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Short communication

Phytotherapeutic potential of iridoid-rich plant species native to the Balkan peninsula

Danijela Mišić*

Department of Plant Physiology, Institute for Biological Research "Siniša Stanković", University of Belgrade, Bulevar despota Stefana 142, 11108 Belgrade, Serbia

Introduction

Iridoids are a large class of cyclopentane pyran monoterpenes that are among the most pharmacologically active constituents of many medicinal plants native to the Balkan Peninsula. Despite their clear phylogenetic separation across plant lineages, many taxa within families such as Plantaginaceae, Gentianaceae, Scrophulariaceae, Rubiaceae, Verbenaceae, Lamiaceae, Caprifoliaceae, and Apocynaceae share the common biochemical trait of iridoid production. Iridoid-containing plants can be systematically classified according to the predominant structural type of their iridoids—namely secoiridoids, iridoid glycosides, and non-glycosilated iridoids—with each group being associated with characteristic pharmacological effects. Recently, more extensive studies revealed that iridoids exhibit a wide range of bioactivities, including neuroprotective, antinflammatory and immunomodulator, hepatoprotective and cardioprotective (Wang et al., 2020).

Iridoid rich plants of the Balkan Peninsula

The Balkan flora contains phylogenetically diverse groups of plant genera primarily producing three groups of iridoid compounds: iridoid glycosides (e.g. *Plantago, Veronica Lonicera, Vinca, Scrophularia, Ajuga, Stachys, Nepeta*), secoiridoid glycosides (e.g. *Gentiana, Gentianella, Swertia, Centaurium, Blackstonia*), and non-glycosidic iridoids (*Nepeta*). Simple iridoids in the form of aglycones usually occur as intermediates in the iridoid glycosides biosynthesis and are thus present as minor constituents, but the exclusivity of the genus *Nepeta* is that this group of iridoids, represented by nepetalactone-type compounds, is predominant (Banjanac et al., 2026).

This points to the existence of the three major chemotypes that can be used for the taxonomy-assisted prediction of pharmacological activities, prioritization of species for drug discovery, elucidation of evolutionary transitions in secondary metabolism, and for identification of convergent evolution across unrelated plant families.

Integrated chemical evolution-pharmacologic effects approach and implication for drug discovery

The phylogenetic distribution of iridoids in the plant kingdom suggests that evolution of iridoid metabolism is associated with the emergence of distinct pharmacological effects. Closely related taxa produce structurally related iridoids that converge on similar biological functions, resulting in recognizable evolutionary–pharmacological clusters. Thus, secoiridoid-rich Gentianaceae species are associated primarily with digestive and hepatometabolic regulation (Andryszkiewicz et al.,

*dmisic@ibiss.bg.ac.rs

2025), while representatives of the family Plantaginaceae, rich in aucubin and catalpol display cytoprotective and anti-inflammatory activities (Aly et al., 2025). On the other hand, harpagide-rich Scrophulariaceae and allied Lamiaceae are connected with anti-inflammatory and analgesic effects (Kumar et al., 2025). Loganin and secologanin are intermediates in the biosynthesis of secoiridoids and alkaloids, but in some species of the families Caprifoliaceae, Apocynaceae, and Rubiaceae these compounds are present as dominant iridoid constituents with neuroprotective and cytoprotective effects (Martins and Nunez, 2015). Non-glycosilated iridoids of the nepetalactone type are usually linked with neuroactive, antimicrobial, and anti-inflamatory effects (2018). One of the most striking patterns across the phylogeny is that anti-inflammatory activity repeatedly emerges in unrelated iridoid lineages. This repeated convergence suggests that the iridoid scaffold itself may constitute a privileged pharmacophore for modulation of inflammatory pathways.

Conclusion

A simplified phylogenetic framework of selected Balkan medicinal plant genera, derived from published molecular phylogenies, reveals clear associations between evolutionary lineages, dominant iridoid structural classes, and characteristic pharmacological activities. This pattern highlights the value of integrating phylogenetic and chemotaxonomic information to better understand the distribution of bioactive metabolites and their therapeutic potential. From a drug-discovery perspective, the phylogenetic approach is founded on the premise that taxa closely related to known iridoid-producing genera are likely to synthesize structurally similar compounds, including previously uncharacterized analogues with enhanced or complementary biological activities. Similar strategies have proven successful in the discovery of bioactive alkaloids and flavonoids, suggesting that phylogeny-guided exploration of Balkan medicinal plants may represent an effective avenue for identifying novel iridoid-based pharmacophores and advancing multi-target therapeutic development.

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