Bioinformatics Analysis of Opioids: Correlating Physicochemical Properties with Pharmacokinetics, Pharmacodynamics, and Molecular Interactions

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Abstract
Opioids are widely used in pain management but pose significant risks, including dependence and adverse effects. This study applies bioinformatics methods to investigate the physicochemical properties, pharmacokinetics, pharmacodynamics, and molecular interactions of selected opioids. Key molecular descriptors (e.g., partition coefficient [logP], polar surface area [PSA], hydrogen bond donors and acceptors) were calculated to assess physicochemical properties, while absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles were predicted using SwissADME, pkCSM, ADMETlab, and admetSAR. Molecular docking was conducted on the μ-opioid receptor (MOR) using AutoDock, followed by a refinement step to optimize ligand-receptor interactions. The best-scoring complexes were analyzed through molecular dynamics simulations, performed in AMBER and OpenMM, to assess stability and binding persistence. Results indicate that increased ligand hydrophobicity correlates with higher binding affinity for MOR across multiple opioids, with fentanyl exhibiting the strongest interaction due to a combination of hydrogen bonding and hydrophobic contacts. Stability analysis showed ligand-receptor complexes remained intact, with minimal fluctuations and consistent interactions at the active site. Pharmacokinetic and toxicity predictions suggest that lipophilic opioids cross the blood-brain barrier more efficiently, enhancing analgesic potential but also increasing side effects. Based on these findings, structural modifications such as reducing hydrophobic bulk or introducing polar groups could improve opioid selectivity and minimize off-target effects. This study highlights how computational approaches, including molecular docking and molecular dynamics simulations, optimize opioid drug design by predicting ligand-receptor interactions and pharmacokinetic properties before experimental validation.

Keywords. Opioids; μ-Opioid Receptor (MOR); Molecular Interactions; Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET); Bioinformatics; Drug Design.