

DISCOVERY AND OPTIMIZATION OF NEW BENZIMIDAZOLE-BASED COMPOUNDS AS ANTITRYPANOSOMAL AGENTS

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Abstract: Neglected tropical diseases (NTDs) impact more than one billion people living in tropical and sub-tropical regions. NTDS are a diverse group of infectious diseases that are generally transmitted through insect vectors and lack safe and effective drugs. The control and elimination of these diseases remain a challenge. One of such diseases is the human African trypanosomiasis (HAT). HAT is endemic to sub-Saharan Africa. It is caused by the kinetoplastid protozoan *Trypanosoma brucei*. In this work, 400 diverse drug-like molecules were screened against the papain-like cysteine protease, rhodesain, a drug target in *Trypanosoma brucei*. Two of the compounds (MMV7703 and MMV7696) showed promising inhibitory activity against rhodesain, and moderate growth-inhibitory activity against *T. brucei* with up to 10-fold selective indices over HepG₂ cells. Analogues of the benzimidazole-based compound (MMV7703) have been synthesized and being evaluated against *T. brucei*. These benzimidazole-based compounds can serve as lead compounds for new antitrypanosomal drugs.

Keywords: NTDs, MMV pathogen box, HAT, Rhodesain, HepG₂, benzimidazole.

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