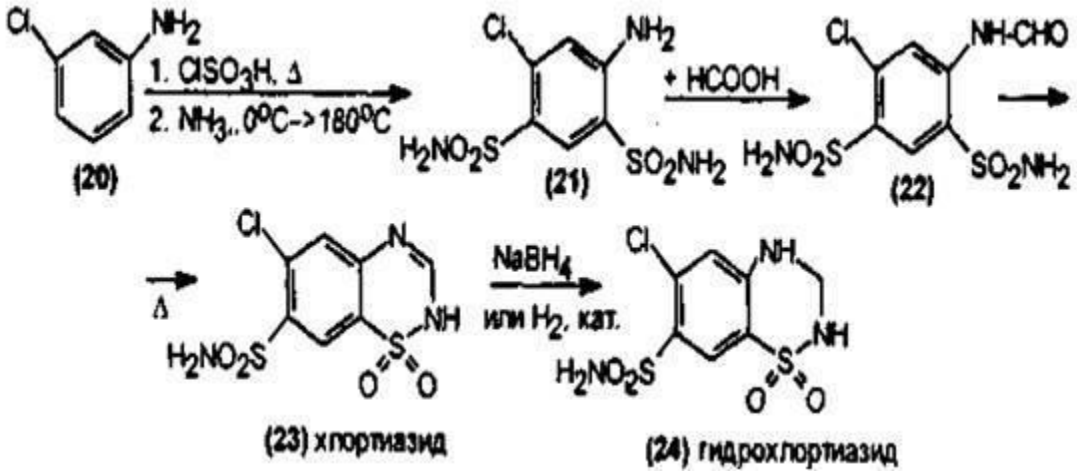
Purpose of the lesson: study of the features of the pharmacological analysis of a number of sulfonic acids

The study of the side effects of sulfonamide antibiotics and the synthesis of their many structural analogues led to the discovery of diuretics and antidiabetic agents among them. Thus, furosemide with diuretic and antihypertensive properties was obtained by nucleophilic substitution of one of the two chlorine atoms in an acid with a primary amine (the regio selectivity of this reaction is dictated, apparently, by steric hindrances created by the sulfamoyl substituent).



A number of disulfamides, for example, and in which the second sulfamide group forms a thiadiazine nucleus, have similar bioactivity. They are synthesized by the introduction of two sulfamoyl groups by the action of chlorosulfonic acid on m-chloroaniline. Disulfanilamide is then heated in formic acid, which leads to N-formylaniline, which is cyclized by heating in

benzo-1,2,4-thiadiazine (chlorothiazide. When it is hydrogenated over the catalyst or using sodium borohydride in an aqueous alkaline medium, another diuretic is obtained - hydrochlorothiazide:



Lecture 11

Topic: IR spectroscopy method in the analysis of drugs. Types of IR spectrometers recommended by HF GF.

Given the widespread use of tablet antisecretory drugs and, in particular, ranitidine hydrochloride preparations, methods of identifying these drugs, as well as substances for their manufacture, are of great importance. IR spectroscopy is used in the pharmacopeia analysis of ranitidine hydrochloride tablets, but the spectrum is obtained only after the extraction of the active substance [1]. The objective of this work was to develop a method for identifying ranitidine hydrochloride in the dosage form “coated tablets” by IR spectroscopy without prior isolation from the dosage form.

IR spectroscopy is based on the phenomenon of absorption of infrared radiation by chemicals with the simultaneous excitation of molecular vibrations. Infrared radiation is an electromagnetic wave and is characterized by a wavelength λ, a frequency.

Lecture 12

Topic: UV spectroscopy in pharmaceutical analysis of drugs. Methods for determining the authenticity of drugs and specific impurities**.**

The purpose of the lesson: the development of spectrometric analysis in establishing quality and medicinal compounds.

The nature and methods of imaging electronic spectra. When a substance absorbs electromagnetic radiation corresponding to the ultraviolet (180-400 nm) and visible (400-800 nm) spectral regions, the transition of valence electrons from occupied orbitals of the ground electronic state to the vacant orbitals of the excited state occurs. Therefore, the absorption spectra in these regions are called electronic,

and the state of the molecule is called excited.

The energy of the electronic transition □□ is related to the frequency of electromagnetic radiation □ and the wavelength □ by the relation

□E = h□ = hc / □,

where h is the Planck constant; c is the speed of light.

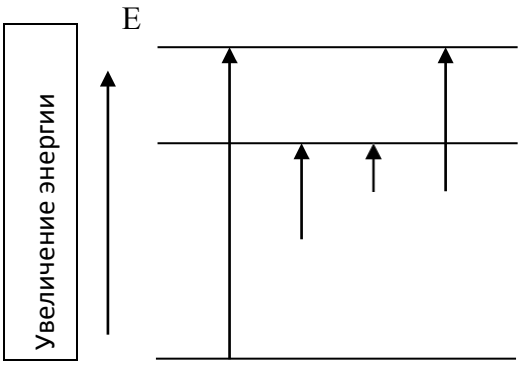
Organic molecules contain single and multiple bond electrons (□- and □-electrons) and electrons of unshared pairs of heteroatoms (n-electrons). Electrons interacting with a quantum of light, absorbing energy, can transfer from a higher occupied orbital to a lower vacant orbital. Electrons are firmly held by the nucleus, therefore, their excitation requires large energies and, therefore, electromagnetic radiation having short wavelengths (120-800 nm).

Depending on the structure of the organic molecule, several types of electronic transitions can occur that require different energies and will be observed at different frequencies.

There are four types of electronic transitions from connecting and non-binding orbitals of the ground state to the loosening orbitals of the excited state: □□□ *, □□□ *, n□□ * and n□□ *.

These transitions are characterized by different values of □E (Fig. 1.1). The highest quantum energy is necessary for the transition □□□ *, i.e. To excite the electrons of the strongest связи bond, light quanta of minimum length (up to 190 nm) are required. The presence of atoms with unshared electrons in saturated compounds gives rise to n□□ * transitions lying in a longer wavelength region than □□□ *. The n□□ * transitions are observed in compounds in which the heteroatom is connected by a multiple bond to another atom, for example, C = N. In simple non-conjugated systems, these transitions are the longest wavelengths.

When conjugated, the highest binding □-orbit can have a higher energy than the non-binding n-orbit, and then the transition band □□□ * will be the longest wavelength band:



* - loosening orbital

□ * - loosening orbital
n - non-binding orbital
□ - binding orbital

□ - binding orbital

Lecture 13

Subject: Mass spectrometry as a method of qualitative and quantitative analysis of drugs, based on direct measurement of the ratio of mass to the number of elementary positive or negative ion charges (m / z) in the gas phase obtained from the test substance.

Mass spectrometers are used to analyze drug substances.

Organic samples in most cases are complex mixtures of individual substances. For example, it is shown that the smell of fried chicken is 400 components (that is, 400 individual organic compounds). The task of analytics is to determine how many components make up organic

matter, find out what components it is (identify them) and find out how much each compound is contained in the mixture. For this, a combination of chromatography with mass spectrometry is ideal. Gas chromatography is the best suited for combination with the ion source of a mass spectrometer with electron impact or chemical ionization, since the compounds in the column of the chromatograph are already in the gas phase. Instruments in which a mass spectrometric detector is combined with a gas chromatograph are called chromato-mass spectrometers ("Chromass").

Many organic compounds cannot be separated into components by gas chromatography, but it is possible by liquid chromatography. To combine liquid chromatography with mass spectrometry, ionization sources in electrospray (ESI) and chemical ionization at atmospheric pressure (APCI) are used today, and the combination of liquid chromatographs with mass spectrometers is called LC / MS. The most powerful systems for organic analysis, demanded by modern proteomics, are built on the basis of a superconducting magnet and operate on the principle of ion-cyclotron resonance. They are also called FT / MS because they use Fourier transform of the signal.

Lecture 14

Subject: Adsorption spectroscopy in the quality control of drug substances and dosage forms.

Medicines (PM), pharmaceutical substances, biologically active substances, general concepts. Definition, legislation (regulatory documents), sources and methods of obtaining drugs. International Nonproprietary Names (INNs) of pharmaceutical substances. Trade names for medicines. Proprietary drug names. The principles of the classification of drugs used in pharmaceutical chemistry: classification of drugs depending on their chemical structure, anatomical and therapeutic chemical classification (ATC), etc. Regulatory requirements: state registration of drugs. Modern requirements for medicines: safety, efficacy and quality. A system for ensuring the quality of medicines at all stages of their creation and use. Standards of Good Practice: Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Manufacturing Practice (GMP). Drug Quality Control System.

Lecture 15

Topic: Chromatographic methods of analysis in pharmaceutical analysis. HPLC (high performance liquid chromatography).

High performance liquid chromatography (HPLC, English HPLC, High performance liquid chromatography) is one of the effective methods for the separation of complex mixtures of substances, widely used both in analytical chemistry and in chemical technology. The basis of chromatographic separation is the participation of the components of the mixture to be separated in a complex system of Van der Waals interactions (mainly intermolecular) at the interface. As an analysis method, HPLC is part of a group of methods, which, due to the complexity of the studied objects, includes preliminary separation of the initial complex mixture into relatively

simple ones. The resulting simple mixtures are then analyzed by conventional physicochemical methods or by special methods created for chromatography.

The HPLC method is widely used in such fields as chemistry, petrochemistry, biology, biotechnology, medicine, food industry, environmental protection, the production of drugs and many others.

Literature

1. Analysis of medicinal mixtures / A.P. Arzamastsev, V.M. Pechennikov, G.M. Rodionova et al. - M.: Sputnik + Company, 2000. - 275 p.
2. Glushchenko NN Pharmaceutical Chemistry: A Textbook for Stud. wednesday prof. textbook. institutions / N.N. Glushchenko, T.V. Pleteneva, V.A. Popkov; Ed. T.V. Wicker. - M.: Publishing Center "Academy", 2004. - 384 p.
3. Loginova N. V., Polozov G. I. Introduction to pharmaceutical chemistry: Textbook. - Mn .: BSU, 2003.-250 p.
4. The State Pharmacopoeia of the USSR, XI edition. - M.: Medicine, 1987 (Issue 1), 1989 (Issue 2).
5. The State Pharmacopoeia of the USSR, X edition. - M.: Medicine, 1968.
6. The State Register of Medicines, 1998, 1999, 2000.
7. Pharmaceutical chemistry: Textbook. allowance / Ed. L.P. Arzamastseva. - M.: GEOTAR-MED, 2004 .-- 640 p.
8. Certification system of pharmaceutical certification systems of GOST RF (Regulation on the Certification System of Medicinal Products Certification Systems of GOST RF), 1998, 28 p.
9. Pharmaceutical analysis of drugs / Ed. V.A. Shapovalova. - Kharkov: IMP Rubicon, 1995.
10. Pharmaceutical Drug Analysis Ed. Shapovalova V.A., Kharkov, 1995, 396 p.

Internet resources:

1. Information portal. - Access mode: http://www.xumuk.ru;
2. Information portal. - Access mode: http://www.alhimikov.net;
3. Information portal. - Access mode: http://www.chemport.ru;
4. Russian State Library. - Access mode: www.rsl.ru;
5. Information and reference portal. - Access mode: www.librari.ru;