Molecular Modeling Design of Anti-Inflammatory Drugs

Zhang, Kerrick (School: Brookings High School)

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are widely used medications to treat pain, fever, and inflammation. These drugs function by inhibiting Cyclooxygenase (COX) enzymes, specifically COX-1 and COX-2, which regulate prostaglandin production. NSAIDs account for over 37% of the over-the-counter (OTC) drug market, with over 43 million Americans using them daily. Given their widespread use, refining NSAIDs could lead to improved therapeutic outcomes. ChemDraw and Chem3D were utilized to generate 15 analogs of both Aspirin and Ibuprofen, which then, utilizing molecular modeling with OpenEye's docking software FRED (Fast Rigid Exhaustive Docking), were evaluated against COX enzymes. Among the aspirin analogs, 10 exhibited stronger docking scores against COX-1, while 4 showed improved binding with COX-2. For ibuprofen, 8 analogs outperformed the base drug against COX-1, and 3 were superior against COX-2. The addition of functional groups such as fluorine and nitrogen appeared to enhance docking scores. Additionally, the study explored Lipinski's Rule of Five to assess the drug-likeness of aspirin and oil of wintergreen, particularly in relation to LogP (Octanol-Water Partition Coefficient), which influences drug solubility and pharmaceutical applications. The findings provide insights into how molecular modifications affect drug efficacy and suggest a balance between efficacy and production costs when optimizing NSAIDs.

Awards Won: