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Review Article

Future perspective of *Cicerbita alpina* (L.) Wallr. (Asteraceae): Review on its phytochemistry and biological potential

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Abstract

Cicerbita alpina (L.) Wallr. (Asteraceae), alpine sow-thistle, is a perennial alpine herb distributed throughout European mountain regions. Traditionally used as an edible wild or cultivated vegetable, the species has attracted scientific attention due to its recently established promising biological and pharmacological potential. The systematic survey on the phytochemistry and bioactivity of the species was completed via PubMed, Google Scholar, and Scopus (1990–2025). *C. alpina* remains underestimated compared to related taxa within the Cichorieae tribe. Comprehensive phytochemical studies reveal the presence of guaianolide-type sesquiterpene lactones, acylquinic and acyltartaric acids, and flavonoids. The profiling is related to its antioxidant, enzyme inhibitory, and antidiabetic activities, highlighting its pharmacological significance. Moreover, the species exhibits antiparasitic and anti-methanogenic effects. This review summarizes current data on *C. alpina* secondary metabolites and bioactivity, emphasizing it as a potential α-glucosidase inhibitor that alleviates oxidative stress markers and carbohydrate metabolism parameters. It could also be applied in nutraceutical and veterinary practice.

Keywords

alpine sow-thistle, *Cicerbita alpina*, biological activity, phytochemistry

Introduction

Cicerbita alpina (L.) Wallr., commonly known as the alpine sow-thistle, is a perennial mountainous herb belonging to the Asteraceae family, Cichorieae tribe (World Flora Online 2025). It is widely distributed across the Alpine arc, the northern Balkans, and the Carpathians, typically occurring at altitudes between 1000 and 1800 m a.s.l. (Funk et al. 2009). In Italy, it is found in the Alps and northern Apennines, where the young shoots are harvested in early spring for the preparation of traditional delicacies such as "Radicchio dell'Orso" and "Radic di mont" (Martinidou et al. 2023). Usually, its use has been largely culinary; the species has commercial value, and lately, some research and trials for cultivation have been conducted (Scartezzini et al. 2012; Alexandru et al. 2013). Thus, a project was developed with the aim of collecting local samplings of alpine sow-thistle, based on their morphological characteristics, and establishing domestication and cultivation techniques. However, recent researches have revealed *C. alpina*'s potential medicinal applications, particularly in the treatment of metabolic and oxidative stress disorders as well as neurodegenerative diseases (Zheleva-Dimitrova et al. 2023, 2024).

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The phytochemical composition of *C. alpina* is characterized by a diverse range of specialized metabolites such as sesquiterpene lactones, flavonoids, and caffeic acid conjugates (Zheleva-Dimitrova et al. 2023). An earlier study on the species identified the guaianolides 11*β*,13-dihydrolactucin, and a new derivative, 8-acetyl-15-*β*-D-glucopyranosyllactucin, which constitutes a major compound of both roots and leaves (0.13% and 0.15% dw, respectively) (Appendino et al. 1991). Then, 8-acetyl-lactucin, 8-acetyl-11*β*,13-dihydrolactucin, and lactucin were identified in alpine sow-thistle roots by comparison with spectral data (Djordjević et al. 2004). More recently, hyphenated mass spectrometry analyses (UHPLC-HRMS, LC/ESI-MS) have expanded *C. alpina* metabolite profiling, identifying caftaric acid, cichoric acid, chlorogenic acid, and 3,5-dicaffeoylquinic acid, as well as various flavonoids (Alexandru et al. 2013; Zheleva-Dimitrova et al. 2023). Flavonoids such as apigenin-7-*O*-glucoside, luteolin-7-*O*-glucoside, and their aglycones have also been reported as predominant components (Martinidou et al. 2023).

Among these compounds, caffeic acid derivatives and sesquiterpene lactones are the most extensively studied due to their biological significance. Sesquiterpene lactones, particularly guaianolide-type lactones like 8-*O*-acetyl-15-*β*-D-glucopyranosyllactucin, 8-acetyl-lactucin, 8-acetyl-11*β*,13-dihydrolactucin, and lactucin, are considered chemotaxonomic markers of the Cichorieae tribe and are associated with bitterness and insect anti-feedant properties (Djordjević et al. 2004; Zidorn et al. 2005). They also exhibit promising pharmacological activities, including antioxidant and enzyme inhibitory as well as antiparasitic and antidiabetic effects (Martinidou et al. 2023; Zheleva-Dimitrova et al. 2023, 2024). Additionally, caffeic acid derivatives contribute significantly to the plant's antioxidant potential (Alexandru et al. 2013; Zheleva-Dimitrova et al. 2023).

Despite these promising findings, the current knowledge on the chemical profile and pharmacological properties of *C. alpina* remains fragmented, with most studies focusing on cultivation and genetic variability and often limited by regional sampling (Michl et al. 2007; Fusani et al. 2009; Fusani and Zidorn 2010; Stachurska-Swakon et al. 2011; Scartezzini et al. 2012; Alexandru et al. 2013; Martinidou et al. 2023).

Overall, *Cicerbita alpina* appears as an underestimated alpine plant with notable nutraceutical and pharmacological potential. Thus, a review on the alpine sow-thistle will emphasize its chemical profiling combined with biological activity, delineating its future perspectives as a valuable plant.

Methods of systematic review. Search strategy and data organization

A thoroughly comprehensive survey using PubMed, Google Scholar, and Scopus was completed for the period 1990–2025 (up to November 2025). The data searching comprised all combinations of the following keywords: *Cicerbita alpina*, alpine sow-thistle, phytochemistry, chemical compounds, pharmacology, and biological activity.

Afterwards, all duplicates of the bibliographies were removed by the citation manager program Mendeley (Elsevier-Mendeley Ltd., London, UK). The articles were thoroughly evaluated and studied; only studies published in English were considered. The inclusion criteria for important relevant references selected all experimental papers reporting the chemical composition and biological activity of an extract or fraction as well as single compounds from *C. alpina*. The exclusion criteria were researches related to the species, such as its genetic variability or compounds related to plant growth.

This review compiles and highlights data on the chemical compounds and biological activity of *Cicerbita alpina*.

Results and discussion

After duplicate elimination, 45 articles were further surveyed. Lastly, twenty-two studies met the inclusion criteria.

Taxonomy, botanical description, and distribution

Cicerbita alpina (L.) Wallr. belongs to genus *Cicerbita* Wallr., subtribe Lactucinae Dumort., tribe Cichorieae Lam. & DC., subfamily Cichorioideae Chevall. of plant family Asteraceae (World Flora Online 2025).

The species common names in Europe are Cicerbitë alpine (Albania) , Алпийска цицербита (Bulgaria), Lletuga alpine, Lechuga de monte (Spain), Ljubičasti mliječ (Croatia), Mléčivec alpský (Czech Republic), Fjeld-Turt (Denmark), Alpine Blue-sow-thistle (Great Britain), Pohjansinivalvatti (Finland), Laiteron des montagnes, Laitue des Alpes, Mulgédie des Alpes (France), Cicerbite des Alpes, Laitue-des-Alpes (Switzerland), Alpen-Milchlattich (Germany), Fjallablámi (Iceland), Cicerbita violetta (Italy), Turt (Norway), Modrzyk alpejski, Modrzyk górski (Poland), Torta (Sweden) (Kilian et al. 2009+).

Cicerbita alpina has the following synonyms: *Lactuca alpina* (L.) A.Gray, *Mulgedium alpinum* (L.) Less., *Aracium alpinum* (L.) Monnier, *Sonchus alpinus* L., *Sonchus multiflorus* Desf., *Sonchus alpestris* Clairv., *Garacium alpinum* (L.) Gren. & Godr. and etc. (World Flora Online 2025/).

C. alpina is a perennial herb, 50–250 cm high. The flowering stems are erect, ribbed, hollow, glandular above and hispid below, robust, unbranched, or branched. Cauline leaves are 8.0–25.0 cm long and 2.0–12.0 cm wide; dark green on upper surface and glaucous on lower surface. Lower cauline leaves are runcinate or lyrate, denticulate, petiole-like attenuate with a winged petiole, glabrous; terminal lobe is broadly triangular, acuminate; lateral lobes are triangular. Middle and upper cauline leaves are ovate or narrowly oblong, amplexicaul or petiole-like attenuate with a winged petiole, glabrous. The inflorescence is paniculiform with glandular peduncle. Involucre is

10.0–15.0 mm long, at flowering 7.0–10.0 mm in diameter; involucral bracts are linear, 10.0–15.0 mm long and 1.0–1.5 mm wide, obtuse, green, and tinged purple, usually glandular. Receptacle is flat and naked. Corolla is ligulate, pale blue to violet, 15.0–18.0 mm long. Achenes are cylindrical in outline, compressed and 4.5–5.0 mm long, with five prominent main ribs, attenuate. Pappus has simple bristles, 7.0 mm long (Kilian et al. 2009+).

The species is distributed in Eastern Europe (North European Russia, Ukraine); Middle Europe (Austria, Czechoslovakia, Germany, Poland, Switzerland); Northern Europe (Finland, Great Britain, Norway, Sweden); Southeastern Europe (Albania, Bulgaria, Greece, Italy, Romania, Yugoslavia); and Southwestern Europe (France, Spain) (World Flora Online 2025).

Cultivation trials on *Cicerbita alpina*

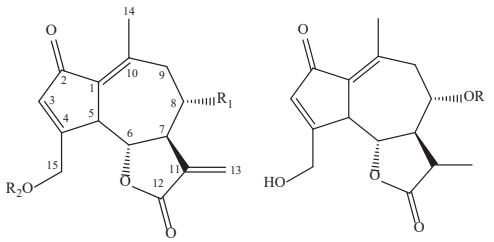
Attempts to domesticate and cultivate *C. alpina* have gained momentum over the past two decades, driven by its culinary value and increasing interest in its bioactive properties. To protect the long-term survival of the species, a research project was launched in Italy in 2004 investigating the potential for domestication of the species and replacing wild harvest with cultivation (Scartezzini et al. 2005). In parallel, the rise in commercial use of canned shoots produced from wild materials has been documented (Cividino et al. 2006). A study done by Fusani et al. (2009) emphasized the species' potential as an "alpine vegetable resource," noting significant variation in shoot yield and bitterness among accessions. Then, Scartezzini et al. (2012) presented a six-year domestication trial, demonstrating that *C. alpina* can be successfully cultivated at lower altitudes when provided with adequate moisture, shade, and humus-rich soils, although bolting and reduced shoot tenderness remained challenges. Afterwards, Alexandru et al. (2013) compared wild and cultivated shoots, revealing markedly higher levels of total phenolics (up to 93.58 mg gallic acid equivalent per gram dry weight (GAE/g dw)) and flavonoids (up to 145.00 mg rutin equivalent per gram dry weight (RE/g dw)) in cultivated material, suggesting that controlled growth conditions may enhance phytochemical accumulation. Further genetic and phenotypic assessments confirmed extensive variability among cultivated and wild populations, contributing to the development of selection strategies for optimal domestication traits (Michl et al. 2007; Fusani and Zidorn 2010; Martinidou et al. 2023). Overall, these cultivation studies highlight both the agronomic potential and challenges of domesticating *C. alpina*, forming an essential basis for its future use as a functional food and medicinal plant.

Phytochemical profile

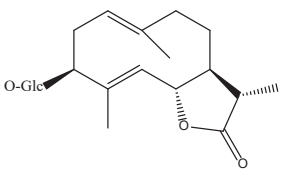
Based on the reviewed investigations, *C. alpina* is a chemically diverse representative of the Cichorieae tribe, Asteraceae family. The plant contains numerous sesquiterpene lactones, phenolic acids, and flavonoids. Below are presented the species' main secondary metabolites (Table 1).

Sesquiterpene lactones

Sesquiterpene lactones (STLs) constitute the most characteristic metabolites of the species. First, the guaianolide-type compounds lactucin (1), 8-acetyl-lactucin (3), 8-acetyl-15*β*-D-glucopyranosyllactucin (4), 11*β*,13-dihydrolactucin (5), and 8-acetyl-11*β*,13-dihydrolactucin (6) were isolated from the roots of the species (Appendino et al. 1991; Djordjević et al. 2004) (Table 1, Fig. 1).



Compound	R_1	R_2	Compound	R
lactucin (1)	OH	H	11*β*,13-dihydrolactucin (5)	H
8-deoxylactucin (2)	H	H	8-acetyl-11*β*,13-dihydrolactucin (6)	$COCH_3$
8-acetyl-lactucin (3)	$OCOCH_3$	H		
8-acetyl-15*β*-D-glucopyranosyllactucin (4)	$OCOCH_3$	Glc		



sonchuside A (7)

Figure 1. Sesquiterpene lactones isolated from *Cicerbita alpina.*

Table 1. Secondary metabolites in *Cicerbita alpina*.

Group of compounds/compound	Plant part/identification method	Reference
Sesquiterpene lactones		
***guaianolide*s**		
lactucin (1), 8-deoxylactucin (2), 8-acetyl-lactucin (3), 8-acetyl-15*β*-D-glucopyranosyllactucin (4), 11*β*,13-dihydrolactucin (5), 8-acetyl-11β,13-dihydrolactucin (6)	Leaves, flowering heads, aerial parts, roots/silica gel and Sephadex LH-20 CC, HPLC, UHPLC–HRMS, UHPLC-DAD, ESI-MS, NMR	Appendino et al. 1991; Djordjević et al. 2004; Zidorn et al. 2005; Fusani and Zidorn 2010; Martinidou et al. 2023
***germacranolide*s**		
sonchuside A (7)	Leaves, flowering heads, aerial parts/silica gel and Sephadex LH-20 CC, UHPLC–HRMS, ESI-MS, NMR	Zidorn et al. 2005; Zheleva-Dimitrova et al. 2023
Carboxylic, hydroxybenzoic acids, and their glycosides		
gallic acid (8), gallic acid-*O*-hexoside (9), syringic acid-*O*-hexoside (10), protocatechuic acid-*O*-hexoside (11), vanillic acid (12), protocatechuic acid (13), 4-hydroxybenzoic acid-*O*-hexoside (14), 4-hydroxybenzoic acid (15), quinic acid (16), gentisic acid (17), shikimic acid (18), salicylic acid (19)	Leaves, flowering heads/ UHPLC–HRMS	Zheleva-Dimitrova et al. 2023
Hydroxycinnamic acids and derivatives		
caffeic acid-*O*-hexoside (20), rosmarinic acid (21), *p*-coumaric acid (22), caffeic acid (23), ferulic acid (24), caffeoylmalic acid (25), caffeoylcitramalic acid (26)	Leaves, flowering heads/ UHPLC–HRMS	Zheleva-Dimitrova et al. 2023
Acylquinic acids		
neochlorogenic (3-caffeoylquinic) acid (27), 3-*p*-coumaroylquinic acid (28), chlorogenic (5-caffeoylquinic) acid (29), 4-caffeoylquinic acid (30), 5-*p*-coumaroylquinic acid (31), 3-caffeoyl-5-hydroxydihydrocaffeoylquinic acid (32), 5-feruloylquinic acid (33), 1/3/5-caffeoyl-4-hydroxydihydrocaffeoylquinic acid (34), 1-caffeoyl-3-hydroxydihydrocaffeoylquinic acid (35), 1,3,4-tricaffeoylquinic acid (36), 1,3,5-tricaffeoylquinic acid (37), 3,4-dicaffeoylquinic acid (38), 3,5-dicaffeoylquinic acid (39), 1,5-dicaffeoylquinic acid (40), 4,5-dicaffeoylquinic acid (41), 3-*p*-coumaroyl-5-caffeoylquinic acid (42), 3-feruloyl-5-caffeoylquinic acid (43), 1,3-dicaffeoyl-5-hydroxydihydrocaffeoylquinic acid (44), 4-*p*-coumaroyl-5-caffeoylquinic acid (45), 4-caffeoyl-5-p-coumaroylquinic acid (46), 3,4,5-tricaffeoylquinic acid (47)	Leaves, flowering heads, aerial parts, shoots/ HPLC, UHPLC–HRMS, UHPLC–TOF–MS	Fusani and Zidorn 2010; Alexandru et al. 2013; Martinidou et al. 2023; Zheleva-Dimitrova et al. 2023
Acyltartaric acids		
caftaric acid (48), tricaffeoyltartatric acid (49), dicaffeoyltartaric acid (cichoric acid) (50), *p*-coumaryltartaric acid (51), caffeoyl-*p*-coumaroyltartaric acid (52), caffeoyl-feruloyltartaric acid (53)	Leaves, flowering heads, aerial parts, shoots/ UHPLC–HRMS, UHPLC–TOF–MS, LC/ESI-MS	Fusani and Zidorn 2010; Alexandru et al. 2013; Martinidou et al. 2023; Zheleva-Dimitrova et al. 2023, 2024
Flavones, flavonols, and flavanones		
apigenin (54), apigenin-7-*O*-glucoside (55), apigenin 4′-*O*-hexoside (56), apigenin 7-*O*-hexuronide (57), apigenin 7-*O*-rutinoside (58), apigenin 7-*O*-hexosyl-*O*-hexuronide (59), apigenin 7-*O*-acetylhexoside (60), apigenin 7-*O*-dihydroxybutyryl-*O*-acetylhexoside (61), luteolin (62), luteolin 7-*O*-glucoside (63), luteolin 7-*O*-hexuronide (64), luteolin 7-*O*-dihexoside (65), luteolin 7-*O*-hexosyl-*O*-hexuronide (66), luteolin 7-*O*-pentosyl-*O*-hexoside (67), luteolin 7-*O*-rutinoside (68), luteolin 7-*O*-acetylhexoside (69), luteolin 7-*O*-dihydroxybutyryl-*O*-acetylhexoside (70), chrysoeriol (71), chrysoeriol-4′-*O*-hexuronide (72), chrysoeriol 4′-*O*-dihexoside (73), cirsiliol (74), quercetin (75), isoquercitrin (76), rutin (77), quercetin 3-*O*-hexosyl-*O*-hexuronide (78), quercetin 3,7-*O*-dihexoside (79), quercetin 3-*O*-acetylhexoside (80), isorhamnetin 3-*O*-glucoside (81), isorhamnetin 3,7-*O*-dihexoside (82), isorhamnetin 3-*O*-acetylhexoside (83), eriodictyol (84), eriodictyol-7-*O*-hexoside (85), eriodictyol-7-*O*-hexuronide (86), eriodictyol 7-O-dihexoside (87)	Leaves, flowering heads, aerial parts/ UHPLC–HRMS	Martinidou et al. 2023; Zheleva-Dimitrova et al. 2023
Coumarins		
aesculin (88), 7-hydoxycoumarin (umbelliferon) (89), aesculetin (90), coumarin (91)	Leaves, flowering heads, roots/ UHPLC–HRMS	Zheleva-Dimitrova et al. 2023

These bitter metabolites are typical of the subtribe Lactucinae and play a defensive role against herbivory (Picman 1986; Van Beek et al. 1990). Later, Zidorn et al. (2005) reported the occurrence of sonchuside A (7), representing the first non-guaiane-type STL detected in the genus (Table 1, Fig. 1). According to Zidorn (2008), STLs of the lactucin type predominate within the Cichorieae tribe, and the data for *C. alpina* match well with this pattern. Within the species, the principal STL is 8-*O*-acetyl-15-*ß*-D-glucopyranosyl lactucin (5) (Fusani and Zidorn 2010; Martinidou et al. 2023).

Newly, an UHPLC-HRMS metabolite profiling study on alpine sow-thistle verified the presence of both guaianolides and germacranolides in the aerial parts, thus con-

firming the chemotaxonomic significance of the species (Zheleva-Dimitrova et al. 2023) (Table 1).

Overall, STLs occurred in the edible shoots of the plant, contributing to its bitterness (Fusani and Zidorn 2010).

Phenolic compounds

Phenolic compounds represent another major class in the *C. alpina* chemical profile, including acylquinic, acyltartaric, and phenolic acids alongside flavones, flavonols, and flavanones, abundant in the shoots, leaves, and flowering heads (Table 1, Fig. 2). Chlorogenic (29), caftaric (48), cichoric (50), and 3,5-dicaffeoylquinic (39) acids, apigenin-7-*O*-glucoside (55), and luteolin-7-*O*-glucoside (63) were determined as dominant components (Fusani and Zidorn 2010; Alexandru et al. 2013; Martinidou et al. 2023). Another quantitative data set reported by Zheleva-Dimitrova et al. (2024) showed cichoric acid (50) (91.9 mg/g dw) as the most abundant caffeoyltartaric acid, followed by caftaric (48) (11.36 mg/g dw) and chlorogenic acid (29) (9.25 mg/g dw). Indeed, a great variety of acylquinic and acyltartaric acids was annotated – witnessed by *p*-coumaroyl-, feruloyl-, hydroxydihydrocaffeoyl-, caffeoyl-feruloyl-, caffeoyl-*p*-coumaryoyl-, and caffeoyl-hydroxydihydrocaffeoylquinic acid – together with caffeoyl-*p*-coumaroyltartaric acid (52) and caffeoyl-feruloyltartaric acid (53) (Zheleva-Dimitrova et al. 2023) (Table 1). Within the flavone glycosides, chrysoeriol-*O*-hexuronide and dihexoside were established along with luteolin/apigenin 7-*O*-dihydroxybutyryl-*O*-acetylhexoside (Zheleva-Dimitrova et al. 2023). Additionally, the authors identified a series of carboxylic, hydroxybenzoic, hydroxycinnamic, acylquinic, and acyltartaric acids in *C. alpina* leaves and flowering heads (Table 1). Cichoric, caftaric, and chlorogenic acids dominated in the leaves, while apigenin and 3,5- and 3,4-dicaffeoylquinic acids dominated in the flowering heads profiling.

Other compounds

The review survey on the chemical constituents of alpine sow-thistle revealed the occurrence of coumarins too (Table 1). Simple coumarins are represented by aesculin (88), 7-hydroxycoumarin (umbelliferone) (89), aesculetin (90), and coumarin (91) (Zheleva-Dimitrova et al. 2023) (Table 1). Nevertheless, the earlier report of furanocoumarins (imperatorin, isoimperatorin, oxypeucedanin, and ostruthol) by Appendino et al. (1991) was later rebutted (Moreno Cardenas et al. 2025). The authors announced that these compounds originated from *Peucedanum ostruthium*, not from *C. alpina*, as well as that furanocoumarins have not been described from any other taxon of the Cichorieae tribe of the Asteraceae family.

Comparative quantitative data profiling of valued Cichorieae tribe species *Cicerbita alpina*, *Cichorium intybus*, and *Cynara scolymus*

Cicerbita alpina is special among Cichorieae species for its remarkably high content of cichoric acid and related hydroxycinnamic acids. Newly, quantitative profiling of

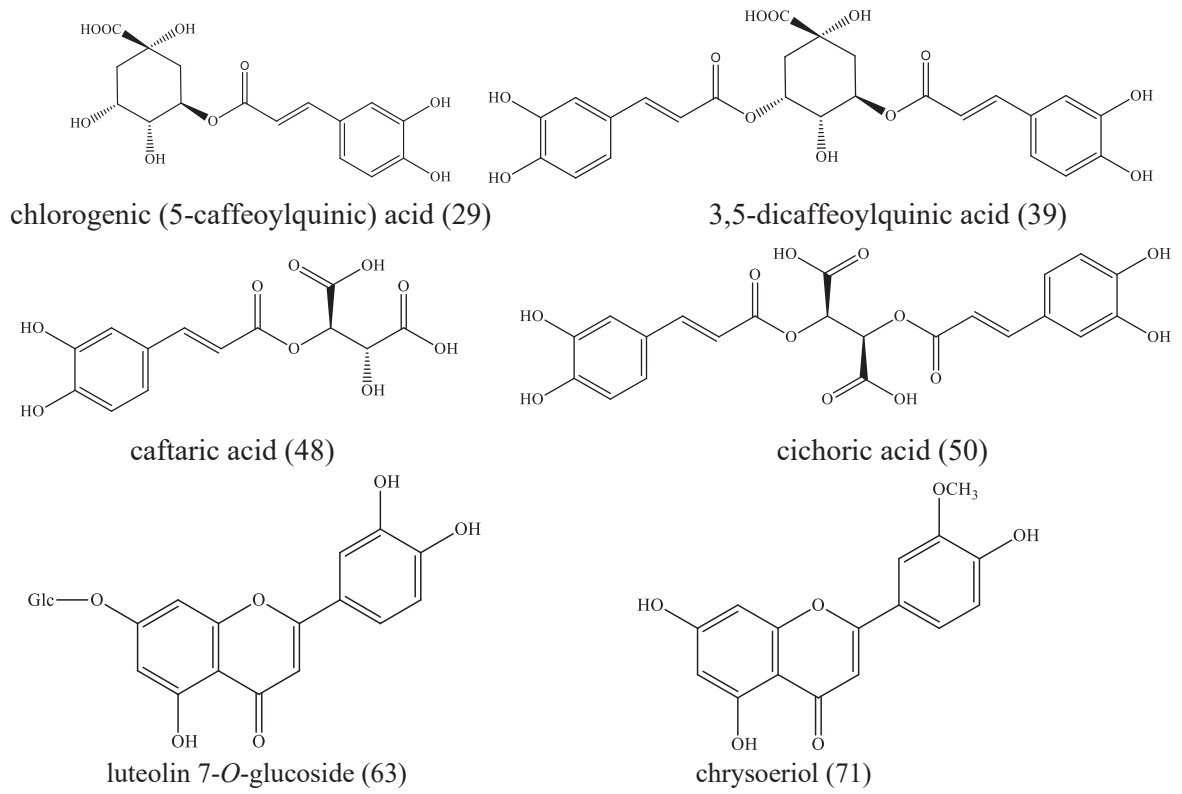


Figure 2. Main phenolic compounds identified in *Cicerbita alpina*.

alpine sow-thistle leaves revealed total phenolic (75.13 mg GAE/g dw) and flavonoid (17.59 mg QE/g dw) contents dominated by cichoric acid (91.9 mg/g dw), alongside caftaric acid (11.36 mg/g dw) and chlorogenic acid (9.25 mg/g dw) in Bulgarian wild provenance (Zheleva-Dimitrova et al. 2024). Previous analyses of edible shoots also reported notable levels of caffeic acid derivatives such as cichoric acid (54.63 mg/g dw), 3,5-dicaffeoylquinic acid (5.44 mg/g dw), caftaric acid (5.14 mg/g dw), and chlorogenic acid (2.66 mg/g dw), further highlighting the species' unusually rich phenolic profile (Fusani and Zidorn 2010).

In comparison, highly valued artichoke (*Cynara scolymus*) had a total polyphenol content of 8.89 mg GAE/g dw; a great quantity of 1,5-dicaffeoylquinic acid (7.6 mg/g dw) has been reported in Italian cultivar stems, while chlorogenic acid has achieved 4.78 mg/g dw, followed by 3,5-dicaffeoylquinic acid (up to 0.31 mg/g dw) (Ayuso et al. 2024). Regarding *Cichorium intybus* (chicory), significantly higher total phenolic (23.94 mg GAE/g dw) and flavonoid (5.06 mg RE/g dw) contents than artichoke have been established in wild Romanian samples (Epure et al. 2021). Among the major compounds, cichoric acid has reached 18.45 mg/g dw, followed by chlorogenic (0.91 mg/g dw) and caftaric acid (0.74 mg/g dw). Thus, unlike chicory and artichoke, *C. alpina* stands out within the Cichorieae tribe for its unique dominance of cichoric and caftaric acids over caffeoylquinic acids, making it one of the richest natural sources of these bioactive compounds and a promising candidate for nutraceutical application.

Biological activities

Herein, the biological activities of *C. alpina* have been intensively studied during the last decade, confirming both traditional use and novel pharmacological potential, including antioxidant and enzyme inhibitory, cytotoxic, and antidiabetic activity, as well as antiparasitic and anti-methanogenic effects (Table 2).

Antioxidant and enzyme inhibitory activity

Phenolic compounds, especially caffeic acid derivatives and flavonoids with *o*-dihydroxy structure, contribute significantly to the radical-scavenging capacity and UV protection of plant species (Rice-Evans et al. 1996; Spitaler et al. 2006). Previously, a high abundance of antioxidant caffeic acid derivatives in the edible shoots of *C. alpina* has been reported (Fusani and Zidorn 2010). Among these compounds, cichoric acid has been associated with multiple bioactivities, including antioxidant, anti-inflammatory, anti-obesity, and neuroprotective effects (Lee and Scagel 2013; Peng et al. 2019).

In a comparative study of wild and cultivated *C. alpina* edible shoots, the contents of total phenolics (10.54 and 93.58 mg GAE/g^{-1} dw, respectively) and flavonoids (25.22 and 145.00 mg RE/g^{-1} dw, respectively) were significantly higher in the cultivated samples (Alexandru et al. 2013) (Table 2). On the other hand, recent results on wild sampling with Bulgarian provenance revealed that the flavonoids dominated in the flowering heads (27.72 mg QE/g), while the leaves had higher phenolics (75.13 mg GAE/g) (Zheleva-Dimitrova et al. 2023) (Table 2). The authors provided the first systematic study on antioxidant activity of both leaves and flowering heads, exploring their radical scavenging activity, reducing power, metal chelating capacity, and total antioxidant potential (Table 2). It is worth noting that the leaves had prominent reducing power in CUPRAC (212.93 mg trolox equivalent per gram dry extract (TE/g)) and FRAP (141.12 mg TE/g) assays. Also, the leaves possessed higher activity in the phospho-molybdenum method and metal chelating test than flowering heads (Table 2). With this respect, multivariate analysis discriminated the profiling of leaves and flowering heads (Zheleva-Dimitrova et al. 2023). Thus, rosmarinic acid and salicylic acid, syringic acid-*O*-hexoside alongside hydroxycinnamoyltartaric acids, 8-acetyl-15β-D-glucopyranosyllactucin, and 15-hydroxytaraxacin occurring in the leaves extract had an impact on the antioxidant activity. Moreover, dicaffeoyl derivatives cichoric acid and 1,5-dicaffeoylquinic acid demonstrated higher DPPH activity compared to monocaffeoyl derivatives, caffeoyltartaric acid (caftaric acid), and chlorogenic acid, respectively (Pellati et al. 2004). Overall, phenolic compounds could be a major component of the antioxidant potentials of foods (Parr et al. 2000), and thus, *C. alpina* could be considered a natural source of antioxidants.

Enzyme inhibitory activity of *C. alpina* leaves and flowering heads methanol–aqueous extracts was evaluated towards selected enzymes involved in metabolic disorders (α-glucosidase, α-amylase, and lipase), neurodegenerative diseases (cholinesterases: AChE, BChE), and hyperpigmentation (tyrosinase) (Zheleva-Dimitrova et al. 2023) (Table 2). Leaves had stronger antioxidant activity compared to flowering heads, as well as lipase (4.75 mg orlistat equivalent per gram dry extract (OE/g)), AChE (1.98 mg galantamine equivalent per gram dry extract (GALAE/g)), BChE (0.74 mg GALAE/g), and tyrosinase (49.87 mg kojic acid equivalent per gram dry extract (KAE/g)) inhibitory potential. Flowering heads revealed the highest activity against α-glucosidase (1.05 mmol acarbose equivalent per gram dry extract (ACAE/g)) and α-amylase (0.47 mmol ACAE/g) (Table 2).

Formerly, the AChE potential of sesquiterpene lactones (lactucin and lactucopicrin) in different chicory extracts was established together with calorimetric and docking simulation studies (Jaśkiewicz et al. 2022). The data revealed that lactucopicrin had more beneficial properties for AChE inhibition compared to lactucin. Additionally, enzyme inhibition was more effective in the case of ex-

Table 2. Biological activity of *Cicerbita alpina*.

Compound/Extract	Mechanism	Model	Reference
Antioxidant and enzyme inhibitory activity			
Phenolic acids and flavonoids/MeOH extract of shoots	Wild and cultivated shoots: total phenolic (10.54 and 93.58 mg GAE/g dw, respectively) and flavonoid (25.22 and 145.00 mg RE/g dw, respectively) contents	Wild and cultivated plants	Alexandru et al. 2013
Phenolic acids, flavonoids, sesquiterpene lactones/ MeOH extracts of leaves and flowering heads	Leaves and flowering heads: total phenolic (75.13 and 48.41 mg GAE/g dw, respectively) and flavonoid (17.59 and 27.72 mg QE/g dw, respectively) contents; antioxidant activity: DPPH (132.80 and 45.36 mg TE/g, respectively), ABTS (139.54 and 99.48 mg TE/g, respectively), FRAP (141.12 and 85.97 mg TE/g, respectively), CUPRAC (212.93 and 157.96 mg TE/g, respectively), chelating (36.97 and 23.92 mg EDTA/g, respectively), PHMD (1.55 and 1.35 mg TE/g, respectively)	*In vitro* antioxidant assays	Zheleva-Dimitrova et al. 2023
Phenolic acids, flavonoids, sesquiterpene lactones/ MeOH extracts of leaves and flowering heads	Leaves and flowering heads: enzyme inhibition: AChE (1.98 and 1.94 mg GALAE/g, respectively), BChE (0.74 and na mg GALAE/g, respectively), α-glucosidase (0.60 and 1.05 mmol ACAE/g, respectively), α-amylase (0.28 and 0.47 mmol ACAE/g, respectively), lipase (4.75 and na mg OE/g, respectively), tyrosinase (49.87 and 33.02 mg KAE/g, respectively)	*In vitro* enzyme assays	Zheleva-Dimitrova et al. 2023
Cytotoxicity			
Phenolic acids, flavonoids, sesquiterpene lactones/ MeOH extracts of leaves and flowering heads	Evaluation of the extracts toward the immune system: cytotoxicity of 70% (flowering heads extract) and nearly 90% (leaves extract) at 2000 and 3000 μg/mL concentration	Human monocytic cell line (THP-1 cells)	Zheleva-Dimitrova et al. 2023
Antidiabetic activity			
Phenolic acids (cichoric, caftaric, and chlorogenic acid)/MeOH extract of leaves	Administration of low (250 mg/kg) and high (500 mg/kg) extract doses, 28 days, p.o.; Blood glucose (mmol/L): DMT2 = 9.2; DMT2 + Acarb = 6.9; DMT2 + ECAld = 7.1; DMT2 + ECAhd = 6.6. Serum lipids: cholesterol reduced from 2.29 to 1.66 mmol/L; triglycerides reduced from 1.30 to 0.59 mmol/L. Hepatic enzymes: ASAT decreased from 143.8 to 111.0 U/L; ALAT decreased from 160.6 to 133.2 U/L. Renal parameters: urea reduced from 14.2 to 12.3 mmol/L; creatinine reduced from 65.5 to 52.2 μmol/L. Modulation of oxidative stress markers (liver): malondialdehyde (MDA) reduced from 5.15 to 3.62 nmol/g; glutathione (GSH) increased from 4.11 to 5.24 nmol/g; glutathione peroxidase (GPx) increased from 1.39 to 2.36 nmol min^{-1} mg^{-1} protein; superoxide dismutase (SOD) increased from 1.15 to 1.79 nmol min^{-1} mg^{-1} protein; catalase activity (CAT) increased from 6.8 to 7.31 nmol min^{-1} mg^{-1} protein	*In vivo* model of streptozotocin-induced type 2 diabetes in Wistar rats	Zheleva-Dimitrova et al. 2024
Anthelmintic activity			
MeOH extract of aerial parts	Microtubule inhibition of egg hatch and larval development; possible interference with neuromuscular signaling in nematodes; the effect of different extract concentrations (0.500, 0.325, and 0.200 mg/mL) was assessed on the embryonic development of the *Ascaridia galli* eggs; EC_{50} = 0.27 mg/ mL; flubendazole control EC_{50} = 0.11 mg/mL; embryonic development (% ED): FL = 25%, *C. alpina* = 47%; at 0.5 mg/mL, *C. alpina* inhibited ED by 35%	*In vitro* model of nematodes (*A. galli* eggs)	Poulopoulou et al. 2023
MeOH extract of aerial parts	Fractions of MeOH extract: BuOH and EtOAc at 500 μg/mL (embryos) and 150 μg/mL (adults); embryo development (*A. galli*): EtOAc 65.5% ED; BuOH 68% ED vs. flubendazole 25% ED at 1.6 μM. Worm motility (*C. elegans*): BuOH fraction → 49% motility at 150 μg/mL; EtOAc → 64% motility. Active phytochemicals: 11-*β*,13-dihydrolactucin 58% ED at 1.8 μM; luteolin 46% ED at 1.7 μM; luteolin inhibited egg hatching by 65% at 10 μM (10 h). No cytotoxicity at ≤ 50 μg/mL.	*In vitro* model of nematodes (*A. galli* embryos and *Caenorhabditis elegans* adult worms)	Horgan et al. 2025
Anti-methanogenic effect			
MeOH extract of aerial parts	Reduction of methanogenic archaea activity; modulation of fermentation pathway via phenolic–STL synergy	*In vitro* rumen fermentation model	Massaro et al. 2025
Non-allergic activity			
STLs/leaves	Occurrence of systemic allergic dermatitis caused by sesquiterpene lactone-containing plants	Literature survey via textbooks and the Medline/PubMed database	Paulsen 2016

tracts. Dose-dependent (2–8 μg/mL) inhibitory activity of caffeic and chlorogenic acids on α-amylase and α-glucosidase was earlier evaluated (Oboh et al. 2015). As a result, caffeic acid had a significantly higher inhibitory effect on α-amylase and α-glucosidase than chlorogenic acid.

Cytotoxicity

To evaluate the cytotoxicity of *C. alpina*, a human monocytic cell line was used, as it mimics the interaction of the extracts with the immune system (Zheleva-Dimitrova et al. 2023) (Table 2). After an incubation of THP-1-derived macrophages with both flowering heads and leaf extracts, a slight increase in metabolic activity was observed at concentrations ranging from 2 to 200 μg/mL. However, noteworthy cytotoxicity was detected at higher concentrations, reaching approximately 70% for flowering head extract and nearly 90% for leaf extract at 2000 and 3000 μg/mL. These concentrations are significantly high and could be considered meaningless (Zheleva-Dimitrova et al. 2023).

Antidiabetic activity

The protective effect of *C. alpina* leaves extract on metabolic disorders and oxidative stress in Wistar rats with streptozotocin-induced type 2 diabetes was examined (Zheleva-Dimitrova et al. 2024) (Table 2). Treatment with low and high doses of the extract significantly improved serum biochemical and lipid parameters. Diabetic rats showed increased total cholesterol (up to 2.29 mmol/L), triglycerides (up to 1.30 mmol/L), and elevated liver enzymes (ASAT 143.8 U/L, ALAT 160.6 U/L), as well as higher urea (14.2 mmol/L) and creatinine (65.5 μmol/L). The treatment with a *C. alpina* extract reduced cholesterol and triglyceride levels by about 25% and 55%, respectively. ASAT and ALAT were normalized to 111.0 U/L, while urea and creatinine declined to 12.3 mmol/L and 50.12 μmol/L, respectively. A beneficial effect of treating diabetic animals with the extract was revealed by the high increase in GSH levels by 27%, while the quantity of MDA decreased by 30% compared to diabetic rats. Treatment of non-diabetic animals with the two doses of the extract alone did not change the parameters considered, nor did acarbose change these parameters in STZ-treated rats. Also, administration of both doses of the extract to the last mentioned enhanced relatively the same range of values of the examined biochemical parameters, and no dose-dependent effect was established (Table 2). Histopathology revealed restoration of normal hepatic and pancreatic architecture, with reduced steatosis and regeneration of β-cells. UHPLC-DAD analysis showed cichoric acid (91.93 mg/g dry extract), caftaric acid (11.36 mg/g), and chlorogenic acid (9.25 mg/g) as major secondary metabolites responsible for the observed antidiabetic, antioxidant, and hepatoprotective effects (Zheleva-Dimitrova et al. 2024). These results should be considered as evidence of the health-beneficial properties of edible Cichorieae species on carbohydrate-related diseases.

Anthelmintic activity

Biological studies have lately drawn attention to the anthelmintic effect of *C. alpina*. Extracts of the aerial parts have demonstrated potent in vitro activity against gastrointestinal nematodes, such as *Ascaridia galli*, a parasite responsible for substantial production losses in poultry (Poulopoulou et al. 2023) (Table 2). As a result, the effect of the extract had time and dose dependence, and there was a promising effect in inhibiting embryonic development of the parasite. Newly, the results are confirmed by Horgan et al. (2025) too (Table 2). The anthelmintic assays of BuOH and EtOAc fractions revealed that the more polar fractions were the most active against *A. galli* embryos and *Caenorhabditis elegans* adult worms, suggesting the fractions' constituents possess dual anthelmintic activity against multiple life-cycle stages (i.e., eggs, worms) of helminths. Also, the BuOH fraction was non-cytotoxic to human cell lines. Moreover, 11-*β*,13-dihydrolactucin and luteolin proved bioactivity against the embryo phenotype within the range of the flubendazole control, and luteolin was found to inhibit *C. elegans* egg hatching (Table 2). Given the increasing resistance of nematodes to synthetic drugs and the growing restrictions on chemical anthelmintics in organic farming, *C. alpina* and its specialized metabolites represent a promising herbal alternative for sustainable parasite prevention and control.

Anti-methanogenic effect

Massaro et al. (2025) observed the anti-methanogenic effect of *C. alpina* together with other pasture plants in rumen fermentation assays, suggesting potential applications in animal nutrition and environmental management (Table 2). The alpine herbs, harvested during their balsamic period, exhibited low gas production, mainly due to poor rumen degradability and reduced microbial growth efficiency. This was partially compensated by a lower CH_4 yield than predicted from the volatile fatty acid profile, indicating that part of the hydrogen not used for methanogenesis or microbial synthesis was redirected toward alternative sinks, such as acetogenesis. The observed shift in fermentation pathways likely reflects the influence of the bioactive compounds characteristic of the studied alpine plants.

Non-allergic activity

Research on systemic allergic dermatitis caused by sesquiterpene lactones has been completed (Paulsen 2016). Shoots of *C. alpina*, widely used as a vegetable in Italian and Finnish kitchens, have not revealed contact allergy, despite the content of lactucin and lactucin derivatives, which cause dermatitis (Table 2).

Conclusion

Based on the comprehensive survey, *C. alpina* appears to be an underappreciated but valuable plant, revealing

a rich phytochemical profile with promising therapeutic potential. The presence of guaianolide-type sesquiterpene lactones and phenolics such as acylquinic, acyltartaric, and other phenolic acids alongside flavones, flavonols, and flavanones holds significance for antioxidant and antidiabetic activity. The obtained data evidenced improvement of glycemic control, lipid metabolism, and oxidative stress parameters in metabolic disorders. An anthelmintic activity as well as an anti-methanogenic effect toward rumen fermentation was also established. Moreover, alpine sow-thistle appears to be one of the richest natural sources of cichoric and caftaric acids, far exceeding typical quantities in both wild and cultivated Cichorieae species. Thus, *C. alpina* emerges as a promising plant material for further development in the fields of nutraceuticals, functional foods, and veterinary practice.

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Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Use of AI

No use of AI was reported.

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Author contributions

Vessela Balabanova: Conceptualization; Methodology; Investigation; Resources; Data curation; Writing - Original draft preparation; Reneta Gevrenova: Writing - Original draft; Data curation, Review & Editing; Supervision. Dimitrina Zheleva-Dimitrova: Investigation; Visualization; Writing - Original draft, Review & Editing; Project administration; Funding acquisition.

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Data availability

All of the data that support the findings of this study are available in the main texts.

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