Cyanobacteria as a Source of Innovation in Bioactive Compound Discovery

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Abstract

Cyanobacteria, among the oldest photosynthetic organisms on Earth, have thrived for over 3.5 billion years by adapting to diverse ecological niches, including marine environments. These long-standing adaptations have led to the evolution of specialized biosynthetic pathways and unique metabolites, making cyanobacteria a rich yet underexplored source of structurally diverse natural products with biotechnological potential.
The Blue Biotechnology and Ecotoxicology Culture Collection (LEGE-CC) at CIIMAR is a valuable resource for natural product discovery, comprising over 1,000 cyanobacterial strains from marine, freshwater, and extreme environments collected across diverse geographical regions.

We present recent advances in accelerating the discovery of novel bioactive compounds from cyanobacteria through an integrated approach combining natural product library fraction screening, physiologically relevant bioassays, metabolomics for early dereplication, and genome mining. Screening 60 cyanobacterial strains and testing 512 fractions enabled the selection of promising strains, leading to the discovery, isolation and structure characterization of several novel compounds. These include: 1) phormidolide E, a 16-membered macrolactone polyketide with potent cytotoxic activity against human colon carcinoma spheroids; 2) two novel metallophore families, lusichelins and leptochelins, which combine metal-chelating activity with cytotoxic potential; and 3) a pseudospumigin-type compound with appetite-modulating activity.

These results highlight the potential of cyanobacteria as a source of novel bioactive compounds and emphasize the importance of multidisciplinary screening approaches in accelerating the discovery of promising new marine drugs and nutraceuticals.
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