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CHEMICAL COMPOUNDS OF HOUTTUYNIA CORDATA THUNB AND THEIR SPECIFIC PHARMACOLOGICAL ACTIVITIES

Resume: *Today, research into herbal medicines is one of pressing issues, because herbal medicines are less toxic, more costly and even more effective than synthetic medicines.*
This review focuses on a literature review of medicinal plant material that bears the name Houttuynia cordata Thunb, which has scientifically proven pharmaceutical activity against infections and viruses.
Key words: *Houttuynia cordata Thunb, medicinal herbs, anti-infective and antiviral activities.*

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HOUTTUYNIA CORDATA THUNB ХИМИЯЛЫҚ ҚҰРАМЫ ЖӘНЕ ОНЫҢ ЕРЕКШЕ ФАРМАКОЛОГИЯЛЫҚ ҚЫЗМЕТІ

Түйін: Бүгінгі таңда шөптік препараттарды зерттеу өзекті тақырыптардың бірі болып табылады, өйткені шөптік препараттар синтетикалық препараттарға қарағанда аз уытты, баға санатына адал және кейде тиімдірек.
Бұл мақала Houttuynia cordata Thunb дәрілік өсімдік шөбіне әдеби шолуға арналған. Бұл дәрілік өсімдік шикізаты халық медицинасында ұзақ уақыт бойы қолданылып келеді және оның инфекциялар мен вирустарға қарсы ерекше фармакологиялық белсенділігі ғылыми дәлелденген.
Түйінді сөздер: Houttuynia cordata Thunb, дәрілік өсімдік материалы, инфекцияға қарсы және вирусқа қарсы белсенділік.

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ХИМИЧЕСКИЙ СОСТАВ HOUTTUYNIA CORDATA THUNB И ИХ СПЕЦИФИЧЕСКАЯ ФАРМАКОЛОГИЧЕСКАЯ АКТИВНОСТЬ

Резюме: На сегодняшний день исследование фитопрепаратов является одной из актуальных тем, потому как,, растительные препараты менее токсичны, лояльны по ценовой категории и временами эффективнее по сравнению с синтетическими лекарственными средствами.
Эта статья посвящена литературному обзору по лекарственному растительному сырью Houttuynia cordata Thunb. Данное лекарственное растительное сырье применятся в народной медицине продолжительно время и научно доказаны его специфические фармакологические активности против инфекций и вирусов.
Ключевые слова: Houttuynia cordata Thunb, лекарственное растительное сырье, противоинфекционная и противовирусная активность.

INTRODUCTION

Houttuynia belongs to a polytypic genus of herbaceous plants in Saururaceae family, this family includes only two species, Houttuynia cordata and Houttuynia emeiensis, but with its broad spectrum and high number of bioactive substances is a variety Houttuynia cordata Thunb [1]. Botanical illustration is shown in figure 1.

Figure 1 - Botanical illustration of Houttuynia cordata Thunb

This genus was named after the Dutch botanist Martin Houttuynia [2].

Houttuynia cordata Thunb is a medicinal herb with a long history of use in Oriental folk medicine.

Thanks to its wide range of uses due to its rich composition and long history of use in traditional medicine over 8 centuries in Asian countries, especially China, this plant was first listed in the 7th Revised Japanese Pharmacopoeia (1961), but also in the European Pharmacopoeia (edition 9) and Pharmacopoeia of the people's Republic of China (edition of 2015).

Botanical description

Houttuynia cordata Thunb is a perennial herbaceous plant, which can grow to a height of 20-30 cm, but in warm climates it can reach a height of up to 80 cm.

The rhizome is sinuous and creeping, upright and rooted at the nodes. The stems are erect and/or slightly twisted, furrowed, glabrous. Leaves are entire, growing in alternating sequence, broadly ovate, ovate-lanceolate or triangular-ovate, pointed, the base deeply cordate; petiolate, however, they are shorter than the leaves, oblong, obtuse and furrowed, also entire. Flowers are bipartite, with no perianth; inflorescence: Spike-like; 10-30 mm long, with four large, oval-oblong, whitish, petal-like bracts growing at the base, which in turn form a corolla-shaped covering. The flowers are about 1 cm in diameter [4]. The fruits are round in shape and have a multi-seeded box; the fruits of this medicinal plant material are usually fleshy (Figure 1).

Flowering occurs during summer months, usually from May to June. This plant has heart-shaped petals and a bright colour, in which bright red, yellow and green colours are mixed, also during flowering, it produces small white buds.

Houttuynia cordata Thunb requires little attention and is an unpretentious plant. It thrives in damp and wet soils as well as near ponds and shallow water. However, it prefers fairly moist soils. Moreover, the plant is tolerant of sunlight, which means it can grow in both shade and in the open air, although its chemical composition depends on this factor. Winter hardiness: 5 (from -29°C to -23°C), i.e., in conditions of the middle zone it may die out in cold snowy winters, but in mild snowy winters it survives without shelter [5].

Also, an excess of nitrogen in the soil and in fertilizers is undesirable because it negatively affects the overwintering.

Distribution

This medicinal herb is widely distributed throughout Southeast Asia, also found from the Himalayas to the Japanese archipelago, the islands of Ryukyu, Taiwan and Java. Moreover, this herb is widely used in Oriental medicine and is also used as a vegetable crop [6].

This species prefers damp places, open ponds and wetlands, also, prefers non-active sunlight.

Ethnomedical uses

Houttuynia cordata Thunb has a rich chemical composition, as evidenced by centuries of scientific work, and use of this herb in traditional medicine for over 8000 years in Asian countries [7].

In China, for example, it was used to treat anisolobis ulcers. In Korea, it was used to treat cough, pneumonia, bronchitis, dysentery, dropsy, leucorrhoea, uteritis, eczema, herpes simplex, acne, chronic sinusitis and nasal polyps [7, 8]. In Thailand, it has been used for immunostimulation and as an anti-cancer agent. In Japan, it was mainly used as a diuretic, but also to treat gastric ulcers, control infection and as an antimicrobial, antitumour, promoter agent for the production of an antibiotic by a strain of Gram-positive spore-bearing bacilli [7, 9].

In India, these shoots were used for freshness, good sleep and heart disease by the Apatani, who traditionally settled in seven villages in the Ziro Valley in Lower Subansiri district of Arunachal Pradesh in the East Himalayan region of India. Apart from general medicinal uses, Houttuynia cordata Thunb is used as food and in cosmetic preparations.

In Korea and Japan, it is often used in combination with other medicinal herbs as cosmetic products. Its extracts are used as cosmetic compositions to prevent or treat wrinkles, prevent cracked skin, anti-ageing and improve skin condition, remove freckles and whiten skin [10].

Fermented extract with other medicinal herbs is used to alleviate atopic dermatitis and other skin conditions due to the anti-inflammatory and soothing effect, itching reducing and moisturising effect of this composition. The extract is also used to protect or nourish hair and prevent dandruff. It is also used to prepare a massage mask that can treat acne, chloasma, atopy and freckles without leaving scars [11].

Phytochemical composition and their pharmacological activity

Houttuynia cordata Thunb composition is dominated by secondary metabolites such as, phenolic compounds, flavonoids, alkaloids, tannins, saponins, essential oils, terpenes and coumarins in large amounts.

The chemical composition of this medicinal herb material depends on the type of extractant and its polarity, for example, when using high-polarity extracts (methanol), polyphenols, phenolic compounds and other high polarity connections are released. In a solvent of medium polarity (ethanol), alkaloids, cardiac glycosides, simple phenolic compounds, flavonoids, etc. pass. Saponins, coumarins, polysaccharides, lignans and other weakly polar compounds dissolve in a weakly polar solvent.

Thai scientists Shu-Chen Chou, Chung-Ren Su and their colleagues from National Cheng Kung University identified with using a methanolic extractant with a batch introduction of water and CHCl3 then purified with n-hexane, then after additional purification with n-BuOH, the scientists isolated Houttuynoside 1 and Houttuynoside 2. The structure was proved using an IR spectrum at a wavelength at 3391cm-1 and 1688 cm-1 and 3353 cm-1 and 1700 cm-1, respectively.

According to a 2013 study by scientists from Central South University in Shanghai, China, scientists identified 346 components in the composition of Houttuynia cordata Thunb. The percentage of components isolated by GC-MS is given below: terpenoids (27.0%), hydrocarbons (16.8%), esters (11.9%), alcohols (11.6%), ketones (7.2%), aldehydes (4.9%), acids (3.8%), phenols (1.7%), esters (0.9%) and mixed compounds (14.2%) [12].

Flavonoids and polyphenols

This group of compounds is one of the large classes of bioactive substances in medicinal herbs. Flavonoids play an essential role in plant metabolism and are very widespread in higher plants.

According to scientific work of scientists of National University of Singapore, flavonoids, namely, quercitin, quercitrin and rutin which were isolated from Houttuynia cordata Thunb, have anti-infective and immunomodulant properties. Quercitin presented an activity against MHV and DENV-2 with method in vitro; quercitrin showed ability to inhibit DENV-2, not MHV.

Quercetin has a capability to forbid H+-ATPase of lysosomal membrane and because of this it prevents the removal of a virus envelope.

The isolated compound (quercetin-7-rhamnoside) from an ethanol extract showed that it has pharmacological activities against MHV and DENV-2 in vitro.

In addition, quercetin has shown a significant inhibitory effect on ATPase of drug-resistant proteins, which increases the bioavailability of anticancer and antiviral drugs in vivo [13].

According to a recent 2021 study, scientists isolated 177 phytocomponents from a methanol extract and used a docking method to study their inhibitory ability against coronavirus. For this Scientists isolated 2 components, such as Quercitin and 6-Hydroxyondansetron with GC-MS/LC-MS, then a molecular docking was performed on ligands (compounds from H. cordata) against three different SARS-CoV-2 receptors, namely Mpro (PDB ID 6LU7), PLpro (PDB ID 7JRN) and ADRP (PDB ID 6W02), respectively, and using Schrödinger suite 2020-3 Glide molecular docking software (Switzerland), determined igand binding to the selected receptors.

The results of this study show that the compound 6-Hydroxyondansetron showed great affinity binding to the two SARS-CoV-2 receptor proteins Mpro and PLpro, as well, Quercitrin showed to be a promising inhibitor as it showed the best binding to the ADRP protein.

Also, rutin (8.8%), hyperin (26.7%), isoquercitrin (9.9%) and quercitin (31.7%) were isolated from the medicinal plant material, reducing infuenza A (IAV)-induced acute lung injury (ALI) in mice byInhibition of infuenza virus neuraminidase and Toll-like receptor signalling [14].

Alkaloids

Alkaloids are organic heterocyclic substances that have mainly nitrogen groups in their structure, but may also have chlorine, bromine and phosphorus. Alkaloids are known to inhibit or excite the central nervous system in large quantities, others paralyse nerve endings, dilate or constrict blood vessels, another group has an analgesic effect.

Over the past 20 years, several alkaloids have been isolated from Houttuynia cordata Chameleon (Houttuynia cordata Thunb), including apomorphine, pyridine and their derivatives [15].

Apomorphines is a group of alkaloids that trace their biogenetic origin to a benzyltetrahydroisoquinoline-laud-nosoline derivative P-12b, in turn formed from two tyrosine molecules. A salt of this compound i.e., apomorphine hydrochloride, is an antiemetic and is used especially in cases where gastric lavage is not possible.

Pyridine and its derivatives are used as nootropics, also as antioxidants, calcium channel blockers, analeptics, anti-tuberculosis drugs and antidepressants.

The best-known group of compounds in this class, 3-hydroxy-2-methylpyridine is converted in a human body into pyridoxal phosphate (PLP), a cofactor of enzymes that catalyse a deamination of amino acids.

Researchers from North East Hill University, India, performed a docking method using ACD/ChemSketch (Freeware) 2019 on 49 molecules among them 22 alkaloids, 11 flavonoids and 16 polyphenols from H.cordata Thunb which were reported in the literature. These studies tested the potential of three classes of substances, such as alkaloids, flavonoids and polyphenols, as inhibitors of the SARS-CoV-2 enzyme RdRp.

The scientists found that compounds 14 (7-oxodehydroazimilobin), 3 (1,2,3,4,5-pentamethoxy-dibenzo-quinoline-7-one) and 21 (1,2-dimethoxy-3-hydroxy-5-oxonorporphine) were the most potent bioactive molecules to interact with the target enzyme with affinity binding higher, the control drug being Remdevir. Of the above 3 compounds, Compound 14 showed a significant inhibitory effect on protein-tyrosine phosphatase 1B (PTP1B) values, which IC50 2,672 μM, while 3 (10 μM) presented a modest hepatoprotective efficacy against D-galactosamine-induced cell damage WB-F344 [16].

Organic and fatty acids

The following acids are present in this medicinal plant material: palmitic, stearic, heptanic, nonanic, undecanoic, octanoic, hexanoic, lauric, capric, heptadecanoic tetradecanoic, tridecanoic, pentadecanoic, octadecenoic, hexadecenoic, octadecadiene, aspartic acid and etc.

Acids such as glutamic acid, capric acid, lauric acid, palmitic acid in H.cordata Thunb were identified by gas chromatograph. In addition, chlorogenic acid, crypto-chlorogenic acid, non-chlorogenic acid, quinic acid and caffeic acid were identified using mass spectra and fragmentation samples.

Also, chemical components: houttuynoside A and houttuynamide A separated and purified by solvent extraction, thin layer chromatography and column chromatography on silica gel and identified the structures by IR, EI-MS, 1H-NMR and 13C-NMR [17]. These compounds have an antioxidant and anticancer pharmacological activities [17].

Takagi and colleagues extracted chlorogenic acid, moreover, found palmitic acid, linoleic acid, oleic acid and stearic acid in the benzene fraction [18].

Bauer and colleagues identified linolenic acid, linoleic acid, oleic acid, palmitic acid and stearic acid by phytochemical investigation [19].

Qinge and his colleagues isolated and purified succinic acid from the dried rhizome of this plant using solvent extraction, silica gel and column chromatography on Sephadex LH-20 [20].

Conclusion

Houttuynia cordata Thunb has a wide spectrum of pharmacological activity, as evidenced by its long-term use in traditional medicine and scientific papers from around the world. According to the literature this medicinal plant has the following activities: anaphylactic inhibitory, antimutagenic, anti-inflammatory, antiviral, fat burning, antibacterial, anti-cancer and antioxidant, anti-allergic, antidiabetic.

But in light of recent developments in 2019, that is, since the outbreak of pandemics due to coronavirus infection (SARS-CoV-19), scientists from all over the world have begun to study this respiratory disease, its causes and most importantly its treatment methods. There is a myriad of scientific papers that have an evidence base for the prevention of this disease, these studies have mainly been carried out in Asian countries.

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