

β-Carboline Alkaloids from *Galianthe thalictroides* Leaves: Uncovering a Novel Indole-Monoterpene–Flavan-3-ol Subclass

Pedro Becker Kerber^{*}, Wilson Hino Kato Jr¹, Júlia Freire de Araújo¹, Ana Camila Micheletti², Fernanda Rodrigues Garcez¹, Walmir Silva Garcez¹, Nidia Cristiane Yoshida¹, Patrícia de Oliveira Figueiredo¹

pedro.beckerkerber@gmail.com

1- PRONABio, Instituto de Química, INQUI, UFMS, Av. Sen. Filinto Müller, 1555, Campo Grande, MS, Brazil. 2 - SINTMOL, Instituto de Química, INQUI, UFMS, Av. Sen. Filinto Müller, 1555, Campo Grande, MS, Brazil.

Galianthe thalictroides (Rubiaceae) is a South American shrub with a restricted distribution and a traditional use of root decoctions in folk medicine for cancer treatment in Brazil. Ethnopharmacological relevance has guided phytochemical research on this species, with root investigations previously leading to the discovery of β-carboline alkaloids and Rubiaceae-type cyclopeptides exhibiting potent in vitro cytotoxic activity. Phytochemical exploration of the leaves (unpublished data) revealed remarkable chemical diversity, with the isolation of eleven β-carboline alkaloids. Among them, a series of indole–monoterpene β-carbolines was identified, as well as novel hybrid molecules in which a flavan-3-ol (epicatechin) moiety is integrated into the monoterpene framework. This unprecedented arrangement constitutes a new subclass of β-carboline alkaloids, never previously described in the literature, significantly expanding the structural landscape of this alkaloid family. In addition to structural novelty, selected leaf-derived β-carbolines exhibited antibacterial activity. One compound showed strong inhibitory effects against *Staphylococcus aureus*, including resistant strains, moderate effects against *Enterococcus faecalis*, *Escherichia coli*, and vancomycin-resistant *E. faecium*, as well as synergistic or additive interactions with ampicillin. Other β-carbolines displayed moderate activity across multiple resistant strains. Furthermore, additional β-carboline alkaloids and other secondary metabolites remain under structural elucidation. Their chemical diversity, together with the unprecedented β-carboline–flavan-3-ol hybrids, provides a strong rationale for future anticancer investigations, aiming to validate their cytotoxic potential and explore pharmacological applications. In summary, *G. thalictroides* emerges as a rich source of novel β-carboline alkaloids, some with antibacterial activity and others with promising structural features for cytotoxicity, thereby expanding phytochemical knowledge and offering new avenues for the discovery of bioactive natural products within Rubiaceae.

Keywords: *Galianthe thalictroides*; alkaloids; β-carboline alkaloids; NMR

