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Article



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THE GENUS THALICTRUM L. FROM THE FLORA OF AZERBAIJAN AS A RICH SOURCE OF BIOLOGICALLY ACTIVE SUBSTANCES

Abstract: The representatives of genus *Thalictrum* L., belonging to the *Ranunculaceae* family, have been used as medicinal plants for centuries due to their various pharmacological effects. Many species of these plants are used in medicine due to their investigated and confirmed therapeutic effects. In general, plants belonging to this genus are widely used in various regions of the world for stomach pain and ulcers, rheumatism, joint pain, nerve problems, fever, diarrhea, tumors, etc. The chemical composition of plants from *Thalictrum* genus is quite rich and many of their components are of great importance for the medical and pharmaceutical fields. In this regard, interest in this plant is increasing day by day. In Azerbaijan, 10 species of this genus are found and some species are being studied by our colleagues as a prospective plants.

Key words: The Genus *Thalictrum* L., the Flora of Azerbaijan, Biologically Active Substances, medicinal plants.

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Introduction

The representatives of the genus *Thalictrum* L. belonging to the *Ranunculaceae* family have been used as medicinal plants for centuries due to their

various pharmacological effects. Many species of these plants have been studied and are used in medicine for their confirmed therapeutic effects. In general, in different regions of the world, plants from

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this genus are widely used for stomach pains and ulcers, rheumatism, joint pain, nervous disorders, fever, diarrhea, tumors, etc.

The chemical composition of plants from the *Thalictrum* genus is quite rich, and many of their components are extremely important for the fields of medicine and pharmaceuticals. As a result, interest in this plant is increasing day by day. In Azerbaijan, 10 species of this genus are found, and some of them are being studied by our colleagues as promising medicinal plants.

Members of the genus *Thalictrum* L., belonging to the buttercup family, have been used as medicinal plants for centuries due to their diverse pharmacological effects. Many species of these plants are used in medicine due to their researched and proven therapeutic effects. In general, plants belonging to this genus are widely used in different parts of the world for the treatment of stomach pains and ulcers, rheumatism, joint pains, nerve problems, fever, diarrhea, tumors, etc. The chemical composition of plants of the genus *basilistnik* is extremely rich, and many of their components are of great importance for medicine and pharmaceuticals. In this regard, interest in this plant is growing day by day. There are 10 species of this genus in Azerbaijan, some species are studied by our staff as promising plants.

General information about plants of the *Thalictrum* L. genus

Plants of the genus *Thalictrum* L., which belong to the buttercup family (Ranunculaceae), include approximately over 190 species that are distributed in temperate regions. [12]. The majority of the representatives of this genus are herbaceous plants. The Ranunculaceae family is a large family that encompasses a wide variety of plant species and is widely distributed around the world. This family is classified based on various characteristics, including morphological features and molecular structure. [12].

It has been established that the Ranunculaceae family consists of approximately 62 genera and more than 2,500 species. These species are mainly distributed in the Northern Hemisphere, with some found in the Southern Hemisphere as well. Most members of the family are herbaceous plants, while some are shrubs or climbing, liana-like plants. Studies on their pollination have shown that most genera are pollinated by insects, whereas the *Thalictrum* genus (meadow-rue) is pollinated by wind. [16]. Their leaves are arranged alternately. The flowers contain both male and female reproductive organs, and their structure can be either simple or double. A characteristic feature of this family is the prominent floral receptacle, the large number of floral parts, and their spiral arrangement. The perianth (the outer parts of the flower) may be simple or double. The types of fruits found in this family are mainly follicles, achenes, and in some species, berries or nutlets.

This family was divided into three subfamilies by Tamura (1995) based on chromosome number, as well as fruit and flower structures. [12].

1. **Subfamily Ranunculoideae** – This is the subfamily with the greatest number and diversity of species. Among the plants in this subfamily, the genus *Ranunculus* (buttercup) is the most widespread. These plants are mainly herbaceous and are notable for the distinct symmetry of their flowers. Their fruits consist of many small seeds, which helps the plants spread over long distances. Representatives of this subfamily possess toxic properties, posing a potential danger to grazing animals and humans.

2. **Subfamily Coptidoideae** – Plants belonging to this subfamily are typically characterized by their elongated seeds and fragrant flowers. They can be found in various climate zones, particularly near bodies of water and in mountainous regions. Some species are used for medicinal or ornamental purposes.

3. **Subfamily Thalicthroideae** – The plants in this subfamily are herbaceous and are distributed across various ecosystems. They are commonly found in Asia, North America, and Europe. Some species can cause poisoning even in very small doses. The genus *Thalictrum* (meadow-rue) is one of the most extensively studied genera within this subfamily.

For centuries, representatives of the genus *Thalictrum* have been used as medicinal plants due to their various pharmacological effects. These plants were initially used in Russia's Siberian region for the treatment of gastrointestinal diseases, women's health issues, various neoplasms, and pulmonary tuberculosis. Later, they began to be widely used in Japan for treating stomach disorders. In China, the use of *Thalictrum* species has a long historical tradition.

In general, it can be stated that plants belonging to this genus are widely used in various parts of the world for the treatment of jaundice, stomach pain and ulcers, rheumatism, joint pain, nervous disorders, fever, diarrhea, tumors, and more. Many species of these plants have been studied and used due to their specific and scientifically confirmed therapeutic effects [7].

Plants belonging to this genus are distributed in various environments - mainly in the Northern hemisphere and subarctic climate zones. They can be found in forests, meadows, and even mountainous areas. They grow best in moist, humid, and shady environments. However, depending on environmental conditions, they have also adapted to different ecosystems. For example:

North America: Many species of this genus grow in various regions of North America, including Canada and the United States. In the United States, it is found especially in the east and northwest.

1. Europe: The species of the *Thalictrum* L. genus are also widespread in Europe. Species of this

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genus can be found in various regions, from England to France and Northern Italy.

2. Asia: Plants belonging to the *Thalictrum L.* genus can be found in areas such as Northern Asia, especially Russia and China. There are also representatives of this genus in some regions of Asia, such as the Himalayan regions.

3. Western and Southern Australia: In Australia, some species of the *Thalictrum L.* genus are widespread, especially in the southern regions.

In Azerbaijan, 10 species of this genus are found, and they are presented in the table below [2]:

Table 1. Plant species of the genus *Thalictrum* (meadow-rue) distributed in Azerbaijan (Fig. 1-4)

No	Species name in Azerbaijani	Species name in Latin
1.	Alpine Thalictrum	<i>Thalictrum alpinum</i> L.
2.	Foul-smelling Thalictrum	<i>Thalictrum foetidum</i> L.
3.	Isopyron Thalictrum	<i>Thalictrum isopyroides</i> C.A.Mey.
4.	Small Thalictrum	<i>Thalictrum minus</i> L.
5.	Curled Small Thalictrum	<i>Thalictrum minus</i> ssp. <i>Flexuosum</i>
6.	Buschianum Small Thalictrum	<i>Thalictrum minus</i> ssp. <i>buschianum</i>
7.	Simple Thalictrum	<i>Thalictrum simplex</i> L.
8.	Sultanabad Thalictrum	<i>Thalictrum sultanabadense</i> Stapf.
9.	Yellow Thalictrum	<i>Thalictrum flavum</i> L.
10.	Takabikum Thalictrum	<i>Thalictrum tacabicum</i> Pakravan & Assadi



Fig 1. *T. alpinum* L.



Fig 2. *T. foetidum* L.



Fig 3. *T. isopyroides* C.A.Mey.



Fig 4. *T. minus* L.

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The *T. minus* plant is widely distributed in Scandinavia, and its representatives growing in Bulgaria are primarily of endemic origin. In Bulgaria, the species of this plant are divided into two subspecies: *T. minus* L. subsp. *minus* and *T. minus* L. subsp. *Majus*. They mainly grow in meadows and moist, humid forests. However, *T. minus* L. subsp. *Majus* is more commonly found in sunny areas. This subspecies is distinguished from the other by its height, ranging from approximately 60 to 100 cm. Additionally, larger and more colorful flowers are characteristic of *T. minus* L. subsp. *Majus*. The endemic origin of these representatives has sparked significant interest in their phytochemical study, leading to extensive research by many scientists. [11].

The *T. minus* plant is also known by other names such as "qızqaytaran" or "qara qaytarma." In Azerbaijan, this plant is mainly found in forests, along mountain edges, in pastures, and in ravines. Its flower cluster is broom-like, and the flowers are typically reddish or greenish-brown in color. The plant is primarily harvested for use in April and May. Its young above-ground shoots can also be boiled and used for food purposes.

The chemical composition of plants of the genus *Thalictrum*.

The chemical composition of plants belonging to the *Thalictrum* genus is quite rich, and many of their components are of great importance for the fields of medicine and pharmacology. As a result of the development of science and technology, many new chemical components and the bioactivities of these components have been identified, their areas of application have been expanded, their medicinal significance has been studied, and thus, interest in these plants has been increasing day by day. [13].

The chemical composition of *Thalictrum* species can vary depending on the environment in which they grow and the specific plant species. It has been determined that these plants contain toxic alkaloids, glycosides, volatile substances, saponins, coumarins, tannins, flavonoids, and phenolcarboxylic acids. In addition, ascorbic acid has been found in the leaves, steroid saponins in the roots, and various oils in the fruits. [2, 14].

1. Alkaloids: Alkaloids possess a variety of biological effects and are the main chemical components found in these plants. It has been established that many different alkaloids are present in the plants, and each of them is distinguished by specific characteristics depending on the group to which they belong.

2. Saponins: Saponins are, after alkaloids, another major chemical component found in these plants, and they influence their biological activity. In the species *T. minus*, triterpenoid saponins such as Thallicoside A and Thallicoside B, as well as 3-O- α -L-arabinopyranoside, are widely distributed. Due to the properties and biological activity of triterpenoid

saponins, these plants have begun to be used in Japan for the treatment of stomach ulcers.

3. Flavonoids: These compounds are chemical substances that give color to plants and possess strong antioxidant properties. The main flavonoids found in species of the *Thalictrum* genus include rutin, apigenin, myricetin, isorhamnetin, and others.

4. Tannins: The main characteristic of these chemical compounds in plants is their antioxidant and antibacterial properties. Thanks to these features, the plants' resistance to infections is enhanced. Tannins are primarily concentrated in the aerial parts and roots of *Thalictrum* species. They are used to improve the digestive system and nervous function.

5. Essential Oils: Essential oils are substances that give plants their scent and have various therapeutic effects. They possess antibacterial and antifungal properties. The essential oils present in the plant vary depending on the environment in which it grows and the diversity of species.

6. Sugars: These substances provide energy in plants and are components involved in metabolic processes.

7. Fatty Acids: More than 21 unsaturated fatty acids have been identified in 17 species of the *Thalictrum* genus. One of the most notable characteristics of this genus is that it is the only known natural source of fatty acids with trans-double bonds at the 5th position [7]

In addition, protocatechuic acid, caffeic acid, coumaric acid, and β -sitosterol have been identified in the composition of *Thalictrum* species. It has been established that these types of compounds were first isolated and thoroughly studied from the aerial parts of the plant *Thalictrum atriplex* Finet et Gagnep. In the essential oils of *T. minus*, 12 compounds have been identified, including thymol (66.63%), paracymene (13.05%), γ -terpinene (7.32%), carvacrol (3.70%), and 1,8-cineole (according to Taherpour and Maroofi). [5].

Phytochemical analysis and conducted experiments on these species have led to the isolation of many alkaloids, which, in turn, possess a wide range of pharmacological effects. The first alkaloid isolated from *Thalictrum* species was the alkaloid thalicmine.

It was initially isolated from *T. minus* (Pulatova et al., 1966), and later obtained from *T. isopyroides* (Pulatova et al., 1968) and other *Thalictrum* species (Umarov et al., 1968). [3]. However, pharmacological studies on thalicmin are relatively limited.

Although there are numerous references regarding the isolation and identification of alkaloids from plants of this genus, the alkaloids of *T. isopyroides* have not yet been fully studied. Most of the literature covers the isolation, identification, and pharmacology of alkaloids from *T. isopyroides* found in various regions of the former Soviet Union. To date, at least 9 monomer alkaloids and 2 dimer

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alkaloids have been obtained from this plant. [17]. This includes: 1-oxo-2-methyl-6,7-dimethoxy-1,2-dihydro-isoquinoline, a derivative of isoquinoline; berberine, a derivative of protoberberine; protopine derivatives; aporphine derivatives octoteine, kabudine, thalisopine, and magnoflorine; dihydroaporphine derivative dihydrokoteine; oxoaporphine derivative thalicmine; and bisbenzylisoquinoline derivatives thalisopine and thalisopidine [17].

For the first time, scientists S.A. Khalil and P.L. Schiff isolated and extensively studied 12 alkaloids from the aerial parts and 6 alkaloids from the underground parts of the plant. They determined that the alkaloids obtained from the aerial parts include: tembetarin, a derivative of bisbenzylisoquinoline; taliporphine and magnoflorine, derivatives of aporphine; dihydrokoteine, a derivative of dihydroaporphine; thalicmine, a derivative of oxoaporphine; and thalisopidine, a derivative of bisbenzylisoquinoline. [3, 17].

The *T. isopyroides* plant has toxic properties. Therefore, special care must be taken when using it, and the recommended dosage should not be exceeded. To reduce and prevent potential toxicological risks, the dosage and duration of the plant's alkaloids must be carefully considered. Additionally, the interactions of these alkaloids with other plants and medicinal substances should be evaluated, and preliminary trials must be conducted. It has been specifically determined that these substances are not recommended for use in cases of bradycardia (slower than normal heart rate), weak heart function, atonic constipation, individual intolerance, as well as for pregnant women and children. The alkaloids in the plant disrupt metabolic processes in the body and negatively affect the liver and kidney functions.

During poisoning, alkaloids in high doses affect the central nervous system in particular - causing headaches, dizziness, vomiting, etc. and other symptoms. In the digestive system - abdominal pain, diarrhea, other digestive problems are observed. Also, allergic reactions, swelling, rash, redness are among the most common symptoms.

One of the main alkaloids in the plant is magnoflorine. Based on the experiments conducted, various toxic effects of this alkaloid on living organisms have been determined. Thus, magnoflorine was found to be cytotoxic against U251 (brain tumor cell line) and HepG2 (hepatocellular carcinoma cell line). In other experiments, magnoflorine was shown to cause cancer in various cell groups - lung, ovary, skin melanoma. However, acute toxicity and long-term toxicity tests on animals have not yet been conducted. [19]. It should be noted that the roots of this plant are highly dangerous for animals and cause poisoning. In such cases, large livestock show symptoms such as colic—acute or severe pain caused

by various factors—diarrhea, and disruption of the heart, kidneys (including the appearance of protein and even blood in the urine), and central nervous system (anxiety, convulsions). In addition to these symptoms, various studies have been conducted on animals, revealing contraindications. The main symptoms of poisoning in horses include rapid breathing, shortness of breath, restlessness, foamy discharge from the nostrils, coughing, cyanosis of the mucous membranes, a temperature above 40°C, and others. In other experiments, cases of poisoning in pigs were studied, and the main symptoms identified were vomiting, sharp abdominal pain, diarrhea, kidney dysfunction (polyuria), pulmonary edema, etc [2,17].

Another major alkaloid present in the plant is berberine. LD₅₀ values for berberine poisoning may vary depending on the way it enters the body and the body's activity. Berberine poisoning is more common in animals. It is known that diarrhea, nausea, vomiting, paralysis, stomach ulcers, etc. occur. Also, during subacute poisoning, liver and kidney enlargement, body weight gain, and immunotoxicity are observed. During subchronic poisoning with berberine, ALT (alanine aminotransferase) and AST (aspartate aminotransferase) values changed, and lung and liver damage was observed. [15].

The use of *Thalictrum* species in folk medicine, their pharmacological properties, and medicinal preparations. Based on the conducted research and the information obtained, it has become clear that plants belonging to the *Thalictrum* genus have a special role in both folk and scientific medicine. They are used for various purposes, including anti-inflammatory, antiseptic, analgesic, diuretic, antipyretic, detoxification, anti-tumor, hypotensive, and for eye-related problems, among others. Among the most studied effects are anti-tumor, antimicrobial, and anti-inflammatory properties. [9].

Many species of the *Thalictrum* genus contain various alkaloids, especially berberine and magnoflorine, which are widely used for medical purposes. These include neuropsychopharmacological, immunomodulatory, anti-inflammatory, antioxidant, and antifungal activities. A tincture made from *Thalictrum* has effective properties in the early stages of hypertension and is used as a significant substance in the treatment of heart rhythm disturbances and blood circulation problems. Many scientists have even discovered the anticancer properties of magnoflorine. However, these effects are not yet fully understood. [8].

One of the most widespread alkaloids found in plants belonging to this genus is berberine. Since the mid-19th century, berberine has been used for various purposes. This bitter-tasting alkaloid has been applied to improve the digestive system and appetite, and as a hemostatic agent in cases of uterine bleeding. In later periods, it was also used as a laxative. Additionally,

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the berberine alkaloid is used in the treatment of heart rhythm disorders, diabetes, and hyperlipidemia. Based on scientifically proven data, it can be stated that berberine is a plant-derived alkaloid of significant importance in preventing atherosclerosis, type 2 diabetes, regulating high blood pressure, and inhibiting the development of cancers (such as liver, lung, ovarian, and prostate cancers). It stimulates the glycolysis process and helps normalize the body's insulin secretion. Berberine has also been used in the treatment of patients with various neurotic disorders, with positive outcomes. Studies have shown that berberine-containing tablets improved metabolic processes related to Alzheimer's disease and reduced susceptibility to depression. Its antifungal, antibiotic, and antiviral activities have also been confirmed. [4, 20].

In tests conducted on animals, berberine has significantly reduced liver toxicity, acting as a hepatoprotective agent. However, due to its poor absorption when taken orally and a range of toxic effects, the use of berberine is limited. Additionally, common side effects include gastrointestinal issues such as constipation and diarrhea. Berberine-containing dietary supplements can be in the form of

tablets or capsules. However, it is recommended to consult a doctor before starting its use, begin with small doses, gradually increase the dosage, and not exceed the recommended optimal dose. It has been determined that an alcoholic solution made from *T. minus*, one of the most widely distributed species, possesses cytostatic activity. The reason for this activity is the presence of the compound tallikoside A found in it. Tallikoside A has the ability to act against various tumors and eliminate them. Alcoholic tinctures made from the above-ground parts of the plant can also be used to treat high blood pressure and as a sedative. Additionally, this tincture has been found to have diuretic properties.

In addition, in Azerbaijani folk medicine, tea made from dried and purified roots is used as an expectorant to soothe coughs and for colds. Since ancient times, it has been established that aqueous infusions made from its roots are effective in treating diseases such as jaundice, kidney diseases, epilepsy, and malaria. Additionally, an ointment made from the plant's leaves can be used as a supportive remedy to accelerate wound healing. [1].

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