A Study of the Relationship Between Pepsin and HIV-1 Protease Inhibitors

Afryea Henderson, Erica Modeste, Carol Parish

Department of Chemistry

University of Richmond

Pepsin is an enzyme in the stomach that cleaves peptide bonds between hydrophobic and aromatic amino acids to aid in digestion. The Human Immunodeficiency Virus (HIV) is a retrovirus that attacks the immune system of humans by invading the body and destroying CD4 cells which are necessary instruments in fighting diseases. There are several enzymes involved in the maturation of the virus. During replication, HIV- 1 protease in particular acts in a similar cleaving fashion as pepsin as it binds to its substrate and breaks down polyproteins that lead to the maturation of the HIV virus. One of the major side effects of HIV-1 Protease inhibitors (PI) includes a considerable amount of gastrointestinal complications.[1] For this study, the PIs were docked to pepsin using Glide. After running 250 ns of explicitly TIP3P solvated Unrestrained Molecular Dynamics, we will utilize Molecular Mechanics/Generalized Born Surface Area (MMGBSA) to determine binding affinities of several PIs to pepsin. Visual Molecular Dynamics and Root Mean Square Deviation will be used to visualize and measure, respectively, the relationship between PIs and pepsin. Understanding the relationship between Pepsin and PIs could give insight into the occurrence of gastrointestinal problems found in patients taking HIV-1 Protease Inhibitors.

[1] (2006). "Protease inhibitors" in *Meyler's Side Effects of Drugs: The International Encyclopedia of Adverse Drug Reactions and Interactions (0-444-51005-2, 978-0-444-51005-1)*, (p. 2965).