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ANTARCTIC LICHENS AS A PLATFORM TO DISCOVER BIOACTIVE MOLECULES WITH NEUROPROTECTIVE AND ANTI-INFLAMMATORY POTENTIAL

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Antarctic lichens endure extreme cold, intense UV radiation, strong winds, and chronic nutrient scarcity—pressures that drive distinctive secondary metabolism. We investigated eight Antarctic lichens as a source of bioactive molecules with neuroprotective and anti-inflammatory potential. To link chemistry with function, we applied an **effect-directed analysis (EDA)** integrating **HPTLC bioassays**, **LC-MS profiling**, and **molecular docking**, enabling the pinpointing and characterization of **COX-2** and **acetylcholinesterase (AChE)** inhibitors. Chemical profiling revealed a landscape dominated by depsides, depsidones, dibenzofurans (notably usnic acid), naphthoquinones, and fatty acids. Functional assays demonstrated COX-2 inhibition, AChE inhibition, and antioxidant activity, consistent with mechanisms relevant to neuroinflammation and oxidative stress. Docking supported plausible binding of representative metabolites within the catalytic sites of COX-2 and AChE, indicating concordance between structure and mechanism. A salient observation was **polypharmacology**. Several metabolites were active across more than one readout: **usnic acid** and **sphaerophorin** consistently exhibited dual antioxidant and enzyme-inhibitory behavior. In addition, an **unusual fatty acid, pentahydroxyoxoheptacosanoate**, detected in multiple species, showed **remarkable anti-inflammatory activity**, highlighting underappreciated lipophilic contributors to lichen bioactivity. Collectively, these findings expand the chemical and functional map of Antarctic lichen chemodiversity and underscore their value as reservoirs of drug-like natural products. The integrated **EDA–HPTLC/LC-MS–docking** strategy provides a rapid, efficient route to identify mechanism-anchored leads from complex matrices and prioritizes candidates for cell-based validation in **neuroprotection** and **inflammation** research.

Keywords: *lichen, bioactive molecules, neuroprotection, inflammation, COX-2, acetylcholinesterase (AChE)*