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Diversity, Bioactivity, Therapeutic Potential, and Future Challenges of
Bibenzyls and Bisbibenzyls in Bryophytes

Invited Talk

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Abstract

Bryophytes, particularly liverworts, produce a wide range of metabolites, among which bibenzyls and bisbibenzyls are considered signature compounds. Bibenzyls contain two aromatic rings, while bisbibenzyls consist of four. The first bisbibenzyls, marchantin A and riccardin A, were reported in 1982 and 1983, and since then, around 70 different bibenzyls and bisbibenzyls have been identified. These compounds are isolated using various solvent systems and characterized through spectroscopic techniques. Their content often varies with season, geography, and environmental conditions. Bibenzyls, structurally related to dihydrostilbenoids, occur abundantly in liverworts and serve as chemotaxonomic markers. Lunularin, a pre-bibenzyl, is found in species such as *Marchantia polymorpha* and *Ricciocarpos natans*. Other examples include cavicularin, an optically active cyclic compound from *Cavicularia densa*; radulanin, a seven-membered heterocyclic ring compound; and dihydroresveratrol, a stilbenoid from *Blasia pusilla* with antineoplastic properties. Bisbibenzyls, dimeric forms of bibenzyls, occur in cyclic or acyclic forms across various orders of Marchantiophyta. They are biosynthesized from two lunularin molecules and share a core of four aromatic rings with two ethano bridges. Several series of bisbibenzyls have been discovered, including marchantins (A–H), riccardins, and plagiochins. Both bibenzyls and bisbibenzyls exhibit diverse bioactivities, such as antibacterial, antifungal, antitumor, antioxidant, neuroprotective, muscle relaxant, and cytotoxic effects. Their significance has been demonstrated in vitro and increasingly through in silico studies. Despite their promise, the natural yield of these compounds in liverworts is very low, posing challenges for large-scale production. Future prospects lie in applying advanced biotechnological and synthetic approaches to enhance scalability, enabling potential pharmaceutical and industrial applications.

Keywords: Bibenzyls, Bisbibenzyls, Liverworts, marchantin A, riccardin A