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EPIGENETIC MODULATORS AIMING AT IMPROVEMENTS IN THE METABOLIC PRODUCTION OF THE ENDOPHYTIC FUNGUS HYPOMONTAGNELLA MONTICULOSA ISOLATED FROM THE RED MARINE ALGA DICHOTOMARIA MARGINATA

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Recent studies have revealed a wide variety of fungi associated with marine algae, showing great biotechnological potential and pharmacological properties. Complementarily, the modification of gene expression through epigenetic modulators can activate the production of novel metabolites via silenced biosynthetic pathways, contributing to chemical diversity. In this context, this work aimed to evaluate the chemical profile of the fungus Hypomontagnella monticulosa, isolated from the red alga Dichotomaria marginata, focusing on metabolic changes induced by epigenetic modulators. The fungal strain was first cultivated on potato-dextrose-agar (PDA) plates for 35 days and subsequently inoculated into Erlenmeyer flasks containing liquid Malt Extract medium under control conditions and supplemented with sodium butyrate (NaBut, 1 mM) and 5-azacytidine (5-AZA, 100 µM). A growth curve of the fungus in liquid medium was performed with ethyl acetate (EtOAc) extractions at 5, 10, 15, 20, 25, 30, and 35 days to assess metabolic variation during growth. Results showed that both mycelial dry weight and extract yields increased with longer cultivation times. However, cultivation in the presence of modulators was performed specifically at 15, 20, and 25 days, as these time periods presented the most significant fungal growth results in terms of biomass and extract yield. After EtOAc extraction, the samples were analyzed by HPLC-DAD under different chromatographic conditions. Four analyses were performed using gradient elution (5% to 100%) with methanol (MeOH/H_2O), MeOH/H_2O with 1% formic acid, acetonitrile (MeCN/H_2O), and MeCN/H_2O with 1% formic acid. Acidified solvents provided sharper and more intense peaks than non-acidified ones, suggesting that compounds in the extract are more stable or detectable in acidic media, possibly due to facilitated protonation. Epigenetic modulators promoted more intense peaks compared to the control, indicating possible activation of silent biosynthetic pathways. This work reinforces the effectiveness of epigenetic modulators and distinct chromatographic conditions in the detection of fungal secondary metabolites, while also directly contemplating UN Sustainable Development Goals related to Good Health and Well being (SDG 3) and Life under water (SDG 14).

Keywords: *Red algae, epigenetic modulators, marine fungi, chemodiversity.*