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CALTHA PALUSTRIS. ANALYTICAL OVERVIEW

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Мета. Аналіз та узагальнення даних щодо ареалу, вмісту біологічно активних сполук та спектру використання у фармації та медицині *Caltha palustris*.

Матеріали та методи. Літературні та електронні джерела інформації, що стосуються поширення, хімічного складу та фармакологічної активності *Caltha palustris*.

Результати. *Caltha palustris* – багаторічна трав'яниста рослина з родини Жовтецевих (*Ranunculaceae*). Рослина неофіційна, широко застосовується народною медициною як протизапальний, спазмолітичний, бактерицидний, протимікробний, безпечний, діуретичний засіб. Основними біологічно активними речовинами *Caltha palustris* є: дубильні речовини, глікозиди (γ -лактони протоанемонін та анемонін) сапоніни, берберин, гіркоти, вітамін С, холін, каротин, флавоноїди та алкалоїди. *Caltha palustris* відносять до регіонально рідкісних рослин адміністративних територій України. З огляду на актуальність розширення асортименту лікарської рослинної сировини для створення сучасних лікувальних засобів та хімічний склад, фармакологічну дію *Caltha palustris*, доцільним є проведення подальших ресурсознавчих, фітохімічних та інших досліджень рослини.

Висновки. Враховуючи значний досвід застосування в народній медицині, широкий спектр фармакологічної активності, вміст цінних біологічно активних сполук *Caltha palustris* є перспективною та цінною сировиною для одержання та виробництва фітохімічних препаратів та впровадження їх у практичне застосування

Ключові слова: *Ranunculaceae*, *Caltha palustris*, протоанемонін, анемонін, біологічно активні речовини, фармакологічна дія

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1. Introduction

Today, the world pharmaceutical industry is making extensive use of herbal raw materials, which are the basis for the creation of medicines. A large number of drugs that are manufactured worldwide have natural ingredients of plant origin. Therefore, the search for new species of plants that could be a source of biologically active compounds, such as flavonoids, coumarins, hydroxylic acids, alkaloids, saponins, amino acids and so on. There is some evidence to support the efficacy of herbal medicines in the treatment of a number of serious diseases. One of these is representatives of the *Ranunculaceae* family, since they are a source of biologically active compounds that have long been used in traditional medicine as a medicine with various pharmacological effects. One such representative is *Caltha palustris*. The plant is used for a long period in folk medicine of different countries and exhibits a wide range of medicinal properties.

Phytochemical and pharmacological studies of *Caltha palustris* have been partially conducted by separate groups of scientists in different fields.

Scientists from the University of British Columbia and Indian scientists from the Central Research Institute of Medicines conducted research on the content of triterpene [1–3]. In addition, German scientists from Bayreuth University [4] conducted the content of biologically active compounds in some representatives of the *Ranun-*

culaceae family. Researchers from the Wrocław University of Natural Sciences (Poland) conducted studies on the separation of polysaccharide fraction from *Caltha palustris* raw material [5]. Italian scientists from Ferraris University [6] carried out the identification of protoanemonin in the plant.

A group of Indian scientists from Kashmir University [7] carried out pharmacological action, including the determination of anthelmintic, antimicrobial, antioxidant and cytotoxic activity.

Polish scientists study the effect of polysaccharide fractions isolated from *Caltha palustris* on phagocytic cell activity and humoral immune responses in mice with induced arthritis [5, 8].

Caltha palustris has not been sufficiently studied at the present stage of the development of pharmaceutical science, so comprehensive studies of its raw materials are relevant.

The purpose of the research is to analyse and summarize the literature on the distribution, chemical composition of *Caltha palustris* and the features of its use for further pharmacognostic, phytochemical and pharmacological studies.

2. Planning (methodology) of research

For this purpose, the following problems must be solved:

- Analyse current literary sources for data on the distribution of *Caltha palustris* in Ukraine;
- Summarize the literature on the content of biologically active compounds of *Caltha palustris*;
- To analyse and establish the possibilities and peculiarities of the use of *Caltha palustris* in pharmacy and medicine.

3. Materials and methods

Literary and electronic sources of information regarding the distribution, chemical composition and pharmacological activity of *Caltha palustris* were selected.

4. Results of the research

Caltha palustris (Fig. 1, 2) is a plant belonging to the family Ranunculaceae, a subclass of Ranunculidae. The Latin name of the genus Ranunculaceae is derived from the ancient Roman language. The species name in Latin means swamp [9].



Fig. 1. *Caltha palustris*

Botanical description.

It is herbaceous plant with erect, simple or top branching stems, up to 20–50 cm in height. Leaves petiole, entire, kidney- or heart-shaped, serrated toothed, dark green, shiny. Root leaves much larger than the stem ones. The flowers are 2–3 cm in diameter. Perianth simple, corolla of five, rarely - many petals. Petals oval or ovoid, golden yellow colour [10].

Stamens numerous, free. Pestle from 2 to 12. Fruit – aggregate.

The plant blooms in April and May. The first flowering of the plant begins only at the 10th year of its life. Leaf fruits containing up to 10 black shiny seeds that fall out after ripening in May and July.

Propagated by seeds and rhizomes [11, 12].

Formula of flower – * $Ca_5Co_5A_{\infty}G_{(2-12)}$. Flower is androgynous.

The number of chromosomes $2n=32$ and 56 [13].



Fig. 2. *Caltha palustris*

Distribution and harvesting.

Caltha palustris is common in the Ukrainian Carpathians in all highlands.

It grows on the banks of ponds, wet meadows, lakes, wetlands, swamps, along rivers in slow flowing and stagnant waters, near wet channels [14, 15]. The distribution map in Ukraine is presented in Fig. 3 [16].



Fig. 3. Distribution of *Caltha palustris* in Ukraine

From the end of the sixteenth century, the plant began to grow in the gardens of Austria and southern Germany. It has become a valuable garden plant in the collections of connoisseurs of Austria, Switzerland, Germany, England, and Holland [17].

In Ukraine, it has long been used for medicinal purposes. They used all the aboveground part of the plant, which is harvested in the spring during flowering. They are dried in dark and well-ventilated areas, often turning over raw materials. It can be dried in ovens at 50–60 °C.

The roots are harvested in the autumn, washed, crushed, decayed and dried in a dryer.

Shelf life (in pouches or wooden containers) is 1–2 years [18].

Chemical composition.

Caltha palustris contains biologically active substances both primary and secondary synthesis. It consists of alkaloids, saponins, γ -lactones: protoanemonin, anemonin, tannins (8.1 %), ascorbic acid (37 mg %) [19, 20].

All parts of the plant contain triterpenoids (palustrolide, caltolide, epicaltolide, 16,17-dihydroxycauronic-19 and hedrogenic acids), steroids (sitosterol), carotenoids (3-epilutein), coumarins (scopoletin, umbelliferone).

Heterocyclic geleborin compounds have been found in underground organs. The flowers contain flavonoids – campferol, quercetin, 7-rhamnoside, 3-glucoside and 3-glucoside-7-rhamnoside of campferol, 7-rhamnoside, 3-glucoside, 3-glucoside-7-rhamnoside quercetin.

In the *Caltha palustris* grass, 16 connected phenolic structures have been identified: phenolic acids – caffeic, chlorogenic, gallic, chicory, isochlorogenic, ferulic and flavonoids – apigenin, apigenin-3-glycoside, luteolin-7-glycoside, k-glycoside; as well as catechin, epicatechin, epigallocatechin gallate and coumarin. The predominant among phenolic acids are chicory and gallic acids, and the flavonoids are dominated by apigenin [21].

Caltha palustris flowers contain pigments of trolixanthin, xanthophyll, epoxanthine, alloxanthine, seeds – fatty oil (30 %). Caltosides (glycosides of hederagenin and oleanolic acid), which have androgenic properties, have been found in the rhizomes and roots of *Caltha palustris*, which grows in the Far East [22].

The seeds have alkaloids, oils and vitamin C.

Due to the presence of a toxic substance protoanemonin the plant is poisonous, but after drying the toxic properties are lost because protoanemonin is converted into anemonin [15, 23].

The content of protoanemonin in the plant is relatively low compared to other members of the Ranunculaceae family – 0.26p.g/g fro wt. Protoanemonin is a metabolite of stress and serves to protect members of the Ranunculaceae family from external stimuli, so its number may vary [24].

Protoanemonin (Fig. 4) is a volatile, viscous, colourless oily substance with a pungent odour and a burning taste.

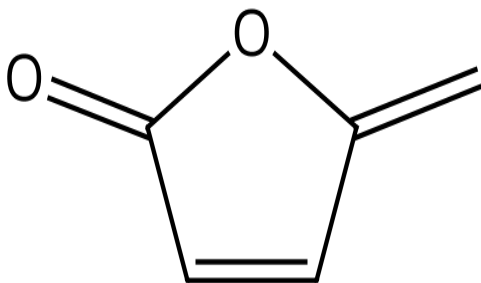


Fig. 4. Protoanemonin

By chemical nature belongs to the group of lactones. With long-term storage of aqueous solutions, the protoanemonic polymerizes and precipitates as crystalline anemonin. The beneficial effect of protoanemonin is

manifested in a stimulating effect on the body: it tones the nervous system, improves haematopoiesis is of great importance In the treatment of purulent wounds and ulcers, as it exhibits antibiotic properties. Actively acts against gram-positive and acid-resistant bacteria [25].

Anemonin (Fig. 5) is found in many members of the Ranunculaceae family, from which it is obtained by distillation of the herbaceous parts. In the processing of chloroform distillation and evaporation of the chloroform solution, there are two crystalline substances: anemone camphor, which has very poisonous properties, quickly turns into amorphous anemonic acid, and anemonin. The latter is a rhombic crystals, melts at 156 ° C, difficult to dissolve in hot water and ethers, easily - in hot alcohol and chloroform. Anemonin is poisonous; its ethereal solution in contact with the eyes leads to dilation of the pupils. However, it has analgesic and antispasmodic properties and is used in asthma, whooping cough, rickets and others [26].

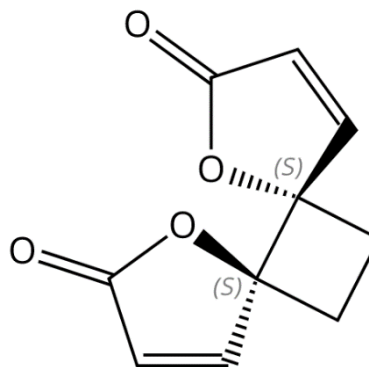


Fig. 5. Anemonin

Pharmacological action and use in medicine.

Caltha palustris is an unofficial plant.

Caltha palustris is used in folk medicine and homeopathy.

In folk medicine of Ukraine, *Caltha palustris* is most commonly used externally as an anti-inflammatory and analgesic agent for burns, wounds, bruises, rheumatism, neurodermatitis, eczema, etc. [27].

In small doses decoction or infusion of *Caltha palustris* grass is used internally for feverish conditions, whooping cough, bronchitis, asthma, metabolic disorders, diathesis, anemia, scurvy, painful menstruation and uterine carcinoma [28].

In Tibetan medicine they used infusion of flowers for the treatment of ascites.

In homeopathy, a plant is used to treat bronchitis and cough, menstrual disorders, and others. Homeopathic anti-cough drug is made from fresh flowering plants [9, 28].

Dosage forms.

On the domestic pharmaceutical market there are preparations containing *Caltha palustris*. These list include the complex homeotic drug Helium-Hel, which is made in the form of drops for oral use by the German company Biologische Heilmittel Heel GmbH.

The drug has immunomodulatory, anti-inflammatory, detoxification and drainage action, which is based on the activation of the body's defences

and normalization of impaired functions due to substances of plant, mineral and animal origin, which are part of the drug.

The tool is used for chronic diseases that are often exacerbated; infections that require stimulation of non-specific immunity; after the consequences of the toxic effects of drug therapy (antibiotics, chemotherapy, radiotherapy) [29].

The American company WHP (Washington Homeopathic Products), founded in 1873 under the name Washington Homeopathic Pharmacy, offers one-component homeopathic remedies from *Caltha palustris*. This company manufactures and markets its own homeopathic remedies and products manufactured by other companies in the world. *Caltha palustris* preparations are available in the form of tablets, granules and pills [30].

External:

• **Decoction** from the whole plant of the *Caltha palustris*. ½ teaspoon of crushed dried raw material is poured into a glass of boiling water, simmered for 5 minutes on low heat and cooled for 1 hour, then filtered. Burned areas of the skin are washed with this decoction.

• **Juice** from fresh leaves and flower buds are used as wound healing agents. Heals wounds, burns, abrasions, rheumatism and removes warts.

• **Poultices** for the treatment of skin diseases, removal of warts, treatment of neurodermatitis, eczema, burns, wounds and abrasions, treatment of rheumatism. To prepare them, fresh leaves are crushed and

boiled, wrapped in cheesecloth and applied to inflamed areas.

Internal:

• **Decoction from the *Caltha palustris***. Pour 1 teaspoon of crushed roots with 1 cup of boiling water, then bring to low heat and bring to a boil. Simmer on low heat for 10 minutes, cool and strain. Take the decoction 3 times a day for 1 tablespoon after meals in violation of metabolism, anemia and colds. 1 teaspoon taken with bronchitis, whooping cough, painful menstruation. Decoction has weak antitumor properties.

• **Decoction from leaves**. 1 teaspoon of the leaves is poured with a glass of boiling water, boiled for 15 minutes in a water bath, cooled for 45 minutes, filtered and boiled with water and brought to initial volume.

• **Infusion**. Take 1 teaspoon of crushed herbs and pour a glass of boiling water, wrap and infuse for 40 minutes. Take 1/3 cup 3 times a day while eating. Treats whooping cough, bronchial catarrh, painful menstruation.

• **Decoction from the whole plant of the *Caltha palustris***. Pour half a teaspoon of shredded raw material with a glass of boiling water; simmer for 5 minutes over low heat. After that, cool and strain. It is necessary to take 50 ml 3 times a day 30 minutes before meals in case of metabolic disorders, anemia, diathesis, colds, fever and as an anti-cingulate agent [23].

Patents

Quite often, *Caltha palustris* is used in oriental medicines. It is used in complex drugs of different spectrum of action. The data are presented in Table 1 [31].

Table 1

Drugs of oriental medicine based on *Caltha palustris*

No.	Name	Author	Country	Patent number	Application
1	2	3	4	5	6
1.	Chinese drug for the treatment of burns	Liu, Baning	China	CN104288359 A 2015-01-21	Astringent, anti-inflammatory, to promote wound healing, reduce exudation and edema, pain relief, reduces blistering, prevent infectious manifestations.
2.	Skin whitening cosmetics containing specific herbal extracts or their alkaline treatment products	Tachikawa, Makoto	Japan	JP2001206819 A 2001-07-31	The cosmetic agent effectively inhibits the production of melanin, whitens the skin and facilitates age-old plaque and freckles.
3.	Chinese drug composition for the treatment of prostatosis	Huang, Xing	China	CN1341427 A 2002-03-27	It can be used to treat prostatitis, prostate hyperplasia, orchitis, epididymitis, urethritis, genital herpes, oliguria, hydronephrosis and cystitis.
4.	Oral care product to improve tartar removal by ultrasound.	Hu, Xiaokun; Liu, Mei; Qin, Tianmu	China	CN109381385 A 2019-02-26	Helps to remove tartar by low power ultrasound, which prevents bleeding and infection.
5.	Non-toxic spray for the treatment of burns and technology of its preparation	Huang, Haining; Tang, Hongquan; Xu, Wenbing; Wang, Jianjun	China	CN107281303 A 2017-10-24	Effectively relieves pain in burns, accelerates the healing of the affected areas, has a bactericidal effect.

Continuation of Table 1

1	2	3	4	5	6
6.	Preparation of Chinese medicinal ointment for the treatment of burns and scalp		China	CN105125769 A 2015-12-09	Improves wound healing, improves blood circulation and reduces swelling. It is used for the treatment of burns.
7.	Chinese medicinal composition for the treatment of lumbar vertebral disorders.	Zhang, Zhongjian	China	CN103263621 A 2013-08-28	Promotes circulation and elimination of stagnation of blood, warming of channels. It can be used to treat lumbar hyperosteoegeny, lumbar intervertebral disc prolapse, lumbar muscle tension, and rheumatic or rheumatoid lumbar without side effects.
8.	Drug used in acute gouty arthritis and method of its use	Zhang, Lizhu	China	CN103585604 A 2014-02-19	Improves blood circulation, eliminates stagnation, promotes absorption of hardness, eliminates swelling and reduces pain. Applies directly to the area of swelling and pain, instantly feeling the cooling effect.
9.	The composition of traditional Chinese medicine for the treatment of hyperplasia of the breast	Dai, Huaying; Bi, Jianyao; Yang, Pengfei; Yu, Hongqiang; Liu, Rong	China	CN105770751 A 2016-07-20	Promotes blood circulation, softening and resorption of solid mass, improvement of immunity, equilibration of the endocrine system for the treatment of various types of lobular hyperplasia of the breast.

Toxicity and contraindications.

The toxicity of *Caltha palustris* is caused by the presence of a protoaneminin in a fresh plant. However, according to the literature, they are destroyed in heat treatment [9].

Fresh juice of the aerial part of the plant, collected in the period before flowering, can cause damage to the skin, namely blisters. Excessive intake of infusions or *Caltha palustris* teas causes pain in the stomach, nausea, vomiting, diarrhoea and allergic reactions [32].

4. Conclusions

Based on the results of the study and analysing the literature on the distribution, content of biologically active substances in the aerial part of *Caltha palustris*, the main aspects of its use in medicine and pharmacy, we can conclude that *Caltha palustris* is a promising medicinal plant of the Ranunculaceae family. The results of the work testify to the prospects of using *Caltha palustris* as a medicinal raw material for further thorough research, since the plant has long experience in ethnomedicine use and contains valuable biologically active compounds.

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