UNIVERSITI TEKNOLOGI MARA
Cawangan Terengganu
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FINAL YEAR PROJECT (FYP)

(CHE367)

Title:

Power of Andrographis paniculata:
Molecular Docking of Andrographolide and its Derivatives Targeting Interleukin-1 Beta to Treat Anti-inflammation

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Abstract

The study revealed the molecular docking of Andrographolide and its derivatives towards Interleukin-1 Beta as a key protein in anti-inflammatory drug design using AutoDock Vina, AMDock and PyMol applications. Among all compounds, CHEMBL4887996 exhibited the highest binding affinity (-8.0 kcal/mol) and stability, followed by andrographolide and its derivatives with scores ranging from -7.3 to -6.8 (kcal/mol). All compounds target the same binding site to form hydrophobic and hydrogen bonds. Therefore, the compound CHEMBL4887996 showed the most stable interaction based on this study. These findings highlight the potential of CHEMBL4887996 as a superior anti-inflammatory agent, especially for treating diabetic patients and optimizing drug design.

Keywords: Interleukin-1 Beta, Diabetic, AutoDock Vina, Binding affinity, anti-inflammatory

Molecular Docking of Andrographolide and its Derivatives Towards Interleukin-1 Beta as Anti-inflammation

1. Background of Study

1.1 Introduction

Inflammation is the immune system response to harmful stimuli like pathogens, damaged cells, toxic substances or radiation. Its main purpose is to eliminate these threats and initiate healing, making it crucial for health. However, uncontrolled acute inflammation can progress to chronic inflammatory disease. Symptoms include redness, swelling, heat, pain and loss of function at the site of injury. Inflammation can be triggered by various factors, including infections and tissue damage. The body responds with chemical signals that guide leukocytes to the injury site, where they produce cytokines to drive the inflammatory response [1]. Interleukin-1 Beta is a cytokine vital for initiating and regulating inflammation. Produced by immune cells like macrophages and monocytes in response to infection or tissue damage, Interleukin-1 Beta is activated by the inflammasome complex. Excess Interleukin-1 Beta is linked to diseases like Rheumatoid Arthritis and diabetes, making it a key target for anti-inflammatory therapies.

Many in vitro studies and clinical trials have been conducted to evaluate the efficacy of drugs used to treat inflammation in diabetic patients. Many therapeutic options such as analgesics, anti-inflammatory drugs, and immunomodulatory agents. Drugs such as cannabis, morphine, aspirin and hydrocortisone have positive results in treating inflammatory disease. However, they have side effects for our bodies. Researchers have found alternatives treatment for inflammation by using Andrographolide as the main compound produced in the drug against the disease [2].

Computational modeling techniques have significantly reduced research timelines and costs by minimizing the need for lab experiments in drug manufacturing. One key method is molecular docking, which predicts interactions between small molecules and proteins at the atomic level. This technique helps researchers understand how drugs interact with their targets, which is essential for drug design and discovery. Molecular docking involves inserting ligands into the binding sites of specific proteins or DNA regions, reforming stable complexes that may show efficacy and specificity. By analyzing these interactions, researchers can characterize molecular behavior and gain insight into biochemical processes. The main goal is to determine the optimal binding pose of ligands to receptors, essential for evaluating binding affinity and identifying lead compounds.

This study aims to use molecular docking simulation to identify the binding affinity of Andrographolide and its derivates and to determine their molecules interaction towards the target protein Interleukin-1 Beta. This study might help to contribute to designing and improving the findings on drugs related to inflammation.

1.2 Literature Review

Inflammation is a vital immune response for eliminating harmful stimuli and starting the healing process. However, chronic inflammation is linked to diseases like diabetes mellitus. Interleukin-1 Beta is a key pro-inflammatory cytokine that can be targeted for anti-inflammatory drug development [1]. Due to the side effects of conventional medications, researchers are investigating natural alternatives such as Andrographis paniculata, which has shown promising anti-inflammatory, antioxidant, and immunomodulatory properties [2].

Molecular Docking in Drug Discovery

Molecular Docking is a computational technique used to predict interactions between small molecules (ligands) and target proteins, which help in drug discovery. This method facilitates efficient screening of potential drug candidates by assessing their binding affinity to specific protein targets [3].

Several studies have utilized molecular docking to evaluate the potential of natural compounds against inflammatory diseases and infections. For instance, studies on phytochemicals from *Momordica Charantia* demonstrated a strong binding affinity to the SARS-CoV-2 main protease, suggesting their potential as antivirus agents [9]. Similarly, Andrographolide and its derivatives have been studied for their inhibitory effects on inflammatory pathways, specifically their ability to bind to Interleukin-1 Beta (5R8E) and modulate immune responses.

Andrographolide as Anti-inflammatory Agent

Andrographolide is a diterpenoid lactone derived from Andrographis paniculata and has been shown to mitigate inflammation through multiple mechanisms. Computational studies have further supported its efficacy by demonstrating strong binding interactions with Interleukin-1 Beta. Recent docking simulations have highlighted the superior binding affinity of certain Andrographolide derivatives, such as CHEMBL4887996, which exhibited the lowest binding energy (-8.0 kcal/mol), indicating higher stability and effectiveness in inhibiting 5R8E activity [8].

Comparison with Related Studies

Research on molecular docking has expanded from focusing solely on inflammatory diseases including virus infections. A study conducted by **Rozani et al. (2024) investigated the docking of phytochemicals from Momordica Charantia against the main protease of SARS-CoV-2** [9]. This study revealed promising inhibitory potential comparable to the results seen with Andrographolide and its derivatives. Both Studies used AutoDock Vina for docking simulations and PyMol for visualization to ensure a consistent methodology in evaluating ligand-protein interactions. These findings highlight the broader applicability of molecular docking in discovering novel therapeutic agents for both infectious and inflammatory diseases.