Leptocarpin

Main functional characteristics: Selective cytotoxicity, anti-inflammatory, immunomodulatory

Molecular weight: ≈344 g/mol (estimated)

[2D structural image not available]

Scientific description

Leptocarpin is a sesquiterpene lactone exclusively found in *Leptocarpha rivularis* (Palo Negro), belonging to the heliangolide subclass. Its structure contains the α-methylene-γ-lactone moiety, a highly reactive group capable of forming Michael adducts with cysteine residues of target proteins. This chemical feature is shared with other bioactive sesquiterpene lactones, such as parthenolide, and is critical for its biological activity.

Pharmacologically, leptocarpin inhibits the NF-κB pathway. By alkylating cysteine residues in IKKβ, it prevents phosphorylation and subsequent degradation of IκB, thereby blocking NF-κB nuclear translocation. As a result, the transcription of pro-inflammatory genes including COX-2, iNOS, TNF-α, IL-1β, and IL-6 is markedly reduced. This underlies its strong anti-inflammatory potential and capacity to modulate the tumor microenvironment.

In cancer research, leptocarpin has demonstrated the ability to induce apoptosis via the intrinsic mitochondrial pathway. This involves mitochondrial membrane potential (ΔΨm) loss, cytochrome c release, caspase-3 and -9 activation, and DNA fragmentation. Furthermore, leptocarpin inhibits migration and invasion of cancer cells, thereby reducing metastatic potential.

Phytochemical studies of *L. rivularis* have confirmed leptocarpin as one of the major active metabolites responsible for the cytotoxic effects of the plant. In vitro assays have shown antiproliferative activity in gastric, colon, and breast cancer cell lines. Additionally, leptocarpin potentiates apoptosis when combined with chemotherapeutic drugs, suggesting a role as an adjuvant in anticancer therapy.

Leptocarpin also exerts immunomodulatory effects by regulating cytokine production, modulating T-cell responses, and shifting macrophage polarization toward an anti-inflammatory phenotype. These properties make it a promising candidate for diseases where immune dysregulation and chronic inflammation are key pathological drivers.

From a biotechnological standpoint, leptocarpin is considered a chemotaxonomic marker of *L. rivularis*. Its unique presence makes it useful for standardization of extracts and as a

quality marker in nutraceutical and pharmaceutical developments derived from this Chilean endemic species.

In conclusion, leptocarpin combines selective cytotoxicity, strong anti-inflammatory capacity, and immunomodulatory effects through well-defined molecular mechanisms. Its exclusivity in *Leptocarpha rivularis* provides a strategic advantage for developing high-value botanical extracts and phytopharmaceuticals, particularly in oncology and immunology.

References

1. 1. Martínez R, et al. Leptocarpin and 17,18-dihydroleptocarpin from Leptocarpha rivularis: isolation and structure. Phytochemistry. 1979;18(11):1923-1926. doi:10.1016/S0031-9422(00)98489-9.
2. 2. Bosio C, et al. Cytotoxic and apoptotic effects of leptocarpin on human cancer cell lines; inhibition of NF- κ B. Bioorg Med Chem. 2015;23(24):7300-7307. doi:10.1016/j.bmc.2015.10.044.
3. 3. Montenegro I, et al. Chemical composition, antioxidant and anticancer activities of Leptocarpha rivularis flower extracts. Molecules. 2021;26(1):67. doi:10.3390/molecules26010067.
4. 4. Carrasco N, et al. Antitumoral activity of Leptocarpha rivularis flower extracts against gastric cancer cells. Int J Mol Sci. 2023;24(2):986. doi:10.3390/ijms24020986.
5. 5. Jiménez-González A, et al. UHPLC-ESI-Orbitrap-MS analysis of Leptocarpha rivularis extracts. J Enzyme Inhib Med Chem. 2018;33(1). doi:10.1080/14756366.2018.1466880.
6. 6. Olea AF, et al. Leptocarpha rivularis extracts against cancer cell lines: micellar encapsulation improves activity. J Chil Chem Soc. 2019;64(2):4437-4442. doi:10.4067/S0717-97072019000204437.
7. 7. Rubio J, et al. Phytochemical profiling and anticancer assessment of Leptocarpha rivularis; micropropagation approach. Plants (Basel). 2022;11(4):546. doi:10.3390/plants11040546.
8. 8. Siedle B, et al. Quantitative structure-activity relationships of sesquiterpene lactones: NF- κ B inhibition. J Med Chem. 2004;47(24):6042-6054. doi:10.1021/jm049937r.
9. 9. Kwok BH, et al. Parthenolide directly binds and inhibits IKKβ; NF- κ B blockade by α-methylene- γ -lactone. Chem Biol. 2001;8(8):759-766. doi:10.1016/S1074-5521(01)00049-7.
10. 10. Hehner SP, et al. Sesquiterpene lactones specifically inhibit activation of NF- κ B. J Biol Chem. 1998;273(50):33508-33516. doi:10.1074/jbc.273.50.33508.