Phytochemical properties of plant species of the Campanulaceae family

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Abstract

The Campanulaceae family, which encompasses approximately 40 genera and 600 species, serves as a substantial reservoir of medicinal plants that are extensively utilized in both traditional and contemporary healthcare modalities. Phytochemical research has elucidated those constituents of this family, particularly those within the genus Codonopsis, harbor a plethora of bioactive compounds including polyacetylene, phenylpropanoids, alkaloids, triterpenoids, flavonoids, and polysaccharides, which underpin their extensive pharmacological effects (Dimitriadis et al., 2024; He et al., 2015).Prominent medicinal attributes ascribed to plants within the Campanulaceae family encompass antioxidant, anti-inflammatory, immunomodulatory, anticancer, adaptogenic, and antimicrobial properties (Dimitriadis et al., 2024; Gao et al., 2018; Liu et al., 2024).For example, Codonopsis pilosula and allied species are distinguished for their roles in enhancing immune function, modulating metabolic processes, and demonstrating anti-tumor efficacy through mechanisms such as the induction of apoptosis and the suppression of cancer cell proliferation (Bailly, 2020; Liu et al., 2024). Other genera, such as Campanula, have demonstrated strong antioxidant and enzyme inhibitory activities linked to their phenolic and flavonoid content (Dimitriadis et al., 2024). Despite these promising findings, further research is needed to elucidate the mechanisms of action, standardize quality control, and validate the clinical efficacy. Overall, the Campanulaceae family represents a valuable reservoir of phytochemicals with significant potential for the development of novel nutraceuticals and therapeutic agents (Dimitriadis et al., 2024; He et al., 2015; Liu et al., 2024).

Keywords: *Phytochemical, Campanulaceae, Medicinal properties, Therapeutic, Nutraceutical*

Introduction

Campanulaceae a widely distributed family of herbs, shrubs, and vines, rarely trees, with about 90 genera and 2,415 species worldwide (Mark T. Strong, 2021). The Campanulaceae family, also known as the bellflower family, has a

*rich history of traditional uses across various cultures. These uses span medicinal, culinary, and ceremonial applications. Native wild edible greens usually include plants with widespread geographical ranges and represent a long tradition associated with well-documented health effects, especially in the frame of the Mediterranean diet. Some Campanulaceae species, such as Campanula pelviformis, have been found to have good nutritional value, containing carbohydrates, proteins, fibers, and various mineral elements(Tsiftsoglou et al., 2023). The purpose of investigating the phytochemical properties of the Campanulaceae family is to identify the properties of this family to enable researchers to study the plant species of this family in more depth and detail. Campanula pelviformis Lam. is not the only edible species of this genus which is part of Mediterranean diet (**Figure 1**). In Italy, many traditional and local recipes have the young aerial parts of C. rapunculus L. and C. trachelium L. (Guarrera & Savo, 2016; Ranfa & Bodesmo, 2017) as ingredients. In Turkey, roots of C. glomerata L. subsp. hispida (Witasek) Hayek (Karık et al., 2018) and the young leaves of C. lyrata Lam. (taşkın & Bitiş, 2016) are consumed as vegetables. According to ethnobotanical studies in Bosnia-Herzegovina, young shoots of C. rapunculoides L., C. trachelium L., C. glomerata L. and C. pyrimidalis L. are used as cooked vegetables (Jman Redzic, 2006). This is not the only research concerning the nutritional value of the plants belonging to this genus. There are many other studies which provide information about the culinary use of Campanula spp. and indicate that, apart from ornamental plants, they are a source of many phytonutrients, fibers and significant amounts of minerals (macro and trace-elements) which play an important role in maintaining human health (Targan et al., 2018). Recently, the medicinal, agro-food and ornamental potential of this species was also studied, along with other neglected local endemic plants of Crete (Krigas et al., 2021). The phytochemical properties of the Campanulaceae family are of significant importance due to their diverse bioactive compounds and associated health benefits. These properties contribute to the family's medicinal, nutritional, and potential therapeutic applications. Introducing the phytochemical properties of this family will guide targeted research.*

Figure 1- (a) Edible parts of the plant Campanula pelviformis Lam. during vegetation period (photo by A. Psaroudaki); (b) Inflorescence of the plant during flowering period (photo by A. Psaroud *(Tsiftsoglou et al., 2023)*

Methodology

The reviewed sources were collected using a systematic and comprehensive search in the literature related to medicinal species and phytochemical properties of the Campanulaceae family. Articles were collected from various online search engines, such as Google Scholar, PubMed, Science Direct and Semantic Scholar.

Results

Phytochemical compounds

The Campanulaceae family exhibits diverse phytochemical constituents across its genera, with significant variations in bioactive compounds. Below is a categorized overview of phytochemical compounds.

Alkaloids

The Campanulaceae family's alkaloids exhibit genus-specific structural diversity, with Lobelia and Codonopsis being the primary sources. Their distinct biosynthetic pathways and pharmacological roles underscore their importance in traditional medicine and drug discovery. Further research is needed to explore lesser-studied species and clinical applications. Codonopsine, codonopsinine, and radicamine A are found in Codonopsis clematidea and C. pilosula. Nicotinic acid and uracil occur in C. pilosula roots (He et al., 2015). Lobelia species contain piperidine alkaloids, a defining feature of this genus (Folquitto et al., 2019). The Campanulaceae family contains several distinct types of alkaloids, which are classified primarily by their chemical structure and the plant genera in which they occur:

1. Piperidine Alkaloids

- ***Structure:*** *Characterized by a 6-membered nitrogen-containing heterocyclic (piperidine) ring.*
- ***Occurrence:*** *Most prominent in the genus Lobelia (subfamily Lobelioideae) (Figure 2).*
- ***Examples:*** *Lobeline, lobelanine, lobelanidine, norlobelanidine.*
- ***Biosynthesis:*** *Derived from lysine.*
- ***Significance:*** *These alkaloids are known for their neuroactive and respiratory effects, with lobeline specifically used as an expectorant and for treating nicotine addiction (DrMukul Tailang Professor, 2018; E.Berry, 2015; Strong, 2007).*

2. Pyrrolidine Alkaloids

- ***Structure:*** *Feature a 5-membered nitrogen-containing heterocyclic (pyrrolidine) ring.*
- ***Occurrence:*** *Found mainly in the genus Codonopsis.*
- ***Examples:*** *Codonopsine, codonopsinine, codonopsinol C, codonopiloside A.*
- ***Biosynthesis:*** *Likely originate from ornithine or polyketide pathways.*
- ***Significance:*** *Associated with immunomodulatory and adaptogenic properties (Cholakova et al., 2005; Strong, 2007).*

3. Polyhydroxylated Pyrrolidine and Piperidine Alkaloids (Iminosugars)

- ***Structure:*** *Sugar-mimetic alkaloids with multiple hydroxyl groups on the pyrrolidine or piperidine ring.*
- ***Occurrence:*** *Occasionally found in some Campanula and related species.*
- ***Examples:*** *DMDP (2,5-dideoxy-2,5-imino-D-mannitol), α-1-C-ethyl-fagomine, 1,4-dideoxy-1,4-imino-D-arabinitol, 1-deoxynojirimycin, 1-deoxymannojirimycin.*
- ***Significance:*** *These compounds act as glycosidase inhibitors and have potential therapeutic effects (Cholakova et al., 2005).*

Table 1- *Summary of the types of alkaloids found in the Campanulaceae family*

Type of Alkaloid	***Core Structure***	***Main Genera***	***Examples***	***Major Activity/Use***
Piperidine	*6-membered ring (N-heterocycle)*	*Lobelia*	*Lobeline, lobelanine*	*Neuroactive, respiratory support*
Pyrrolidine	*5-membered ring (N-heterocycle)*	*Codonopsis*	*Codonopsine, codonopsinol*	*Immunomodulatory, adaptogenic*
Polyhydroxylated pyrrolidine/piperidine (Iminosugars)	*Hydroxylated 5- or 6-membered ring*	*Campanula (rare)*	*DMDP, fagomine derivatives*	*Glycosidase inhibition, therapeutic*

These alkaloids are important chemotaxonomic markers and contribute to the medicinal properties of Campanulaceae plants (Cholakova et al., 2005; Strong, 2007).

Figure 2- Lobelia rotundifolia, photo by P. Acevedo(Strong, 2007)

Phenylpropanoids

Tangshenosides I-VI and syringin are identified in Codonopsis tangshen and C. lanceolata. Coniferaldehyde and sinapinaldehyde appear in C. cordifolioidea (He et al., 2015). Phenylpropanoids are a class of organic compounds biosynthesized from phenylalanine and tyrosine via the shikimic acid pathway, characterized by a six-carbon aromatic ring and a three-carbon propene tail. (Akashi et al., 2005; Hahlbrock & Scheel, 1989). In the Campanulaceae family, these compounds play significant ecological and taxonomic roles, while also contributing to medicinal properties in certain species. The Campanulaceae family exhibits distinctive phenylpropanoid chemical profiles, with several novel compounds identified in recent studies. While exclusivity is challenging to confirm due to limited comparative data, certain phenylpropanoids show restricted distribution across the family .While phenylpropanoids are widespread in plants, their glycosylation patterns and structural modifications (e.g., acylated glucosides in Campanula) may serve as family-specific markers. However, current evidence suggests these compounds are not strictly exclusive to Campanulaceae. For example, neolignans and hydroxycinnamaldehydes occur in other families but are underrepresented in Campanulaceae prior to these studies (Qi et al., 2020c; Tsiftsoglou et al., 2023) .Limited comparative analyses across plant families hinder definitive claims of exclusivity. Further studies are needed to map the biosynthetic pathways of campanulalignans and assess their distribution beyond Campanulaceae. In summary, Campanulaceae produces structurally unique phenylpropanoids like campanulalignans and simplified derivatives, but their exclusivity remains unconfirmed. These compounds highlight the family's chemical innovation and therapeutic potential, particularly in anti-inflammatory applications.

Triterpenes and Sterols

Taraxerol, α-spinasterol, and stigmasterol are prominent in C. pilosula, C. tangshen, and C. lanceolata. Friedelin and echinocystic acid derivatives occur in multiple Codonopsis species (He et al., 2015; Moosavi et al., 2018).Triterpenes and sterols are prominent secondary metabolites in the Campanulaceae family, contributing to both ecological adaptability and medicinal properties. These compounds are distributed across genera

like Codonopsis and Campanula, with structural diversity and tissue-specific accumulation patterns. Triterpene acetates in aerial tissues may enhance plant defense against pathogens or herbivores (Choi et al., 2023). Sterols and triterpenoids in Campanula species correlate with traditional uses, such as antioxidant and potential cardiotonic effects (Moosavi et al., 2018; Yayli et al., 2003). There are limited data on sterol diversity across Campanulaceae genera. Biosynthetic regulation of triterpene acetates remains understudied.This chemical repertoire highlights Campanulaceae's adaptability and underscores its potential for biotechnological and pharmacological applications.

Polyacetylenes

Polyacetylenes are a notable class of bioactive compounds present in the Campanulaceae family, particularly recognized for their chemical diversity and pharmacological potential. Polyacetylenes are part of the chemical profile that helps differentiate Campanulaceae species and may assist in chemotaxonomic classification. Detailed chemical characterization and biosynthetic pathway elucidation of polyacetylenes in Campanulaceae remain limited. More comprehensive studies are needed to explore their distribution across different genera and their ecological roles. In summary, polyacetylenes are important secondary metabolites in Campanulaceae, especially in Lobelia and related genera, contributing to the family's chemical diversity and potential medicinal applications. Lobetyolin and lobetyolinin are widely distributed in Codonopsis pilosula, C. lanceolata, and related species (He et al., 2015).

Flavonoids and Phenolic Compounds

Flavonoids and phenolic compounds in Campanulaceae are diverse and species-specific, with important roles in plant defense, taxonomy, and pharmacology. The family shows a characteristic pattern of flavone and flavonol distribution that aligns with genetic and ecological differentiation among species, particularly in the genus Campanula (Bergonci et al., 2023; Moosavi et al., 2018; Mubariz et al., 2022; Murai et al., 2014). Luteolin, kaempferol, and apigenin glycosides are found in Campanula nervosa and C. thalictrifolia. Phenolic acids like ferulic acid and chlorogenic acid derivatives appear in Campanula takesimana leaves (Qi et al., 2020a; Tsiftsoglou et al., 2023).

Cardiac Glycosides

Campanula latifolia contains cardiac glycosides, reported in both aerial parts and roots (Moosavi et al., 2018). Cardiac glycosides are present but not widespread or highly abundant in the Campanulaceae family. Campanula latifolia is among the species reported to contain these compounds, though detailed phytochemical data remain sparse. These compounds have potent cardiotonic and toxic effects and are chemically characterized by steroidal aglycones linked to sugars. Their pharmacological significance in Campanulaceae is still underexplored compared to other plant families. Thus, while cardiac glycosides occur in Campanulaceae, they are not a defining or extensively studied chemical group in this family, warranting further phytochemical and pharmacological investigation.

Polysaccharides

Codonopsis species produce immunomodulatory polysaccharides, though specific structures require further characterization (He et al., 2015). Campanulaceae polysaccharides are chemically diverse, mainly fructan-based energy storage molecules with complex monosaccharide compositions. They have significant bioactivities, especially in genera like Codonopsis and Platycodon, underpinning their pharmacological potential.This family uniquely stores carbohydrates as fructans rather than starch, distinguishing it biochemically from many other plant families.

Medicinal properties

These compounds underpin the family's traditional medicinal uses, with antioxidant, anti-inflammatory, and adaptogenic properties frequently reported (Erdoğan et al., n.d.; Moosavi et al., 2018; Qi et al., 2020a). Variations in compound profiles often align with taxonomic classifications, supporting chemotaxonomic studies (He et al., 2015; Kim et al., 2017). The Campanulaceae family encompasses species with significant medicinal properties, supported by a rich phytochemical diversity including alkaloids, polysaccharides, phenolics, flavonoids, triterpenes, and cardiac glycosides. These compounds contribute to traditional uses in respiratory therapy, immune support, anti-inflammatory treatments, and as nutritional supplements. Ongoing phytochemical and pharmacological studies continue to validate and expand the therapeutic potential of Campanulaceae plants.

Anti-inflammatory Properties

The Campanulaceae family contains multiple compounds phenylpropanoids, flavonoids, lobetyolin, and sesquiterpenes that exhibit potent anti-inflammatory effects through inhibition of key inflammatory enzymes and mediators. Experimental studies confirm these activities in vitro and in vivo, validating traditional medicinal uses and highlighting the family's therapeutic potential. Extracts from Campanulaceae plants, especially Codonopsis and Campanula species, inhibit pro-inflammatory mediators such as TNF-α, nitric oxide, and IL-6. The key compounds effective in this property are triterpenoids (e.g., lansemacid A), phenolic acids, flavonoids (Jung et al., 2018; Qi et al., 2020b).

Anticancer Activity

The Campanulaceae family contains flavonoids, phenylpropanoids, and polyacetylene derivatives with significant antioxidant properties that underpin their potential anticancer activity. Compounds like lobetyolin and quercetin glycosides contribute to reducing oxidative stress, a key factor in cancer prevention. Although direct anticancer studies are sparse, these phytochemicals provide a promising foundation for future research into Campanulaceae derived anticancer agents. Saponins and polyacetylenes from Codonopsis species induce apoptosis and inhibit proliferation in various cancer cell lines. The key compounds effective in this property are Saponins, polyacetylenes(Jin et al., 2022; Wang et al., 2022).

Immunomodulatory Effects

Description: Polysaccharides from Codonopsis roots enhance immune response, supporting traditional use for immune deficiency. The key compounds effective in this property are Polysaccharides (Long et al., 2024). Campanulaceae polysaccharides and extracts stimulate innate immune responses by activating macrophages, enhancing phagocytosis, and promoting cytokine secretion (NO, TNF-α, IL-6). These effects are mediated through key signaling pathways like NF-κB and MAPK, leading to improved immune defense and regulation. The family's immunomodulatory properties support its traditional medicinal uses and highlight its potential as a source of natural immune-enhancing agents. This immunomodulatory profile makes Campanulaceae species promising candidates for developing therapies aimed at boosting immune function and managing inflammatory diseases.

Antioxidant Activity

Methanol and ethanol extracts from Campanula and Codonopsis species show strong free radical scavenging activity. The key compounds effective in this property are Flavonoids and phenolic acids (Figure 3) (Sarikurkcu et al., 2017). The antioxidant activity in Campanulaceae is largely attributed to flavonoids, phenolic acids, phenylpropanoids, and polyacetylenes, which effectively scavenge free radicals and reduce oxidative stress. Several Campanula species exhibit antioxidant capacities comparable to standard antioxidants like Trolox, making the family a promising source of natural antioxidants with potential applications in health and industry.

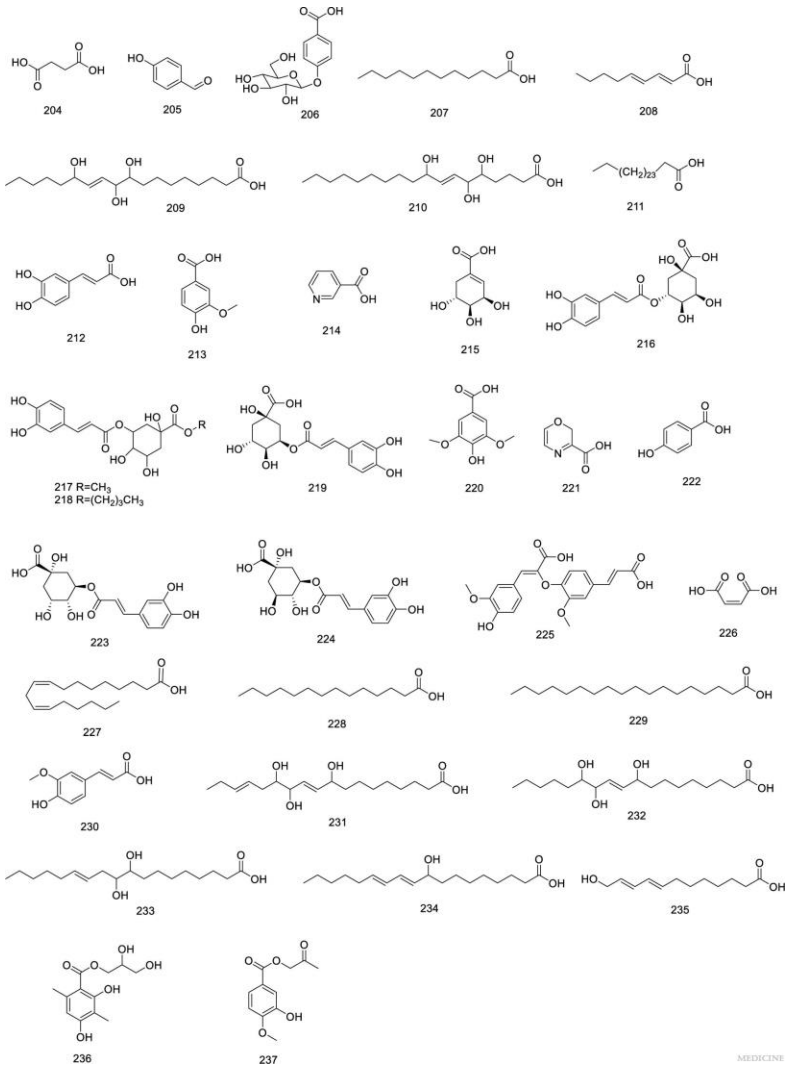

Figure 3- Structural of phenolic acids and organic acids from genus Codonopsis*(Chu et al., 2024)*

Neuroactive and CNS Effects

Piperidine alkaloids, especially lobeline from Lobelia species, show potential in treating addiction and neurodegenerative diseases. The key compounds effective in this property are Lobeline, lobinaline (Dwoskin & Crooks, 2002; Folquitto et al., 2019). While direct evidence is limited, the Campanulaceae family likely possesses neuroactive and CNS effects through polyacetylenes and other secondary metabolites. These compounds may

influence neurotransmitter systems and provide neuroprotective or neurotoxic effects. Traditional medicinal uses support potential CNS benefits, but detailed pharmacological and toxicological studies are required to clarify these properties.

Respiratory Support

Lobelia extracts are traditionally used for asthma and bronchitis due to bronchodilatory and expectorant effects. The key compounds effective in this property are Lobeline (Ge et al., 2020).
The Campanulaceae family supports respiratory health through multiple mechanisms: respiratory stimulation, bronchial relaxation, expectoration enhancement, anti-inflammatory action, and antioxidant protection. Lobelia inflata is historically and currently valued as a respiratory stimulant and expectorant, primarily due to lobeline. Platycodon grandiflorus offers antitussive, anti-asthmatic, and anti-inflammatory benefits, making it effective against chronic bronchitis and asthma.These properties validate traditional uses and highlight Campanulaceae species as valuable botanical resources for respiratory therapies.

Antimicrobial Activity

Extracts from Lobelia and Campanula species show antimicrobial effects against bacteria, including Mycobacterium tuberculosis. The key compounds effective in this property are Alkaloids, phenolic compounds (Ge et al., 2020). The Campanulaceae family contains species with broad-spectrum antimicrobial activity against both bacteria and fungi. Extract efficacy depends on species, solvent used, and microbial strain tested, with organic solvent extracts generally showing stronger activity. These findings support the traditional medicinal use of Campanulaceae plants and highlight their potential as sources for developing new antimicrobial agents. Further isolation and characterization of active compounds are needed to fully harness their therapeutic potential.This antimicrobial profile positions Campanulaceae as a promising family for natural product research targeting infectious diseases.

Blood System Regulation

Codonopsis extracts have been shown to reduce cholesterol, triglycerides, and improve blood viscosity, beneficial for metabolic disorders. The key compounds effective in this property are Polysaccharides, saponins (Chu et al., 2024). Campanulaceae species, especially Codonopsis, exhibit protective effects on erythrocytes and tissues by reducing oxidative damage and apoptosis. They regulate blood lipid profiles and improve blood rheology, contributing to cardiovascular health and resolving blood stasis. Immunomodulatory polysaccharides enhance hematopoietic function and immune responses, supporting overall blood system regulation. These multifaceted effects validate the traditional use of Campanulaceae plants in managing blood-related disorders and highlight their therapeutic potential in cardiovascular and hematological health.

Discussion

The Campanulaceae family, comprising approximately 40 genera and 600 species, is an important source of medicinal plants with a wide range of bioactive compounds and pharmacological activities (Dimitriadis et al., 2024). Extensive phytochemical investigations have revealed that members of this family, especially the genera Codonopsis and Campanula, are rich in diverse classes of secondary metabolites, including alkaloids, flavonoids, terpenoids,

polyacetylenes, lignans, fatty acids, phenolic acids, and polysaccharides (Dimitriadis et al., 2024; He et al., 2015; Yilmaz et al., 2023). These constituents are responsible for the notable medicinal properties observed in various species. Codonopsis species, particularly Codonopsis pilosula and C. lanceolata, have been widely used in traditional medicine for their immunomodulatory, anti-inflammatory, and adaptogenic effects (He et al., 2015; Liu et al., 2024). Recent pharmacological studies have highlighted the anti-cancer potential of Radix Codonopsis, attributing its activity to compounds such as luteolin, stigmasterol, polyacetylenes, lobetyolin, and glycitein, which act through mechanisms like inhibition of cancer cell proliferation, suppression of epithelial-mesenchymal transition, and induction of apoptosis (Liu et al., 2024). In addition, Codonopsis extracts are commonly used in health products and functional foods to nourish qi, enrich blood, and promote vitality, reflecting their integration into both traditional and modern therapeutic practices (Liu et al., 2024). The genus Campanula has also demonstrated significant medicinal value. Recent studies on species such as Campanula baskilensis have identified high levels of phenolic acids and flavonoids, including quinic acid, protocatechuic acid, rutin, hesperidin, and nicotiflorin, which contribute to strong antioxidant and enzyme inhibitory activities (Yilmaz et al., 2023). Extracts from other Campanulaceae plants have shown potent antioxidant effects, with methanol and ethanol extracts frequently exhibiting the highest activity in radical scavenging assays (Dimitriadis et al., 2024; Yilmaz et al., 2023). Additionally, certain hot water extracts from Campanula takesimana have demonstrated anti-inflammatory effects by inhibiting pro-inflammatory mediators such as prostaglandin E2 in macrophage models (Qi et al., 2020b). Beyond antioxidant and anti-inflammatory properties, some Campanulaceae species display notable antimicrobial and enzyme inhibitory activities, further supporting their potential as sources of novel nutraceuticals and therapeutic agents (Dimitriadis et al., 2024; Yilmaz et al., 2023). However, while the pharmacological promise of these plants is clear, gaps remain in the comprehensive understanding of their mechanisms of action, standardization of extracts, and clinical validation of their effects (He et al., 2015). Moreover, the phytochemical diversity within less-studied species of the family suggests that further exploration could yield additional bioactive compounds with unique medicinal properties (Dimitriadis et al., 2024; He et al., 2015).

Conclusion

The Campanulaceae family is a valuable reservoir of phytochemicals with diverse and significant medicinal properties, including antioxidant, anti-inflammatory, immunomodulatory, anticancer, and antimicrobial activities (Dimitriadis et al., 2024; He et al., 2015; Liu et al., 2024; Yilmaz et al., 2023). The therapeutic potential of well-studied genera such as Codonopsis and Campanula has been substantiated by both traditional use and modern pharmacological research, largely due to their rich content of polyacetylenes, flavonoids, phenolic acids, and other secondary metabolites. Nevertheless, further research is warranted to elucidate the mechanisms underlying these bioactivities, standardize quality control measures, and expand investigations to lesser-known species within the family (He et al., 2015). Advancing such studies will not only enhance the scientific understanding of Campanulaceae phytochemistry and pharmacology but also support the development of new natural products for health promotion and disease prevention.

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