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Posted Date: 13 February 2024

doi: 10.20944/preprints202402.0696.v1

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Communication

Investigating the Inhibitory Potential of Amentoflavone Against HIV-1 Protease: A Molecular Docking Study

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Abstract: This study investigates the potential of natural compounds against HIV-1 protease, a critical enzyme in the replication cycle of human immunodeficiency virus type 1 (HIV-1). HIV-1 protease is essential for cleaving large precursor proteins into smaller functional proteins necessary for viral maturation and infectivity. Protease inhibitors, specifically targeting HIV-1 protease, effectively suppress viral replication, aiding in the management of HIV infection. Using the SWISS DOCK Server, several natural compounds were investigated for their potential as inhibitors of HIV-1 protease. Docking results revealed that Amentoflavone showed excellent binding affinity with high Estimated ΔG values, suggesting its potential as an inhibitor of HIV-1 protease. Additionally, Amentoflavone exhibited similar promising results when tested against Roussarcoma virus protease. These findings indicate the potential of Amentoflavone as a natural compound against HIV and warrant further investigation into its therapeutic applications.

Keywords: HIV-1 protease 2; SWISS DOCK Server; Roussarcoma virus protease; Human Immunodeficiency Virus

1. Introduction

HIV, the Human Immunodeficiency Virus, targets the body's immune system, particularly CD4 cells crucial for fighting infections, leading to Acquired Immunodeficiency Syndrome (AIDS), the advanced stage of HIV infection [1–5].

Transmission occurs through specific bodily fluids like blood, semen, vaginal fluids, and breast milk. Unprotected sexual contact, sharing needles contaminated with HIV-infected blood, and mother-to-child transmission during childbirth or breastfeeding are common modes.

Once inside the body, HIV infects CD4 cells, using them to replicate and generate more virus. Continuous replication results in a decline in CD4 cell count, weakening the immune system and making the body susceptible to infections and diseases [1–5].

While HIV has no cure, effective management is possible with antiretroviral therapy (ART), a combination of medications suppressing virus replication, reducing viral load, and slowing disease progression. With proper treatment and medical care, individuals with HIV can lead long and healthy lives [1–5].

The HIV genome's sequence can differ among viral isolates because of mutations and genetic diversity. This variability is a key factor in HIV's ability to evade the immune system and develop resistance to antiretroviral drugs. Scientists employ genetic sequencing methods to investigate HIV's genetic diversity and devise approaches for diagnosis, treatment, and prevention [6–8].

This work focused on The HIV-1 protease using Molecular Docking methods [9] through SWISS DOCK Server (SwissDock - The online docking web server of the Swiss Institute of Bioinformatics - Home) [10].

This viral protease is crucial for cleaving large precursor proteins, called viral polyproteins, into smaller functional proteins necessary for viral maturation and infectivity.

The precise cleavage of these precursor proteins at specific sites by HIV-1 protease is essential for generating structural and functional proteins vital for the assembly of new viral particles. Without the activity of HIV-1 protease, the virus fails to mature properly, leading to significant impairment of its replication [11–13].

Given its central role in the viral life cycle, HIV-1 protease has become a prime target for the development of antiretroviral drugs. Protease inhibitors, a class of antiretroviral drugs, specifically target HIV-1 protease, disrupting its proper functioning. By inhibiting the activity of HIV-1 protease, these drugs effectively suppress viral replication, contributing to the management of HIV infection, especially when used in combination therapy [11–13].

2. Material and Methods

- Structure of Crystal Structure HIV-1 virus protease was taken from SWISSDOCK Server (PDB Code:1b6l). Docking investigation was performed automatically by Blind Docking method.
- Structure of Crystal Structure Rous sarcoma virus protease was taken from SWISSDOCK Server (PDB Code:1bai). Docking investigation was performed automatically by Blind Docking method.

3. Results and Discussion

In this study, the SWISS DOCK Server [10] conducted an investigation on several natural compounds targeting HIV-1 protease, a key enzyme in the replication cycle of human immunodeficiency virus type 1 (HIV-1). This viral protease is crucial for cleaving large precursor proteins, called viral polyproteins, into smaller functional proteins necessary for viral maturation and infectivity.

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Docking results revealed that Amentoflavone demonstrated excellent binding affinity, with a high estimated ΔG (-10.1 kcal/mol), indicating its potential as an inhibitor of HIV-1 protease. Additionally, Amentoflavone was assessed against Rous sarcoma virus protease, exhibiting a similarly high estimated ΔG (-9.93 kcal/mol). These findings are promising, suggesting that this natural compound could serve as a potential candidate against HIV.

Figure 1 is shown the Docking outcomes of the potential Ligand Binding Site of Amentoflavone in the crystal structures of Rous Sarcoma Virus Protease (RSV Protease) and HIV-1 Protease. Indeed, Panel (A) reports Crystal structure of Rous Sarcoma Virus Protease (RSV Protease). The potential ligand binding site of Amentoflavone is highlighted in blue. Amentoflavone is docked within the binding site and is represented as a blue-colored molecule. Panel (B) shows Crystal structure of HIV-1 Protease. Similarly, the potential ligand binding site of Amentoflavone is highlighted in blue, and Amentoflavone is docked within this site, shown as a blue-colored molecule. The figure was reproduced using the Chimera program, a molecular visualization software commonly used for analyzing protein structures and ligand interactions.

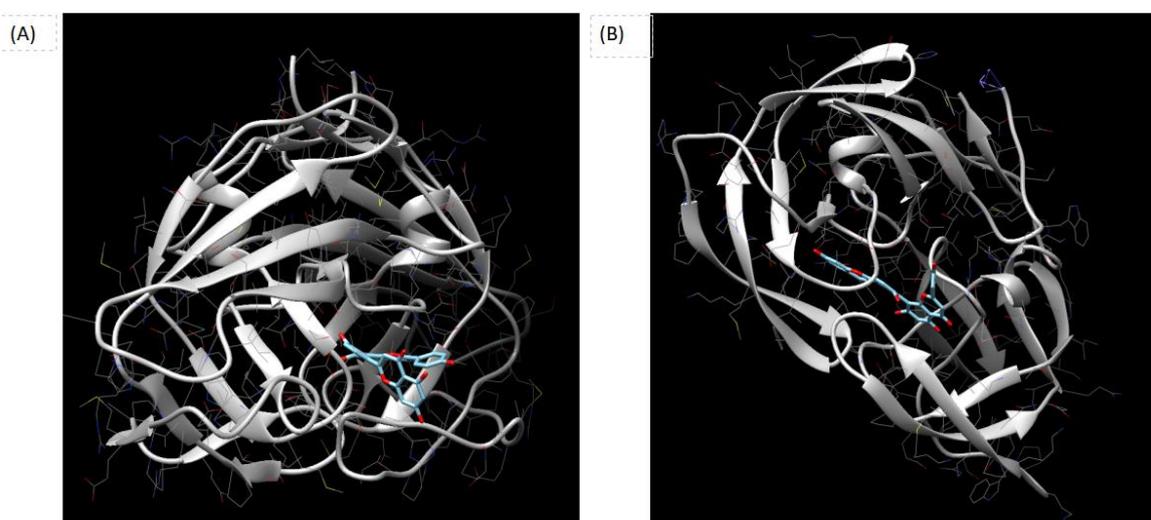


Figure 1. depicts the docking results of Amentoflavone within the potential Ligand Binding Site of the crystal structures of Rous Sarcoma Virus Protease (RSV Protease) and HIV-1 Protease, denoted as (A) and (B) respectively. The docked Amentoflavone is highlighted in blue. This figure was generated using the Chimera program.

4. Conclusion

In conclusion, this study highlights the potential of natural compounds, particularly Amentoflavone, as inhibitors of HIV-1 protease. The docking results, obtained using the SWISS DOCK Server, demonstrated excellent binding affinity of Amentoflavone with HIV-1 protease, suggesting its potential as an effective inhibitor. Furthermore, Amentoflavone exhibited similar promising results when tested against Rous sarcoma virus protease, indicating its broad-spectrum inhibitory activity against viral proteases.

These findings underscore the importance of exploring natural compounds as potential therapeutic agents against HIV and other viral infections. Amentoflavone, in particular, shows promise as a natural compound with inhibitory activity against HIV-1 protease, which is crucial for viral replication and infectivity.

Conflicts of Interest: The authors declare no conflicts of interest.

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