

# Understanding the Interaction Between HIV Reverse Transcriptase Inhibitor Drugs and Human Pepsin

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Human Immunodeficiency Virus (HIV) is a retrovirus that attacks CD4 cells in the human immune system. The virus requires many enzymes in order to function and thrive in the human body, one of which is reverse transcriptase. This enzyme functions by producing a complementary strand of DNA from RNA so that the virus can continue to reproduce after it infects a human cell. Pepsin is a human protease enzyme located in the digestive tract that cleaves the peptide bonds preferably between hydrophobic and aromatic amino acids, which allows food to be digested properly. One of the side effects of HIV Reverse Transcriptase inhibitors includes gastrointestinal issues. Through the use of molecular dynamics, we studied the interaction between HIV Reverse Transcriptase inhibitors and Human Pepsin in order to get a better understanding of the side effects associated with this class of drugs. We used GLIDE to dock several different RTI drugs into Pepsin and generated different poses. Then, we utilized Unrestrained Molecular Dynamics from AMBER to run 250 nanosecond simulations in explicitly TIP3P solvated complexes. Molecular Mechanics/Generalized Born Surface Area (MMGBSA), Visual Molecular (VMD), and Root Mean Squared Deviation (RMSD) will allow us to calculate binding affinities, investigate key residue interactions, and measure the stability of the interaction respectively.