Uncovering Bioactive Metabolites in Cyanobacteria Using OSMAC and Metabolomic Profiling

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Abstract

Over recent decades, marine biodiversity has gained attention as a source of novel natural products, with cyanobacteria standing out for their ability to produce bioactive metabolites. However, under standard laboratory conditions, many biosynthetic gene clusters remain transcriptionally silent, limiting their biotechnological exploitation. The "One Strain Many Compounds" (OSMAC) strategy-through modulation of environmental parameters-has emerged as a powerful tool to induce differential metabolite expression.1-3
In this study, five cyanobacterial strains isolated from hypersaline environments were subjected to the OSMAC approach via salinity modulation (15, 25, and 60g/L synthetic sea salts) under controlled photoperiods in Z8 medium. Extracts obtained from lyophilized biomass (CHCl:MeOH, 2:1 v/v) were fractionated via reverse-phase HPLC, yielding 120 fractions screened for health and environmental bioactivities. Health-oriented assays included lipid-reducing activity in zebrafish larvae (Nile Red assay) and HepG2 hepatocytes (anti-steatosis), as well as glucose uptake stimulation (2-NBDG assay) in zebrafish. Environmental bioassays targeted antifouling activity against *Mytilus galloprovincialis* larvae and antibacterial effects on five marine bacterial strains.

LC-HR-ESI-MS/MS-based metabolite profiling was performed on the most promising fractions to identify compounds potentially responsible for the observed bioactivities. Preliminary results indicate that a single cyanobacterial strain can produce distinct bioactive metabolites depending on the cultivation conditions, such as variations in salinity. This supports the potential of the OSMAC strategy as a valuable approach for diversifying and uncovering bioactive compounds from cyanobacteria.

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