Bionectin F from marine derived *Clonostachys rogersoniana* as a potential inhibitor of *Mycobacterium tuberculosis* β-ketoacyl-ACP reductase (MabA)

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The number and diversity of drugs in tuberculosis (TB) drug development process have increased over the years, yet the attrition rate remains very high, signaling the need for continued research in drug discovery. In this study, extracts from marine derived fungi associated with ascidians were evaluated for antimycobacterial activity and their metabolites were identified through untargeted mass spectrometry-based metabolite profiling. Molecular docking and molecular dynamics simulations were performed on the bioactive extract. The methanol extract from *Clonostachys rogersoniana* MK33 was found to be a potent inhibitor of growth of *Mycobacterium smegmatis* mc^2155 and *Mycobacterium tuberculosis* H37Rv. Metabolite profiling of six marine fungal isolates led to the identification of 66 metabolites, among them was bionectin F from *C. rogersoniana* MK33 which had a docking score of -11.17 kcal/mol against *M. tuberculosis* β-ketoacyl-acyl carrier protein reductase (MabA, PDB ID = 1UZN), an essential enzyme involved in mycolic acid biosynthesis. Molecular dynamics simulation of the bionectin F and MabA complex revealed that bionectin F binds with A:SER140, a residue vital for the transformation of MabA to a holo-form. These findings provided strong evidence to conclude that bionectin F is a potential candidate for TB-drug development. Further studies on bioassay- guided purification of the methanol extract from *C. rogersoniana* MK33 are required to validate this conclusion.

Keywords: Tuberculosis; drug-discovery; marine fungi; MabA; Bionectin F.