



CYTOTOXIC THIAZOLE-PRODUCING *Myxococcus* sp. BRX-014 ISOLATED FROM A BRAZILIAN MANGROVE

Renan da Silva de Oliveira^{1*}, Luís Guilherme Pereira Feitosa², Elthon Gois Ferreira³, Anna Caroline Campos Aguiar⁴, Leticia Veras Costa-Lotufo³, Paula Christine Jimenez¹

*rs.oliveira@unifesp.br

1- Instituto do Mar, Departamento de Ciências do Mar, Universidade Federal de São Paulo, Santos, SP – Brazil, 11.070-100. 2- Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP – Brazil, 14.040-903. 3- Instituto de Ciências Biomédicas, Departamento de Farmacologia, Universidade de São Paulo, São Paulo, SP – Brazil, 05.509-900. 4- Departamento de Microbiologia, Imunologia e Parasitologia, Universidade Federal de São Paulo, São Paulo, SP - Brazil, 04.023-900.

Myxobacteria are recognized as prolific producers of structurally diverse and biologically active metabolites. Although predominantly studied from terrestrial soils, their occurrence in coastal ecosystems such as mangroves remains largely underexplored. This gap is particularly evident in Brazil, where studies on myxobacterial diversity and biotechnological potential are still scarce. In this context, the present study investigates the potential of strain BRX-014, isolated from the Portinho Mangrove in São Paulo, Brazil. Phylogenetic analysis based on 16S rDNA sequencing identified the strain as a member of the genus *Myxococcus*, forming a distinct clade that suggests a potentially novel lineage. Its organic extracts demonstrated potent and selective cytotoxicity against human fibrosarcoma (HT-1080) and colorectal carcinoma (HCT-116) cell lines. Bioassay-guided fractionation afforded a dichloromethane fraction with pronounced bioactivity, displaying potent cytotoxicity (IC₅₀ = 0.58 µg/mL) and strong antiparasitic activity against *Plasmodium falciparum* 3D7 (IC₅₀ = 0.9 µg/mL). Metabolomic analysis of the BRX-014 extract (HRMS/GNPS) revealed a large cluster of ions annotated as myxothiazol correlates, suggesting the presence of novel thiazole-related metabolites. Fractions enriched in these ions were purified by HPLC and will be subjected to further structural elucidation. The detection of ions consistent with myxothiazol derivatives provides a plausible mechanistic rationale for the observed bioactivities, given that myxothiazols are potent inhibitors of the mitochondrial cytochrome bc₁ complex. This study highlights the unexplored potential of myxobacteria for the discovery of novel bioactive molecules, while also underscoring the importance of Brazilian mangroves as reservoirs of distinctive microbial diversity.

Keywords: Myxobacteria; Myxothiazol; Marine natural products; Anticancer; Antimalaria

