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Contributed Paper

Evaluation of Biphenylalanine and Its Derivatives as Potential HIV-1 gp120 Attachment Inhibitors Based on Molecular Docking, CD4 Capture ELISA and Cytotoxicity Analysis

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ABSTRACT

Biphenylalanine and its derivatives (BPAs) are novel attachment inhibitors that target HIV-1 gp120 and prevent its binding to CD4 on host cell, designed via molecular modelling and docking using gp120-CD4 protein complex crystal structure. In this study, molecular docking showed that L-biphenylalanine has highest binding probability than D-biphenylalanine and L-methyl-biphenylalanine and exhibited low negative docked energy. The CD4 capture ELISA experiments indicated that L-biphenylalanine has an IC_{50} at submicromolar concentration. The Vero cell cytotoxicity test revealed that BPAs were non-toxic up to 400 μM. L-biphenylalanine fulfils "the Lipinski rule of five" criteria as a good drug candidate.

Keywords: biphenylalanine, derivatives, attachment inhibitors, HIV-1 gp120, CD4 capture ELISA, cytotoxicity

1. INTRODUCTION

Current drugs administered under HAART regimens to suppress HIV-1 infection target three main viral enzymes: reverse transcriptase, integrase and protease [1, 2, 3] that operates to inhibit viral replication after viral entry without effectively eradicating the infection. Studies have shown that their long term prescription may cause patients to develop toxic side effects and possible resistance of the virus to the drugs [4, 5, 6].

The hunt for new potential inhibitors that prevent viral entry into host cell is required for HIV patients. The mechanism of HIV-1 viral entry depends on three protein-protein interaction phases that consists of attachment, co-receptor binding, and viral fusion into the host cell [7]. The initial attachment phase is characterized by the binding of HIV-1 gp120 protein to host cell CD4 receptor that triggers a cascade of conformational changes in the viral envelope protein. In the second phase, the attachment of HIV-1 gp120 to CD4 exposes its co-receptor (CXCR4 or CCR5)-binding site on CD4 [8]. Finally, the formations of gp41