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PLANT SPECIES OF THE GENUS *Pedicularis* L. IN THE TERRITORY OF THE WESTERN BALKANS: OVERVIEW OF USE IN TRADITIONAL MEDICINE, PHYTOCHEMISTRY, BIOLOGICAL AND PHARMACOLOGICAL ACTIVITY

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ABSTRACT. Modern pharmacotherapy is based on chemical substances derived from plants and herbal medicine from the past. *Pedicularis* L. is one of the largest genera of hemiparasitic flowering plants, with over 500 species known. It is mostly found in the cold highlands of the northern hemisphere. Numerous endemic *Pedicularis* species may be found in the Balkans, demonstrating their significance in plant endemism. However, several of these species may face conservation issues due to human activities like habitat fragmentation, agricultural development, and other pressures. Monitoring their numbers, protecting their habitat, and increasing public understanding of their significance are the goals of conservation initiatives. By conducting field surveys and molecular analysis to comprehend their evolutionary relationships, researchers are still working to improve the taxonomic classifications of Balkan *Pedicularis* species. The chemicals from *Pedicularis* plant species that have been identified so far have been shown to have anti-tumor, hepatoprotective, immunomodulatory, anti-inflammatory, antidiabetic, antibacterial, antifungal, analgesic, and diuretic properties in research published in the literature. This paper provides an overview of previous research in the Western Balkans.

Keywords: *Pedicularis*, traditional medicine, pharmaco-biological activity, phytochemicals.

INTRODUCTION

Natural compounds derived from microbes, minerals, plants, and animals have a significant role in medicine. Since ancient times, when their medicinal properties were first recorded, they have been an important source of pharmaceutical formulations (DHAMI, 2013). The unique chemical diversity of natural products, developed over millions of years, results in a wide range of biological activities and drug-like properties (YUAN *et al*., 2016).

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Using herbs as medicine and searching for bioactive compounds in plants is not a new practice. Native herbs have been used for centuries to treat various illnesses. For example, archaeological evidence indicates that marshmallows were used for various purposes by Neanderthals, who lived 60,000 years ago in what is now Iran (VICKERS and ZOLLMAN, 1999). All around the world, traditional medicine still makes extensive use of these plants. Historically, plants have been used for a wide range of medical purposes, from curing illnesses and alleviating symptoms to causing poisoning or even death. Today, it is estimated that there are between 250,000 and 350,000 distinct plant species on Earth. Less than 10% of it was utilized for human or animal nourishment, but a substantially higher amount was most likely employed for medical purposes (KARTAL, 2007).

With more than 500 species identified, the genus *Pedicularis* L. (family Orobanchaceae) is among the largest genera of hemiparasitic flowering plants and is primarily found in the chilly northern hemisphere's mountains. The word "pediculus" (meaning "louse") refers to the ancient English belief that cattle grazing on these plants would subsequently become infested with lice. This is the source of the genus name, which has Latin origins (VENDITTI *et al*., 2016). Species of this genus are widely distributed across Europe, especially in mountainous regions, as well as in North Asia, North America, and the Mediterranean basin (Fig. 1). With roughly 70 species, Europe has the most biodiversity, followed by India with 83 species and China with 350 species, of which 271 are endemic (LI *et al*., 2014; YATOO *et al*., 2016). These species are typically found in meadows and grasslands with sparse understory vegetation (NICOLINI, 1960).

The Balkans are a significant center for *Pedicularis* species, characterized by a wide variety of floral characteristics and leaf structures. The distribution of these species in the region is influenced by factors such as altitude, soil type, and moisture levels. As a result, they flourish in diverse habitats including alpine meadows, subalpine zones, mountain slopes, and lower-elevation grasslands. *Pedicularis* flowers are arranged in dense spikes or clusters along the stem, displaying a stunning range of colors such as pink, purple, yellow, and white. In the Balkans, the leaves of *Pedicularis* species are deeply divided or lobed, forming basal rosettes or arranged alternately along the stem and resembling fern fronds. Certain species in the region are hemiparasitic, relying on host plants for nutrients through haustoria, which enhances their ability to survive in nutrient-poor soils. The Balkans harbor numerous endemic *Pedicularis* species, underscoring their significance in regional plant endemism. However, human activities such as habitat fragmentation, agricultural expansion, and other pressures present conservation challenges for these species. Conservation efforts focus on habitat preservation, population monitoring, and raising awareness about their ecological importance. Researchers are actively refining the taxonomic classifications of Balkan *Pedicularis* species through field surveys and molecular analyses to better understand their evolutionary relationships (POPOVIĆ *et al*., 2020).

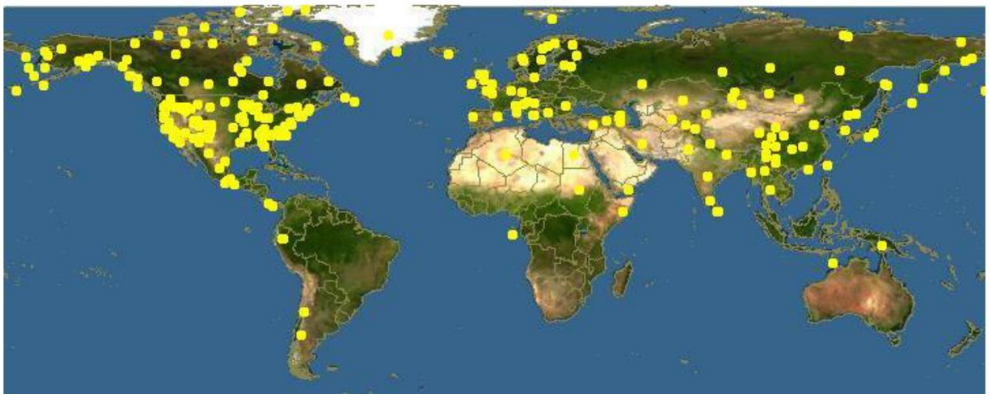


Figure 1. Distribution of plant species of the genus *Pedicularis* (FREZZA *et al*., 2019).

In this review paper, we present a description and the occurrence of *Pedicularis* species in the Western Balkans, along with a wide range of pharmacological and biological activities exhibited by extracts obtained from various parts of different species within the genus *Pedicularis*.

MATERIALS AND METHODS

Our study employed a systematic literature review approach to gather relevant information. Relevant data was extracted from 89 studies. Searches were conducted using the Web of Science, PubMed, Scopus, and Google Scholar databases. The search strategy utilized a combination of keywords including "*Pedicularis* species," "traditional medicine," "pharmacological activity," "biological activity," and "phytochemicals." Articles identified through these searches were screened based on their relevance to the medicinal and pharmacological properties of *Pedicularis* species. Data extraction focused on documented uses in traditional medicine, observed pharmacological activities, biological effects, and analysis of phytochemical constituents reported in the literature.

RESULTS AND DISCUSSION

Plant species of the genus Pedicularis presented on the territory of the Western Balkans

Most *Pedicularis* plants are herbaceous and perennial, and grow up to 50 cm in height. Biennial or annual species are present but extremely uncommon. From a morphological perspective, these species are distinguished by big, fleshy roots, which are frequently central and include special organs called haustoria that feed the lymph of neighboring plants (FREZZA *et al*., 2019). The elegant, long-flowering inflorescences, tidy blooms, and exquisite leaves are the distinguishing features of the genus *Pedicularis*. The crown is colored in shades of purple, red, pink, yellow, orange, pale yellow, and white (LI *et al*., 2014; KRIVKA and HOLUBEC, 2015). Figure 2 shows the plant species of the genus *Pedicularis* that are represented in the territory of the Western Balkans.

a) Pedicularis brachyodonta Schloss. & Vuk. *(„short-toothed louse“)* (Fig 2. m)

The plant species *P. brachyodonta* is an endemic species. It grows primarily in the temperate biome. The original area of this species is the western part of the Balkan Peninsula, i.e. Albania, Bulgaria, North Macedonia, Montenegro, Bosnia and Herzegovina, Croatia, Serbia, and Greece. The tall, upright stems of *P. brachyodonta*, which can grow as high as 30 – 80 centimeters, are one of its defining characteristics, together with finely divided leaves and clusters of yellow to orange flowers. The highly split leaves and clusters of yellow to orange blooms of *P. brachyodonta* are its distinguishing features. It usually grows on rocky or gravelly soils in alpine and subalpine meadows. Due to its adaptation to high altitudes, this species can coexist with other alpine plants. Its ecological role likely includes providing habitat and food sources for pollinators and herbivores (SCHLOSSER and VUKOTINOVIĆ, 1857; MUSTAFA *et al*., 2015).

b) *Pedicularis dasyantha* Hadač (Fig 2. b)

P. dasyantha is indigenous to the Balkan Peninsula, where it can be found in North Macedonia, Serbia, Albania, Bulgaria, Greece, and Bosnia and Herzegovina. It inhabits meadows in the montane and subalpine regions, usually at higher elevations. This species is characterized by clusters of flowers that vary in color from pink to purple, borne on tall stems. Its fern-like leaves are deeply divided or lobed, contributing to its distinctive appearance.

Typically growing in dense tufts or clumps, it enhances the natural beauty of its environment. *P. dasyantha* thrives in montane and subalpine settings with moderately moist soils. As a hemiparasitic plant, it forms associations with other plants, obtaining nutrients through specialized root structures called haustoria. These connections enable its survival in nutrient-deficient conditions. Maintaining species montane and subalpine environments is essential to its continued survival, while precise conservation assessments may differ based on local populations and regional circumstances. The variety of *Pedicularis* species found in the Balkans, of which *P. dasyantha* is just one example, emphasizes the significance of the area for the preservation of biodiversity and botanical study (HADAČ, 1942; ODASZ and SAVOLAINEN, 1996).

Figure 2. Plant species of the genus *Pedicularis* represented in the territory of the Western Balkans: a) *Pedicularis acaulis* Scop., b) *Pedicularis dasyantha* Hadač, c) *Pedicularis ferdinandi* Bornm., d) *Pedicularis friderici-augusti* Tommas., e) *Pedicularis graeca* Bunge, f) *Pedicularis hacquetii* Graf, g) *Pedicularis heterodonta* Pančić, h) *Pedicularis hoermanniana* K. Malý, i) *Pedicularis leucodon* Griseb., j) *Pedicularis limnogena* A. Kern., k) *Pedicularis mixta* Gren., l) *Pedicularis oederi* Vahl, m) *Pedicularis brachyodonta* Schloss. & Vuk., n) *Pedicularis petiolaris* Ten., o) *Pedicularis sceptrum-carolinum* Schrank, p) *Pedicularis sylvatica* Linnaeus, q) *Pedicularis superba* Franch. ex Maxim., r) *Pedicularis verticillata* Linnaeus.

c) Pedicularis sceptrum-carolinum Schrank (Fig 2. o)

Found throughout Bosnia and Herzegovina, Slovenia, and other sections of the Balkans, the species *P. sceptrum-carolinum*, commonly called royal lousewort, bears tall spikes of blooms that range in color from purple to pink (LINNAEUS, 1753). It thrives in alpine and subalpine meadows, often found on rocky slopes or in open grasslands. Adapted to montane and subalpine environments, this plant can coexist with other alpine flora. Its ecological role likely includes providing habitat and sustenance for pollinators and herbivores. Conservation efforts should prioritize preserving the alpine habitats where *P. sceptrum-*

carolinum thrives and monitoring population declines due to habitat degradation or climate change (WRÓBLEWSKA, 2013; NÄRVÄ, 2022).

d) *Pedicularis mixta* Gren. (Synonym is *Pedicularis pyrenaica*) (Fig 2. k)

This species is originally found in the Balkans, which include Serbia, Albania, Bosnia and Herzegovina, and Montenegro. Deeply lobed leaves and spikes of pink to purple flowers define *P. mixta*. Found primarily in moist or swampy habitats, *P. mixta* thrives in montane and subalpine meadows. Its adaptation to damp environments enables its presence in wet meadows and along stream banks. Ecologically, it interacts with diverse species and plants native to wetlands. Inflorescence with many blooms (15–35), slowly opening into a long, spicy raceme. A crown with a delicate pink lower lip and a purple upper lip. Appendices and calyx with thick, woolly pubescence (GRENIER and GODRON, 1853; SORIANO, 2021).

e) *Pedicularis oederi* Vahl (*„Oeder's Lousewort“*) (Synonym is *Pedicularis foliosa* subsp. *oederi – “bearded louse“*) (Fig 2. l)

Found throughout Bosnia and Herzegovina, Slovenia, and Croatia, among other places in the Balkans. The species height is 20–50 cm. Leaves pinnately, the larger ones over 4 cm wide, with toothed tips. The crown is pale yellow. (LINNÉ, 1767; HORNEMAN, 1860; BONNIER *et al*., 1926). It grows in montane and subalpine meadows, frequently in patches of grass or rock. Due to its adaptation to montane environments, this species can coexist with other alpine plants. Its ecological function might involve giving pollinators and herbivores a place to live and food. The goal of conservation activities may be to protect the alpine environments that are home to *P. oederi* (YU *et al*., 2014; LAUBER *et al*., 2018).

f) Pedicularis sylvatica Linnaeus (*„cup louse“ or „Common Lousewort“*) (Fig 2. p)

Found in North Macedonia, Greece, and Bulgaria, among other places in the Balkans. *P. sylvatica* is a semiparasite that grows to a height of 5–20 cm and can be either biennial or perennial. It has creeping runners that emerge from the mid-erect stem's base. The leaves are either pinnate or pinatisect, while the stems remain unbranched. Dorsiventral, light-purple or pink flowers create a inflorescence. Its fruit is an egg-shaped capsule that is concealed within an inflated calyx. The plant can be found in lowland moors and transitional peatlands of the Scheuchzerio-Caricetea nigrae class, moist heathlands of the Sphagno-Ericetalia order, and swards with *Nardus stricta* of the Nardetalia order. Additionally, it can be found in the *Molinion caeruleae* alliance's wet meadows and the *Magnocaricion* alliance's big sedge rushes (LINNAEUS, 1753; RADKE and SOTEK, 2017).

g) Pedicularis verticillata Linnaeus (*„red (vertebrate) louse“*) (Fig 2. r)

Found throughout the Balkans, especially in Bulgaria, Greece, and North Macedonia, *P. verticillata* is distinguished by its deeply lobed leaves and whorls of purple to pink flowers (LINNAEUS, 1753). It usually grows on rocky or gravelly soils in alpine and subalpine environments. Because of its adaptation to high altitudes, this species may coexist with other alpine plants. Its ecological role likely includes providing habitat and sustenance for pollinators and herbivores. Conservation efforts aim to preserve the alpine environments that support *P. verticillata*. Monitoring populations for declines due to habitat degradation or climate change is crucial for conservation planning (MURAYAMA *et al*., 2019).

h) *Pedicularis hacquetii* Graf (Synonym is *Pedicularis exaltata*) (Fig 2. f)

Found in North Macedonia, Bulgaria, Greece, Albania, and other areas of the Balkans. Deeply splited leaves and spikes of pink to purple flowers are produced by *P. hacquetii*. It grows in meadows that are alpine or subalpine, frequently in rocky or grassy settings. Because of its adaptation to high-altitude environments, this species may coexist with other alpine

plants. It interacts with pollinators and other organisms and is involved in the dynamics of the alpine ecosystem. Although not always regarded as a threat, conservation initiatives in the Balkans may involve population monitoring and the evaluation of possible dangers such as habitat disruption and climate change (TĚŠITEL *et al*., 2018).

i) Pedicularis superba Franch. ex Maxim. (Fig 2. q)

Found in North Macedonia, Greece, and Bulgaria, among other places in the Balkans. *P. superba* is distinguished by its highly split leaves and towering spikes of pink to purple flowers (MEYER, 1888). It usually grows in meadows that are alpine or subalpine, with rocky or grassy environments. Because of its adaptation to high altitudes, this species may coexist with other alpine plants. Its ecological function might involve giving pollinators and herbivores a place to live and food. Preserving the alpine environments where *P. superba* is found and keeping an eye on population decreases because of habitat degradation or climate change are two possible conservation goals (YU *et al*., 2013; LI *et al*., 2021).

j) Pedicularis friderici-augusti Tommas. (*„Friedrich-August's louse"*) (Fig 2. d)

Another "royal" species, *P. friderici-augusti*, is named for "Majestati Friderici Augusti, Saxonum Magnanimi Regis" and is found in Greece, Italy, and the Balkan Peninsula. It is only found in a few North-East limestone mountains in Greece, where it grows on exposed rocky slopes typically between 1200 and 1800 meters high where its reddish-pink corollas and densely hairy inflorescence make it stand out (SCHLECHTENDAL and GARCKE, 1839; DIMOPOULOS *et al*., 2013).

k) Pedicularis ernesti-mayeri Stevanović, Niketić and D. Lakušić (*"Ernest Mayer's Lousewort"*)

P. ernesti-mayeri, is a species of flowering plant that is widely distributed in temperate and alpine regions of the world. The native range of this species is Montenegro. It usually grows in alpine and mountainous environments, frequently in bogs, damp meadows, and by streams. The slender, erect stems of *P. ernesti-mayeri* can grow up to 20–40 cm (8–16 inches) in height. Along the stem, the deeply lobed leaves are placed. The flowers are usually purple to pinkish-purple in color and are organized in thick, terminal spikes. Every bloom is shaped like a tubular object. *P. ernesti-mayeri*, like other *Pedicularis* species, is an important pollinator food source for butterflies and bees in their natural habitats. Climate change, competition from invasive species, and habitat loss from human activity are some of the dangers that some populations of *P. ernesti-mayeri* may face, while specific conservation evaluations may differ based on the region and jurisdiction. Population monitoring, habitat restoration, and preservation are examples of conservation activities (STEVANOVIĆ *et al*., 2001; ROALSON *et al*., 2013; DIMOPOULOS *et al*., 2016; SHUKA *et al*., 2017).

l) Pedicularis heterodonta Pančić (*„red louse"*) (Fig 2. g)

It is native to the center region of the Balkan Peninsula and grows in Serbia and eastern Bosnia, extensively distributed over Serbia's southwest and southeast: Kopaonik Mountain, Ivica Mountain, Suva Mountain, Ruplje, Basara, Vidlič, Vlasina, Ozren, Zlatar, environs of Užice, Radan Mountain, and Prokletije Mountain. On the rocks of the spruce belt, mostly serpentinite and silicates; limestone is less common; on the meadows of the subalpine and alpine belts. It has been observed in pastures of the *Poetum violaceae*, *Agrostidetum vulgaris*, *Brometum erecti*, and *Danthonietum calycinae* kinds, as well as in white pine forests. An important species for the world's vascular flora is found in Serbia. The European Red List has it listed. It is not protected as a natural rarity in Serbia. It has the classification LRlc (low probability of danger-last concern) under the IUCN classification system. In the national parks of Kopaonik, Tara, Shar and Prokletije, and it is classified as equally

endangered. Plant is perennial and has thicker roots. Simple stem that is erect and nearly smooth. The leaves have two pinnate divisions, are nearly smooth, and have lobe-toothed tips with short, sharp teeth made of cartilaginous material. The middle and upper parts of the inflorescence are three-lobed or toothed, not longer than the calyx, while the lower part is leaf-like and pinnately divided. The sepals are covered with sparse, curled hairs. Calyx: egg-shaped, three-lobed, with an oblong central lobe and obliquely oval, two-toothed side lobes; smooth or coated in sparse, curly hairs (PANČIĆ, 1884; SINGH *et al*., 2019).

m) Pedicularis hoermanniana K. Malý (*„mountain louse"*) (Fig 2. h)

P. hoermanniana is a shrubby plant that is found in montane and subalpine mesophyllous or wet meadows, and shrubby areas. It is distributed throughout parts of Central and Northeast Italy, Slovenia, and much of the Balkan Peninsula (east to the Stara Mountain in Bulgaria and south to Mts. Pieria and Tymfi in NW Greece, Albania, Bosnia and Herzegovina, and Croatia). A perennial herbaceous plant, mountain oleander can grow up to 40–50 cm and occasionally even 100 cm. The stem has several leaves and is erect, grooved, and naked. The leaves have deeply pinnately divided lobes with serrated edges. Ground leaves are on petioles that are comparatively lengthy. The arrangement of stem leaves, blooming leaves, and flowers alternates. Like an inflorescence, the flowers are arranged in a compact spike or cluster at the apex of the stalk. The flowering leaves are lanceolate in the top half of the flower and resemble the stem leaves in the lower part, which are much longer than the blooms. The corolla is pale yellow, and about 2 cm long. Four viable stamens and an ovary are present in the flower. The fruit has many seeds and resembles a quiver. The life form indicates that it is a hemicryptophyte, with a blossoming period from June to August. It is included in the element of Balkan flora (BECK, 1900; AUTHIER, 2000; NIKOLIĆ and TOPIĆ, 2005; DAKSKOBLER, 2015; TEOFILOVSKI, 2018).

n) Pedicularis leucodon Griseb. (*"colorless/pale colored/louse"*) (Fig 2. i)

This species is indigenous to parts of Europe, especially France, Switzerland, Italy, Austria, Slovenia, North Macedonia, Eastern Albania, and Northern Greece. It usually grows on rocky slopes and alpine meadows in hilly areas. The leaves of *P. leucodon* are strongly lobed and have slender, upright stalks. The leaves may have serrated edges and are arranged along the stalk. The flowers might be white or pale pink, and they are typically carried in dense spikes. *P. leucodon* is a plant species that has evolved to alpine conditions. As such, it contributes to the ecosystem by giving different insects and other wildlife habitat and food. It might also help stop soil erosion and stabilize alpine ecosystems. *P. leucodon's* conservation status may alter in response to various circumstances, including habitat degradation, loss, and climate change. Two previous investigations conducted on the land of Mt. Lozen reported the existence of this Balkan endemic species; however, the floristic region of Sredna Gora was not noted (ASSYOV *et al*., 2012; TEOFILOVSKI, 2017).

o) Pedicularis limnogena A. Kern. (*"water louse"*) (Fig 2. j)

P. limnogena, also referred to as *"Marsh Lousewort"*, is a type of flowering plant. Typically, wetland areas, including marshes, bogs, and stream banks, are home to this species. This species' natural range extends from Romania to the northern Balkan Peninsula. It is mostly found in the temperate biome. The leaves of *P. limnogena* are deeply lobed along the upright stem. The flowers can be many colors, most commonly pink or purple, and are carried in dense spikes (WETTSTEIN, 1863). *P. limnogena*, a plant species that has adapted to wetlands, contributes to the ecosystem by giving different insects and other wildlife a place to live and food. It might also prevent soil erosion and stabilize wetland habitats. *P. limnogena*'s conservation status can change in response to several causes, including fragmentation, degradation, and loss of habitat. Preserving habitat, restoring damaged wetlands, and

monitoring populations to identify trends and hazards are a few examples of conservation initiatives (COLDEA *et al*., 2018).

p) Pedicularis petiolaris Ten. (Fig 2. n)

It grows in the mountains of central Italy, the southwest and central regions of Bulgaria, the west and south of the former Yugoslavia, and the northern Pindos of Greece and Albania. It grows on rocky slopes, alpine grasslands, serpentinites, shales, and limestones at altitudes of 1500–2600 meters. It flowers in June and July. Perennial herb growing up to 20 (-30) cm tall. Base leaves are ovate-lanceolate, 2-pinnatisect, with narrow, incise-dentate, apiculate segments, glabrous save for villous petioles. Though smaller, cauline leaves are similar. Bracts have a glabrous distal petiole that is crispate-hairy and visibly longer than the calyx. Ten to twelve millimeters, calyx tubular-campanulate, lanceolate, whole or sparsely toothed. Purplish-red, 18–22 mm corolla that is glabrous save for a row of hairs on either side of the tube; the upper lip is noticeably curled, short-beaked, and has two teeth close to the apex. The oblong-ovoid capsule is 1.5 times longer than the calyx (STEVANOVIĆ *et al.,* 2001).

q) Pedicularis graeca Bunge (*„petiole-leaved louse"*) (Fig 2. e)

Native to Greece on the northern Peloponnese and the southern half of Albania. The species could be found on Stony alpine grasslands between 1500 and 2400 m, preferably on calcareous substrates but also on schists or serpentinites. It flowers from June to August. Perennial herb with erect or ascending, densely lanate stems up to 20–30 cm of height. Basal leaves: ovate-lanceolate, 2-pinnatisect with ovate-lanceolate, incise-dentate segments, glabrous except for lanate petioles. Lesser, subsessile, and cauline leaves 0–2 mm. After flowering, the inflorescence matures and lengthens. Higher bracts gradually get narrower, lanceolate, and more or less dentate; lower bracts are leaf-like, pinnatifid, and longer than the calyx. Including the narrow, lanceolate, 4-5 mm, shallowly toothed to complete teeth, the calyx is thickly lanate, measuring 10–14 mm. Corolla 20–25 (–30) mm, yellow, glabrous; lower lip crenulate; upper lip distally curled, short beaked. Ovoid capsule, 1.3 times longer than calyx (GRAEFF, 1843; DIMOPOULOS *et al.*, 1992).

r) Pedicularis acaulis Scop. (*„ground louse"*) (Fig 2. a)

It is often referred to as the stemless lousewort. This species is indigenous to parts of Europe, especially the Swiss Alps, the Northwest Balkan Peninsula, France, Switzerland, Italy, Austria, Slovenia, Bosnia анд Herzegovina, and Croatia. It usually grows in mountainous areas, such as grasslands, rocky slopes, and alpine meadows. The blooms of *P. acaulis* are immediately produced from a basal rosette of leaves, giving rise to its characteristic stemless growth pattern (PULEVIĆ, 2005; HASSLER, 2018). The ground aphid is a perennial herb with seemingly terrestrial leaves and blooms that lacks a discernible stem. The dark green leaves measure 5–20 cm in length and 1.5–2.5 cm in width. It is broad, linear-oblong, and pinnately divided into up to 12 pairs of glabrous ovate-oblong segments that are sessile and pinnately divided. The leaf spindle and petiole have hairs. In the center of a rosette of leaves are bluish or pinkish-white blooms that are unisymmetrical, bisexual, and have double flowers. The flowers are 1–3 cm long. There are five connected leaves on the stem. The calyx's tube is as complete as its five free lobes, which are lanceolate, have serrated edges, and have leaves. Five linked petals, each with two lips, measure up to 35 mm in length. The wreath has a long, straight tube that is sickle-curved, with a rounded upper lip and a three-parted lower lip at the top. The calyx and corolla tube are nearly the same length. The flower bears four dioecious stamens, each of which is glabrous and has a point at the base. Two fertile leaves, a head-shaped neck, a snout, and an enlarged two-stage fruiting body make up the pistil. When fully grown, the fruit just barely overhangs or does not overhang the

multi-seeded calyx. It is compressed, globular, and obliquely acuminate in the upper section (NIKOLIĆ and TOPIĆ, 2005).

s) Pedicularis ferdinandi Bornm. (Fig 2. c)

The plant has pubescent to villose stems, glabrous, bipinnatisect leaves, segments that are oblong to lanceolate and dentate, and very short, white lanate racemes with corollas that are 22–25 mm long, 4–5 cm in size, and pale rose in color. Bloom in the spring and form tuft. Fertilization requirements include an alpine home, wet, humous, gravelly soil, and a semi-shaded location. Propagation seed: tiny, slightly covered seed in winter, germinating in 1 to 3 months, and dividing in spring at 10–16 °C, right before new growth starts (DIMOPOULOS *et al.*, 2016; VOGT *et al.*, 2018).

Characteristic of secondary metabolites presented in plant species of the genus Pedicularis

Phenols, phenylethanoids, phenylpropanoids, flavonoids, iridoids, lignans, and alkaloids are among the primary phytoconstituents of the genus *Pedicularis* (YATOO *et al.*, 2017; FREZZA *et al.*, 2019). The two most prevalent compounds in the entire genus *Pedicularis* are the iridoids (Fig. 3) and the phenylethanoid glycosides (Fig. 4). However, certain compounds have also been found exclusively in individual species (VENDITTI *et al.*, 2016; FREZZA *et al.*, 2019). The structures of most of the chemicals found in *Pedicularis* are shown below. The structures are drawn in *Chemdraw Ultra 8.0*.

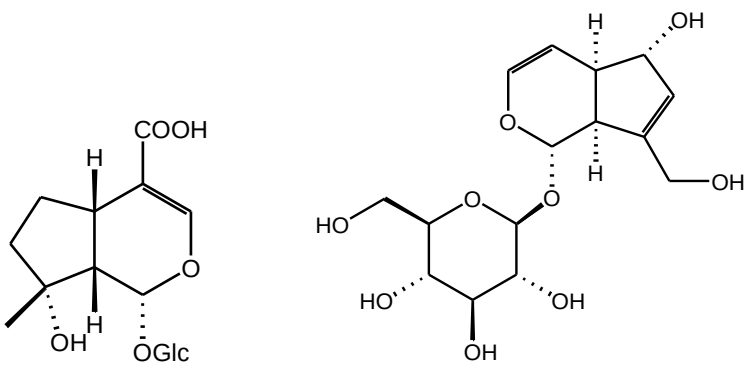
Iridoid glycosides

A class of monoterpenoid chemicals known as iridoids has a broad range of biological activities and a high therapeutic value (LI *et al.*, 2014). Researchers studying *Pedicularis* iridoids found that they have many biological effects, including protecting the liver, stopping DNA mutations, delaying muscle fatigue, fighting tumors, reducing oxidation, and stopping blood clots (SHAO *et al.*, 2018).

Glycosides and iridoid compounds' C1-OH mix readily. At the same time, carbonyl group derivatives are frequently used to replace carbon atom. This genus has yielded 62 identified iridoid glycosides thus far and some of them are shown in Fig. 3 (VENDITTI *et al.*, 2016; FREZZA *et al.*, 2019).

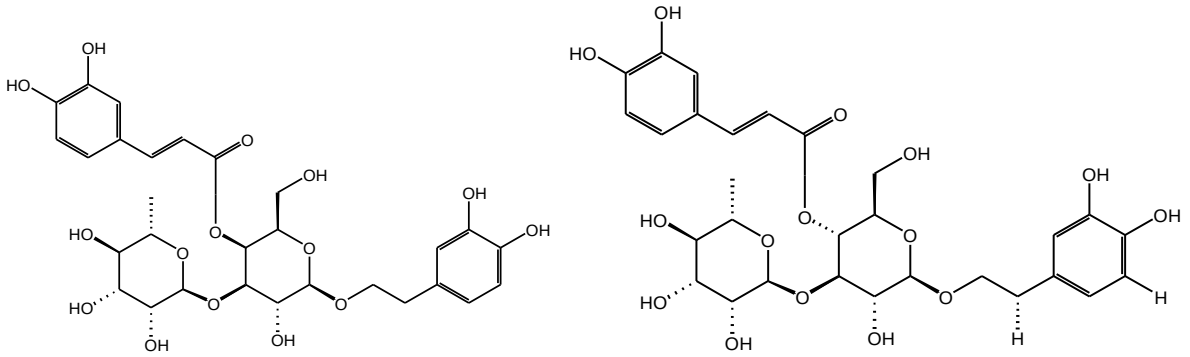
Phenylethane glycosides (PhGs)

Another distinctive and widely acting chemical found in *Pedicularis* plant species are PhGs. From plant species in the genus *Pedicularis*, more than 38 PhGs have been isolated (LI *et al.*, 2014). Fig. 4 displays several of them (VENDITTI *et al.*, 2016; FREZZA *et al.*, 2019).



pedicutroside A aucubin

Figure 3. A few of the iridoids presented in *Pedicularis* plant species.



pedicularioside G verbascoside

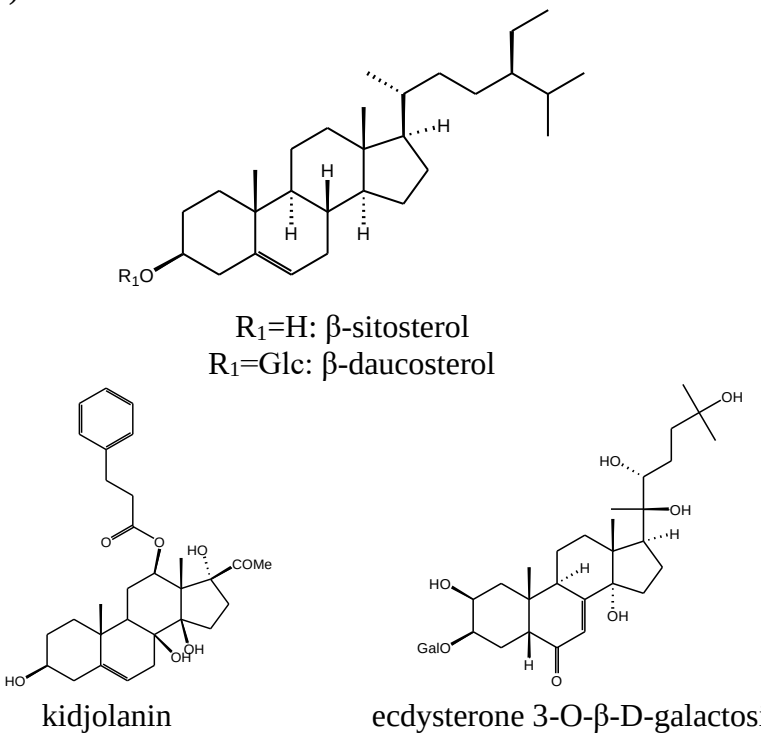
Figure 4. Selected phenylethanoid glycosides found in *Pedicularis* plant species.

Terpenes and terpenoids

The four main categories of plant secondary metabolites involved in stress tolerance and environmental adaptation are terpenoids, flavonoids, alkaloids, and phenolics. Terpenoids are the most diverse class of these compounds and play significant roles in chemical ecology (BONCAN *et al.*, 2020). Fig. 5 displays terpenoids that have been extracted from *Pedicularis* plant species (FREZZA *et al.*, 2019; WANG *et al.*, 2021).

Alkaloids

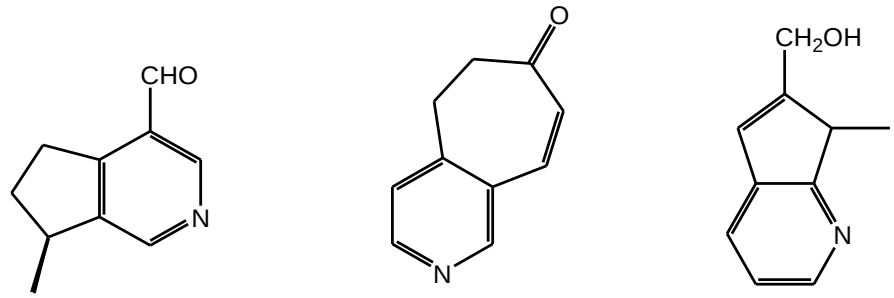
Plant cell membranes naturally contain bioactive substances called phytosterols, which share a chemical structure with cholesterol generated from mammalian cells. Lipid-rich plant foods, including nuts, seeds, legumes, and olive oil, contain a lot of them. Plants are a rich source of β-sitosterol (SIT), the main phytosterol among the others (BABU and JAYARAMAN, 2020). The majority of the pyridine alkaloids that have been isolated from the genus *Pedicularis* are generated from monoterpenes (LI *et al.*, 2014). Fig. 6 displays several of them (FREZZA *et al.*, 2019).



R_1=H: β-sitosterol
R_1=Glc: β-daucosterol

kidjolanin ecdysterone 3-O-β-D-galactoside

Figure 5. Main compounds of terpenoids found in *Pedicularis* plant species.



indicaine pediculidine pediculine

Figure 6. Several of the alkaloids found in *Pedicularis* plant species.

Additional substances extracted from Pedicularis plant species

While not major constituents, certain amino acids, phenolic compounds, and phenolic acids have been identified in the genus *Pedicularis*. For example, *P. decora* roots contain 17 amino acids, including aspartic acid, threonine, serine, glutamic acid, glycine, alanine, cystine, methionine, isoleucine, phenylalanine, alanine, valine, arginine, proline, leucine, and tyrosine (LI *et al.*, 2014).

Pedicularis plant species on the territory of the Western Balkans: pharmacological screening and application in traditional medicine

According to research, compounds isolated from *Pedicularis* plant species exhibit anti-tumor, hepatoprotective, immunomodulatory, anti-inflammatory, antidiabetic, antibacterial, antifungal, analgesic, and diuretic properties. These medicinal plants are used to treat conditions such as leucorrhoea, fever, sterility, rheumatism, general weakness, collapse, and urinary issues. Additionally, they are used to maintain vigor, enhance digestion, and stimulate blood circulation (YATOO *et al.*, 2017). Phenolic compounds are abundant in the genus *Pedicularis*, and numerous phenolic compounds have been identified in plant species within this genus (YUEHUI *et al.*, 2018). Other active components that have various health benefits include phenols, terpenoids, flavonoids, lignans, tannins, iridoids, and phenylpropanoid glycosides. To fully explore the medicinal potential of these significant plants, more comprehensive research is required to characterize the different phytoconstituents of the genus *Pedicularis*. This will allow for the investigation of their molecular mechanisms of action and the identification of additional advantageous applications (YUEHUI *et al.*, 2018; FREZZA *et al.*, 2019).

Antioxidant activity

The phytoconstituents identified in extracts from various studied *Pedicularis* plant species suggest that these plants possess antioxidant properties and can be used to treat oxidative stress. YUEHUI *et al.* (2018) demonstrated the antioxidant and superoxide-influencing properties of phenylpropanoid glycoside. Due to the presence of linoleic acid, phenylpropanoid glycoside has been demonstrated to suppress autoxidation. Phenolic compounds found in *Pedicularis* have been shown to scavenge reactive oxygen species (ROS). It has been observed that the antioxidant activity of *Pedicularis* plants affects both exercise-induced oxidative stress and diabetes.

Table 1. The use of some plant species of the genus *Pedicularis* in the territory of the Western Balkans in traditional medicine, according to the existing literature.

***Pedicularis* sp.**	**Traditional use**	**The plant organ used**	**References**
P. brachyodonta	means for treating inflammation; improving blood circulation; treating wounds and infections, and stimulating the nervous system.	- leaves, petals	SPRAGUE, 1962 PURCELL, 1974 GIBSON *et al*., 1989 TURKER *et al*., 2021
P. dasyantha	It is used as a muscle relaxant; an aphrodisiac; a treatment for respiratory ailments and sore throats; a cure for lice and scabies; and a solution for heart difficulties, anemia, diarrhea, ulcers, stomach pains, and other digestive issues.	- leaves, roots	HADAČ, 1942 TURKER *et al*., 2021
P. sceptrum-carolinum	to reduce inflammation or swelling; to treat digestive problems, including ulcers and stomach aches; for wound healing; a muscle relaxant.	- leaves, roots	LINNAEUS, 1753 TURKER *et al*., 2021
P. mixta	It is used as a muscle relaxant; an aphrodisiac; a treatment for respiratory ailments and sore throats; a cure for lice and scabies; and a solution for heart difficulties, anemia, diarrhea, ulcers, stomach pains, and other digestive issues.	- leaves, roots	STUART, 1911 CHITTENDON, 1956 HUXLEY, 1992 FREZZA *et al.*, 2019 TURKER *et al*., 2021
P. oederi	to cure micturition issues, scabies, rheumatoid arthritis; as a sedative; to treat food poisoning; for headaches, back, and body pain.	- roots/decoction - whole plant/raw vegetable	ANGMO *et al.*, 2012 RINCHEN and PANT, 2014 LI *et al.*, 2014 FREZZA *et al.*, 2019 TURKER *et al*., 2021 AMIN *et al.*, 2024
P. sylvatica	it is used as food.	- flowers/raw plant	FREZZA *et al.*, 2019
P. verticillata	for the treatment of anemia, hydrosis, hypotension, leucorrhoea, fevers, sterility, rheumatism, general debility, collapse, and urinary issues.	- roots/decoction	LI *et al.*, 2014 FREZZA *et al.*, 2019 BEJENARU *et al.*, 2024
P. friderici-augusti	The herb *P. friderici-augusti* has been utilized in traditional medicine in several regions of the world, particularly in Asia and Europe. It is used in traditional medicine to treat various diseases, such as inflammatory processes, coughs, colds, and respiratory problems.	- leaves, flowers	TURKER *et al*., 2021

Table 1. continued

P.hoermanniana	It is used as a muscle relaxant; to reduce inflammation or swelling; to alleviate insomnia and other sleep disturbances; a treatment for respiratory ailments and sore throats; to relieve headaches, migraines, and menstrual cramps; and a solution for diarrhea, ulcers, stomach pains, and other digestive issues.	- leaves, stems, flowers	TURKER *et al*., 2021
P. leucodon	It is consumed as food.	- flowers, nectar	ÇAKIR, 2017
P. petiolaris	It is also employed in traditional medicine, although the effectiveness of its therapeutic effects varies according to custom and usage.	- leaves, flowers	TURKER *et al*., 2021
P. graeca	to treat a range of illnesses, such as digestive issues, discomfort, and inflammation.	- leaves, flowers	TURKER *et al*., 2021
P. rostratocapitata	It is used as a muscle relaxant; to relieve headaches, dizziness; kidney and bladder problems; a treatment for respiratory ailments and sore throats; and a solution for diarrhea, ulcers, stomach pains, and other digestive issues.	- roots, leaves	TURKER *et al*., 2021
P. acaulis	It is used as a muscle relaxant; a treatment for respiratory ailments and sore throats.	- leaves, flowers	TURKER *et al*., 2021
P. ferdinandi	It is used as a muscle relaxant; to reduce inflammation or swelling.	- leaves, flowers, stems	TURKER *et al*., 2021

The 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay was used in the study to demonstrate the high level of free radical-scavenging activity of the *Pedicularis*-methanol extract. Verbascoside from *Pedicularis* was shown to have antioxidant activity and was demonstrated to lower ROS. The genus *Pedicularis* has shown its antioxidant potential by reducing oxidants and increasing antioxidants.

Verbascoside is a well-studied phenylethanoid glycoside with strong antioxidant properties. Its antioxidant activity arises from its ability to scavenge free radicals, inhibit lipid peroxidation, and chelate metal ions. These actions help protect cells from oxidative stress-related damage (LUHATA *et al.*, 2022). Alyssonoside, a glycoside related to iridoid compounds, has shown moderate antioxidant activity, although it is less potent than verbascoside and some other phenolic glycosides. Its antioxidant effects are primarily attributed to its ability to scavenge reactive oxygen species (ROS) and support cellular antioxidant defenses (WU *et al.*, 2020). Boschnaloside, another iridoid glycoside, has shown antioxidant potential in preliminary studies, with actions that include inhibiting ROS and supporting cellular enzymes like superoxide dismutase (SOD). Its antioxidant activity is often linked to its anti-inflammatory benefits, though it's generally weaker than phenolic antioxidants (LIN *et al.*, 2019). Leucosceptoside A, another phenylethanoid glycoside, has potent antioxidant activity. It scavenges free radicals and prevents lipid peroxidation, offering cellular protection from oxidative damage. Like verbascoside, it has a strong radical

scavenging capacity and is used in studies investigating natural antioxidants (FREZZA *et al.*, 2022). Isoverbascoside is an isomer of verbascoside, and it shows similar antioxidant properties, though often slightly less potent than verbascoside itself. It scavenges free radicals and inhibits lipid peroxidation, contributing to its protective effect against oxidative damage (CHEN *et al.*, 2002; PONGKITWITOON *et al.*, 2024). Leucosceptoside B has antioxidant properties similar to leucosceptoside A, with mechanisms involving radical scavenging and inhibition of oxidative damage. It's known for its protective effects against cell damage due to its phenolic structure (FREZZA *et al.*, 2022).

Recent studies demonstrated that an ethanolic extract of *Pedicularis* exhibited antioxidant properties by decreasing lipid peroxides (LPO) and enhancing the activity of glutathione reductase, catalase, and superoxide dismutase (YUEHUI *et al.*, 2018). Notably, a 60% ethanolic fraction outperformed an aqueous fraction, a 40% or 80% ethanolic fraction, and a 60% methanolic fraction in terms of results. In addition, *Pedicularis longiflora* has demonstrated comparatively better antioxidant capability in assays for total phenol, total flavonoid, DPPH RC50, ferric-reducing action potential (FRAP), and total antioxidant capacity (TAC) than *Pedicularis oederi* and *Pedicularis bicornuta* (YUEHUI *et al.*, 2018). Its increased phenol and flavonoid content may be due to its higher scavenging potential, as seen by *P. longiflora* extract's lower DPPH, higher FRAP, and medium TAC levels when compared to *P. bicornuta* and *P. oederi* extract. All things considered, the phytochemical study of the *Pedicularis* plants from Changthang, Ladakh, has demonstrated that these plants have good antioxidant capacity and high concentrations of phenols and flavonoids. Additionally, an *in vivo* investigation employing diabetic rats demonstrated *P. longiflora's* antioxidant capacity by elevating reduced glutathione (GSH) levels, catalase (CAT) activity, superoxide dismutase (SOD), and lowering LPO levels (YUEHUI *et al.*, 2018). To understand the mechanisms underlying *Pedicularis sp.*'s antioxidant properties, which are linked to the presence of flavonoids and phenylpropanoids, more *in vivo* antioxidant assays and molecular research are necessary. Plant extracts known for their high polyphenol content, SOD-like activity, and capacity to scavenge radicals are found in *Pedicularis* plants. These substances, particularly phenylpropanoid glycosides, act as strong natural antioxidants by inhibiting cancer cell growth, repairing oxidative DNA damage, scavenging free radicals, and inhibiting leukotriene B4 production. Supplementation with *Pedicularis muscicola Maxim* enhances the enzyme system that scavenges free radicals by increasing levels of superoxide dismutase and glutathione-stimulating hormone, which in turn reduces hippocampal reactive oxygen species, malondialdehyde, and lipid hydroperoxidation (YUEHUI *et al.*, 2018). In a mouse model of alloxan-induced oxidation injury, *P. muscicola* butanol extract lowered abnormally elevated levels of SOD, GSH-Px (plasma glutathione peroxidase), lipid peroxidation, alanine transaminase, aspartate aminotransferase, alkaline phosphatase, and monoamine oxidase, while improving liver and spleen indices (YUEHUI *et al.*, 2018).

Therefore, substances like phenols and flavonoids are responsible for the antioxidant properties of *Pedicularis* plants (YATOO *et al.*, 2017). Another study established an effective method for screening and purifying potent antioxidants from the aqueous extract *of P. longiflora* using the online combination HSCCC HPLC-DPPH test. This technique identified six main compounds with potential antioxidant activity: verbascoside, alyssonoside, boschnaloside, leucosceptoside A, isoverbascoside, and leucosceptoside B. Among these, boschnaloside, alisonoside, leukosceptoside A, and leukosceptoside B were isolated from *P. longiflora* for the first time. The outcomes demonstrated that the target-guided isolation of antioxidant chemicals from natural plants was a successful technique when the online HPLC-DPPH experiment was combined with HSCCC (YUEHUI *et al.*, 2018).

KHODAIE *et al.* (2012) investigated the antioxidant activity of *Pedicularis sibthorpii* and *Pedicularis wilhelmsiana* growing in Azerbaijan and Iran. The methanolic extract

exhibited superior antioxidant activity compared to other crude extracts (n-hexane and dichloromethane).

Immunomodulatory potential

Extracts from various plant species of the *Pedicularis* genus have shown promise in diabetes treatment by increasing insulin levels and reducing glucose and glycated product levels. However, the immunomodulatory potential of the *Pedicularis* genus, particularly in diabetes, has not been evaluated or compared with standard immunomodulators like vitamin E (YATOO *et al.*, 2018). The genus *Pedicularis* contains many species with potential medicinal properties, including immunomodulatory effects. However, specific research on the immunomodulatory activities of many of the species on the territory of the Western Balkans we have listed is sparse or limited to general descriptions in broader pharmacological studies. Research of the species on the territory of the Western Balkans is limited, but it is part of the *Pedicularis* genus known for phenolic compounds, iridoids, and flavonoids, which often have immune-regulatory properties. Flavonoid and glycoside compounds common in this genus could assist in immune balance by reducing inflammation and oxidative stress. The research on the *in vitro* and *in vivo* immunomodulatory potential of *P. longiflora* and *Allium carolinianum* in alloxan-induced diabetes in Wistar rats was one of the investigations that looked at the immunomodulatory effect (YATOO *et al.*, 2018; BEHL *et al.*, 2021). Lymphocyte stimulation and cytokine release assays were employed to study the in vitro immunomodulatory activity of ethanol extracts from the aerial parts of *P. longiflora* and the whole plant parts of *A. carolinianum*. In the 42-day experimental trial, doses of 500 mg/kg b.wt. for *P. longiflora* and 250 mg/kg b.wt. for *A. carolinianum* were used to assess the cell-mediated immune (CMI) and humoral immune (HMI) responses in 5 groups of 6 rats each, including alloxan-induced diabetic and plant extract-treated rats. The median effective dose for *P. longiflora* was determined to be 500 mg/kg. *P. longiflora* had a substantially greater *in vitro* lymphocyte stimulation index (1.73 ± 0.04, $p < 0.05$) than *A. carolinianum* (1.27 ± 0.06). On the other hand, *P. longiflora* substantially released 15.63 ± 1.00, $p < 0.05$, more transforming growth factor-β1 (TGF-β1) than *A. carolinianum* (21.61 ± 1.19), indicating that *P. longiflora* had a stronger immunological response. In comparison to *A. carolinianum* (47.57%, 165.83 ± 3.96, and 7.01 ± 0.01, respectively), *P. longiflora* significantly raised the ear thickness (53.12%), inflammatory cellular infiltration (200.00 ± 11.42), and total leukocyte count (7.44 ± 0.02). This is the first study to demonstrate that *P. longiflora* ethanol extract, particularly in alloxan-induced diabetic rats, has more powerful *in vitro* and *in vivo* immunomodulatory activity than *A. carolinianum*. To determine the various molecular pathways driving this immunomodulatory response, more investigation is necessary (YATOO *et al.*, 2018; BEHL *et al.*, 2021). Studies indicate that *Pedicularis densispica* extracts may modulate cytokine production, balancing pro-inflammatory and anti-inflammatory responses. The plant may help modulate immune responses in conditions of immune dysregulation, making it potentially useful for autoimmune or inflammatory diseases (CHU *et al.*, 2011; XIAO *et al.*, 2022). Research suggests that extracts from *Pedicularis kansuensis* can influence immune cell activity, potentially reducing inflammation and promoting immune homeostasis. These effects are linked to the plant's antioxidant potential, which may protect immune cells from oxidative stress. This article focuses on iridoid compounds in *P. kansuensis* and their contributions to the plant's anti-inflammatory and immunomodulatory actions (ZHANG *et al.*, 2011; CAO *et al.*, 2017).

Anti-inflammatory activity

Several plant species within the genus *Pedicularis* contain flavonoids, phenylpropanoids, and iridoids, contributing to their anti-inflammatory properties. Flavonoids and phenols inhibit COX-2, leading to a dose-dependent reduction in TNF-α levels (YATOO *et*

al., 2017). Unlike conventional nonsteroidal anti-inflammatory drugs, plant-based COX-2 inhibitors exert their pain-relieving effects over a longer period. Flavonoids and phenols regulate the activities of inflammatory mediators such as nitric oxide, prostanoids, leukotrienes, cytokines, chemokines, and adhesion molecules, as well as enzymes like tyrosine and serine-threonine protein kinases involved in signal transduction, cell activation, and inflammation (YATOO *et al.*, 2017). They inhibit all isoforms of cyclooxygenase, lipoxygenase, and inducible nitric oxide synthase expression. Additionally, flavonoids block phosphodiesterases crucial for cell activation and prevent the synthesis of prostaglandins and cytokines. These mechanisms collectively support the anti-inflammatory properties of flavonoids and phenols. Some medicinal plants also exhibit anti-inflammatory properties through inhibition of leucocyte migration, histamine release, and pro-inflammatory cytokine production (TNF-α and IL-8); modification of macrophage functions and neutrophil adhesion; and elevation of anti-inflammatory cytokine levels (IL-4, IL-6) (YATOO *et al.*, 2017). Investigations into these impacts are necessary for *Pedicularis* plants. Rats with alloxan-induced diabetes show a reduction in plasma TNF-α and TGF-β1 after receiving 500 mg/kg of *Pedicularis longiflora* extract. The anti-inflammatory effects of *Pedicularis* plant phytoconstituents are achieved through blocking the production of proinflammatory mediators like TNF-α and interferongamma, inhibiting the actions of enzymes like cyclooxygenases, lipoxygenases, and kinases, and encouraging the production of anti-inflammatory mediators like interleukins-4 and 10. The NF-κB signaling pathway controls these effects, but it's also important to investigate alternative pathways controlled by flavonoids and phenols (YATOO *et al.*, 2017).

Alpha-amylase inhibition was employed to examine the antidiabetic effects of *Pedicularis groenlandica* extracts. With an alpha-amylase inhibition value of 74.10 ± 2.65%, PGH exhibits good action. Following this extract, α-amylase inhibition was 48.10 ± 2.43% for PGA, 38.57 ± 1.36% for PGC, and 38.27 ± 3.32% for PGE. It indicates that the PGH extract contains a high concentration of the bioactive ingredients that give it its antidiabetic properties. When compared to the common medication acarbose, the antidiabetic potential showed an inhibition of 90.9 ± 3.1%. Good antidiabetic potential was demonstrated by *P. groenlandica* non-polar extracts, which suggested the nature of the bio-components in the extracts that were in charge of the antidiabetic action. Furthermore, more research should be done on this plant to determine its pharmacological potential, impacts of different stresses, and phytoremediation potential (HAMEED *et al.*, 2021).

Antitumor activity

The phenylethanoid glycoside isoverbascoside was identified in the Chinese traditional medicine plant *Pedicularis striata*. CHUAN *et al.* (2002) demonstrated that isoverbascoside can induce differentiation in the human hepatocellular carcinoma (HCC) cell line SMMC-7721. The average cell population doubling time was delayed, and the proliferation of SMMC-7721 cells was significantly suppressed in a dose- and time-dependent manner when treated with isoverbascoside. When cells were exposed to 20 micromol/l isoverbascoside, their ability to form colonies on soft agar decreased, they experienced G0/G1 arrest, and their levels of the marker enzymes gamma-glutamyltransferase (gamma-GT) and tyrosine aminotransferase (TAT), which indicate the malignance and differentiation stage of HCC, respectively, increased and decreased. These findings imply that isoverbascoside has the ability to stimulate SMMC-7721 cell differentiation.

Neuroprotective activity

Phenylethanoid glycosides act as potent natural antioxidants and possess neuroprotective properties. They inhibit neuronal damage caused by various harmful stimuli, including alcohol, scopolamine hydrobromide, sodium nitrite, hypobaric stress, and free

radicals such as nitric oxide (YATOO *et al.*, 2017). *Pedicularis* plant species are used in traditional medicine to treat inflammatory conditions like rheumatoid arthritis. *Pedicularis* is a genus of plants, the antidepressant qualities of which have not yet been thoroughly studied.

A dysregulated hypothalamic-pituitary-adrenal (HPA) axis is the cause of excessive corticosterone (CORT), which is linked to behavioral abnormalities, including depression and cognitive decline. *Pedicularis resupinata* is used in Korean eastern medicine to treat inflammatory conditions like rheumatoid arthritis. Nevertheless, *P. resupinata's* antidepressant qualities are not well understood. Using *in vivo* models of CORT-induced depression, the antidepressant-like effects of *P. resupinata* extract (PRE) were assessed. Acteoside, a phenylethanoid glycoside, was identified by HPLC as the primary component of PRE. Eight-week-old male ICR mice were given an intraperitoneal injection of CORT (40 mg/kg) and were given PRE orally every day (30, 100, and 300 mg/kg) for 21 days in a row. The open-field test, sucrose preference test, tail suspension test, passive avoidance test, and forced swim test were used to assess depressive-like behaviors. Mice treated with a high dose of PRE showed a significant reduction in CORT-induced depressive-like behaviors. Furthermore, brain-derived neurotrophic factor levels were dramatically decreased by repeated CORT injections, whereas the mice's hippocampal total glucocorticoid receptor (GR) and GR phosphorylation at serine 211 were significantly elevated but improved by PRE therapy. The results of this study imply that PRE may have antidepressant-like effects in mice that exhibit depressive-like behavior when exposed to CORT (LIM *et al.*, 2022).

Aversin, O-methylaverufin, varilactone A, spirosorbicillinol A, and four novel polyketides, aspeversins A-D, were created by *Aspergillus versicolor*, an endophytic fungus connected to the herbal remedy *Pedicularis sylvatica*. Comprehensive spectroscopic data analysis was used to clarify their structures, and $Mo_2(AcO)_4$-induced CD and computed electronic circular dichroism (ECD) data were used to determine their absolute configurations. With an IC_{50} value of 25.57 μM, aspeversins C was discovered to have α-glucosidase inhibitory action. A molecular docking investigation corroborated the findings of an enzyme kinetic study, which showed that 5 was a typical uncompetitive inhibitor toward α-glucosidase. Additionally, compounds demonstrated their neuroprotective potential as antiparkinsonian drugs by enhancing the vitality of PC12 cells in a model of Parkinson's disease caused by 1-methyl-4-phenylpyridinium (MPP^+) (JIANG *et al.*, 2024).

Antimicrobial activity

KHODAIE *et al.* (2012), in addition to the antioxidant activity, investigated the antimicrobial activity of *Pedicularis sibthorpii* and *Pedicularis wilhelmsiana* growing in Azerbaijan and Iran in order to determine whether the plant species of the genus *Pedicularis* show antimicrobial activity. Antibacterial activity was observed in methanolic extracts particularly against Gram positive isolates of *Staphylococcus aureus* and *Staphylococcus epidermidis*. The studied extracts showed no signs of antifungal action. One possible explanation for *Candida albicans's* insensitivity to the studied extracts is that the structure of mushrooms like *C. albicans* has lipophilic properties. In conclusion, it is likely that certain phenolic chemicals, including flavonoids and phenylethanoids (found in other *Pedicularis* species), which have antibacterial and antioxidant properties, are present in methanolic extracts. The antimicrobial and antioxidant properties of methanolic extracts highlight the need for further research on phytochemical analysis and bioassays of various fractions to isolate pure plant compounds. In addition to a phytochemical analysis of the plant's methanolic extract to identify potential potent phytoconstituents, a second study KHODAIE *et al.* (2019), was started to assess the antibacterial activity of the SPE (solid-phase extraction) fractions. Although verbascoside, a common phytoconstituent in the genus *Pedicularis*, was previously reported from *P. wilhelmsiana*, there are no reports of the presence of luteolin, luteolin-7-glucoside, martinoside, aucubin, ipolamiide, 5-hydroxy-8-epi-loganin, or mannitol

in this plant. It is well known that several plant polyphenols have antibacterial qualities. According to earlier research, *P. wilhelmsiana*'s higher levels of flavonoids and total phenol, particularly in the 40% and 60% SPE fractions, may be a contributing factor to the fractions' potent antibacterial activity. This leads to a phytochemical analysis of the *P. wilhelmsiana* methanolic extract. Inhibition can be justified by the presence of luteolin, luteolin-7-glucoside, and martinoside in 60% of SPE fractions, which show antibacterial activity, as well as the emergence of verbascoside, a polyphenolic molecule, in 40% of SPE fractions. Using the approach outlined in this work, no phytochemical substances could be isolated from this fraction. Therefore, more investigation is required to identify the phytochemical component that gives the 80% SPE fraction its inhibitory action against both *S. epidermidis* and *Pseudomonas aeruginosa* (KHODAIE *et al.*, 2019).

CONCLUSIONS

Since ancient times, people vhave relied on various plants for healing. The popularity of several herbs in traditional medicine can be attributed to their easy availability and high safety, as well as their effectiveness, which has been demonstrated through empirical research. Today, the rationale for using traditional plants is validated by both *in vitro* and *in vivo* experiments. The greatest opportunities for safely utilizing and reaping the benefits of plant potential are provided by current understanding. The data presented in this paper show a wide range of pharmacological and biological activities exhibited by extracts obtained from different parts of different plant species of the genus *Pedicularis*. The presence of different groups of secondary metabolites indicates that these plants can serve as a source of active compounds, some of which have potential pharmaceutical importance. There is currently relatively little information available in the literature about the plant species of the *Pedicularis* genus that are widely distributed throughout the Western Balkans. The fact that they haven't been well investigated yet is noteworthy, particularly in light of their chemical composition and biological activity manifestation, since this creates opportunities for the identification of novel compounds. Future studies should focus on other biological activities in addition to a more thorough and comprehensive chemical characterization of bioactive components.

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