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Supramolecular synthesis of cis-1-amino-2-indanol derivatives: An in vitro and in silico analysis of drug efficacy against HIV-1 South African Wild-type C protease

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HIV-1 protease (HIV PR) is an aspartic protease which is considered vital in the cleaving of new viral polyprotein into functional units [1]. These polyproteins are needed in the maturation stage of the viral replication cycle to infect other host cells, this makes the HIV PR a significant drug target for possible therapeutic agents [2]. Due to the distinctive patterns of pharmaceutical drug resistance observed in HIV protease inhibitors, South African HIV-1 subtype C presents its own unique challenges in its management due to lowered drug efficacy [3]. Designing and synthesizing drugs which can adapt to these ever-changing macromolecules has become increasingly important for the management and treatment of patients living with HIV/AIDS. The constituent cis-1-amino-2-indanol has been used as a blueprint for many types of inhibitors including HIV-1 protease and malaria [4].

Cis-1-amino-2-indanol derivatives were synthesized using ketones and aldehydes to produce Schiff base imines to which a series of six compounds were synthesized using one pot synthesis as well as elucidated and characterized by SC-XRD, FTIR and Raman spectroscopy. Using in silico techniques such as molecular docking and dynamics studies the molecules were predicted to behave as dynamic covalent inhibitors which have a high binding affinity for the South African HIV-1 Wild-type C protease, binding to various allosteric sites. The effectiveness of these molecules on the South African HIV-1 Wild-type C protease was evaluated using empirical studies by assessing various kinetic and thermodynamic parameters which can be considered to inhibit proteolytic activity. Additionally, the compounds were also assessed for their cytotoxic effects on Green African monkey kidney cells (Vero cells) to evaluate their respective cytotoxic profiles.

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