Marine metabolites for HIV control: A multi-target *in-silico* approach

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ABSTRACT

This study evaluates the potential of marine sponge-derived metabolites as multi-target inhibitors of Human Immunodeficiency Virus (HIV), aiming to overcome the limitations of current antiretroviral therapies. An in silico molecular docking study was conducted on 15 compounds, including FDA-approved drugs (Efavirenz, Darunavir, Lenacapavir) and marine-derived phytoconstituents from Dysidea, Axinella, and Hippospongia species. The compounds were docked against key HIV targets: reverse transcriptase (RT), capsid protein (CP), and protease (PR). ADMET (absorption, distribution, metabolism, excretion, and toxicity) profiling was performed to assess pharmacokinetic and safety parameters, including blood-brain barrier penetration (logBB) and toxicity indices (LD_{50}, mutagenicity, CYP enzyme inhibition). Hippospongide A showed strong dual-target inhibition against RT (-7.1 kcal/mol) and PR (-9.4 kcal/mol), comparable to Darunavir. Avarone exhibited broad-spectrum efficacy (RT: -7.0, CP: -7.4, PR: -8.7 kcal/mol) and notable CNS penetrability (logBB: 0.26). Hippospongide A was non-mutagenic with low toxicity (LD_{50}: -0.5), although it showed moderate inhibition of CYP2C19/2C9 enzymes. Avarone, despite its mutagenicity, had strong multi-target and CNS potential. Marine sponge metabolites, particularly Hippospongide A and Avarone, show promise as next-generation HIV therapeutics. From this in-silico study, we confirmed that Hippospongide A is ideal for systemic viral suppression, while Avarone offers potential for targeting CNS reservoirs.

Keywords: ADMET profiling, HIV inhibitors, marine sponges, molecular docking