

Abstract

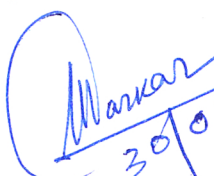
The thesis, **Mathematical Study on Enzyme Catalysed Reaction for HIV-1 Replication: Insight into the Antiviral Drug Treatment**, concentrates on modelling the "within-infected-cell" replication of Human Immunodeficiency Virus Type 1 (HIV-1) infection and conducting an in-depth study of the antiviral drug treatment.

In this thesis, we develop a set of nonlinear differential equations that describe the enzymatic activity of Cytochrome P3A4 (CYP3A4) in HIV-1 infected patients who consume alcohol. We conduct an analytical comparison of the metabolism of protease inhibitors (PIs) between alcoholic and non-alcoholic HIV-1 infected individuals. Additionally, the study examines the role of alcohol consumption in increasing viral load, thereby accelerating the progression of the infection.

Next, we consider a mathematical model comprising a system of nonlinear differential equations that describe the biochemical reactions catalysed by HIV-1 reverse transcriptase (RT) and integrase (IN), based on Michaelis-Menten enzyme kinetics. This model incorporates a dual inhibitor for HIV-1 RT/IN, which functions as both a non-nucleoside reverse transcriptase inhibitor and an integrase inhibitor. To assess the effectiveness of this dual inhibitor against HIV-1 infection, a one-dimensional impulsive differential equation model is developed, leading to the numerical determination of an optimal dosing regimen. The results of the analytical and numerical analyses provide essential insights into identifying the minimum effective dose for the administration of HIV-1 RT/IN dual inhibitors in preventing HIV-1 infection.

Furthermore, we investigate the effect of Tat inhibitor on the suppression of HIV-1 transcription through a mathematical model based on nonlinear differential equations. It frames the analysis as an optimal control problem, assessing the potential of the Tat inhibitor as a therapeutic approach for HIV-1 infection. A one-dimensional impulsive differential equation model is developed to evaluate the maximum concentration of the elongating complex (P_2) and determine the optimal timing for successive dosages. The present findings indicate that impulsive dosing is more effective than continuous dosing in inhibiting HIV-1 transcription. Next, an enzyme kinetic model is formulated to observe the impact of viral proteins Tat and Rev on HIV-1 replication, and the efficacy of combined drug therapy (administering Tat and Rev inhibitor) is examined using an optimal control framework. Applying the Pontryagin maximum principle, the study aims to minimize therapy costs while optimizing its effects on Tat-Rev regulation of HIV-1 replication, supported by numerical simulations with varying system parameters.

Keywords: HIV-1, AIDS, CYP3A4 enzyme, Alcohol, Tat, Rev, Protease inhibitor, Dual Inhibitor, Integrase, Reverse Transcriptase, Impulsive Differential Equation, Optimal Control.


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