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# Molecular docking and toxicity analysis of ribosome-inactivating protein and natural chemical compounds as promising antiretroviral candidates against HIV-1

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## Abstract

**Background:** HIV (human immunodeficiency virus) uses HIV-1 reverse transcriptase as the receptor to convert RNA into viral DNA. In addition, the CD4 receptor is also used by the virus to enter CD4+ T cells and subsequently replicate. **Objective:** To screen several proteins in Indonesian plants for the potential to bind to the CD4 receptor. **Method:** Molecular docking was carried out on Cluspro 2.0 specifically for protein to protein and MOE for protein to ligand. **Results:** The protein ligands were Cinnamomin III, Agglutinin, PAP, PAP-S, Momordin I, MAP30, Beta-luffin, Luffaculin I, Cucurmosin, DAP, Dianthin-30, Bouganin, Maize, Ricin, Abrin, Balsamin, and the bond energy values (Joules/kg.mol) were -602.8, -973.5, -511.3, -439.1, -532.2, -661.9, -487.0, -472.8, -530.9, -413.6, 444.1, -504.5, -617.2, -855.6, -883.9, -558.6, respectively. The best binding energy with CD4 was selected to identify the compound's molecule. These compounds were abrusin, abrusogenin, eicosadienoic acid, heneicosane, precatorine, and trigonelline, and the bond energy values (Joules/kg.mol) were -19.2158, -16.7057, -15.5155, -13.9632, -15.6119, and -9.2620, respectively. The toxicity test of abrusin was carried out against 18 targets, and two targets showed toxic activities. **Conclusion:** The content of RIP and natural chemical compounds in *Abrus precatorius* seeds make them the best candidate for antiretroviral therapy against HIV-1.

## Introduction

HIV-1 reverse transcriptase (RT) is a complex enzyme comprising two related subunits, p66 and p51, forming an asymmetric heterodimer. These subunits are derived from a more significant precursor called Gal-Pol polyprotein. This Gag-Pol polyprotein is synthesised from unspliced viral RNA and cleaved by the viral protease (PR) into its constituents (Seckler *et al*., 2009).

Zidovudine, or Azidothymidine (AZT), is a synthetic nucleoside analogue classified as a nucleoside reverse transcriptase inhibitor (NRTI). It is structurally similar to thymidine, a natural component of DNA, and functions as an antiviral agent by being incorporated into newly synthesised viral DNA in place of thymidine. Once incorporated, zidovudine acts as a chain terminator, blocking further elongation of the DNA strand. This interference with the elongation of viral DNA strands limits the ability of HIV-1 reverse transcriptase to complete viral DNA synthesis, which is a critical step in the viral replication cycle (Yogita *et al*., 2012).

The emergence of HIV-1 resistance to the antiviral drug AZT was first reported in 1989 and represented a significant challenge in managing HIV/AIDS. This resistance was reportedly mediated by specific mutations in the polymerase domain of reverse transcriptase, including D67N, K70R, T215Y/F, and K219Q, which impaired the ability of the drug to inhibit viral replication (Yogita *et al*., 2012). Two additional mutations, M41L and L210W, were subsequently

identified that could confer resistance to AZT (Das & Eddy, 2013). The term "*thymidine analogue mutations*" (TAM) was then coined to describe these mutations, as they were also found to mediate resistance to other thymidine analogues, such as d4T. Each TAM mutation could confer modest resistance to AZT, ranging from 1.5- to 4-fold, with high-level resistance requiring the presence of multiple mutations (Das & Eddy, 2013).

A multitude of monoclonal antibodies (MABs) have been created and are being studied to address different illnesses, including malignancies, autoimmune disorders, and infectious diseases (Becari *et al*., 2019). One such MAb, ibalizumab, has many advantages as an HIV treatment, including a distinctive method of operation, the ability to restore CD4 T cell counts, very little risk of acquired resistance, and low toxicity compared to other antiretroviral drugs. Ibalizumab is the first intravenous MAb for treating HIV-1 infection and a novel agent for managing the disease in over a decade (Becari *et al*., 2019). Following FDA approval in March 2018, ibalizumab has been used in conjunction with other antiretroviral therapies (ARTs) to treat multidrug-resistant HIV-1 infection in severely treatment-experienced adults who are failing their current antiretroviral regimen (Becari *et al*., 2019).

Due to the remarkable chemical diversity in the plant and microbial kingdoms, natural products have long been a focus of drug discovery efforts. With the advent of new technologies and innovative screening approaches, it has become increasingly feasible to identify novel bioactive compounds from natural sources and investigate their mechanisms of action. In the context of HIV-1 infection, natural products have garnered particular attention due to their potential to provide new therapeutic options for combating this devastating pandemic. The broad spectrum of natural compounds exhibiting anti-HIV activity underscores the importance of screening natural product libraries for discovering lead compounds with novel mechanisms of action. Identifying such compounds not only provides new therapeutic options for managing HIV/AIDS but also contributes to the ongoing efforts to combat the emergence of drug-resistant HIV-1 strains (Atanasov, 2021).

The quest to find better and safer antivirals remains a highly researched field, with plants being a commonly utilised source due to their various protein-based defence mechanisms against viral infections. Ribosome-inactivating proteins (RIPs) play a significant role in this research, with PAP (pokeweed antiviral protein) being one of the first RIPs to be purified. While several RIPs have been isolated as protein synthesis inhibitors, many others show powerful antiviral properties. For many years, researchers have focused on RIPs as potent protein synthesis inhibitors that can be used to create immunotoxins. Linked to a monoclonal antibody or a protein that specifically binds to a receptor, these RIPs can target cancer cells. Although initially found to be widely distributed among angiosperms, RIPs have also been found in other taxons (Citores *et al*., 2021).

This study conducted a comprehensive investigation to identify compound components in several plants indigenous to Indonesia. Sixteen ribosome-inactivating proteins (RIPs) were then docked with the CD4 receptor to determine the protein with the best binding energy. Subsequently, the compounds found in plants with the best RIP were identified and tethered to the HIV-1 Reverse Transcriptase Receptor (HRTR) to obtain a compound with the best energy binding.

## Methods

### *Protein-protein docking*

*Receptor evaluation*

The quality evaluation of the models was conducted using the web tools of SAVES (https://services.mbi.ucla.edu/SAVES/) v6.0. The assessment of the receptors was based on the errat score, verify3D, and Ramachandran plot. In the errat score, two ‘lines were drawn on the error axis to indicate the level of confidence in rejecting regions that surpassed the error value. This was expressed as a percentage of the protein for which the calculated error value fell below the 95% rejection limit.

*Docking of the molecules to the receptors*

The interaction between toxin protein and T Cell Surfaced CD4 (TCS CD4) receptor (PDB ID: 3O2D chain A) that has been evaluated was investigated through molecular docking using the auto-docking tool, ClusPro 2.0 webserver. This tool utilises various protein parameters to screen docked complexes and their cluster memberships (Kazakov *et al*., 2017). The ClusPro 2.0 algorithm uses the FFT correlation approach and double logical interaction potentials to expand its usability. Near-native structures were filtered by ClusPro, and the docked confirmations were ranked based on their clustering properties. PyMOL was used to visualise the generated docking modes from Cluspro (Schrodinger, 2015), separate protein complexes to obtain Ibalizumab (IBA) as a control and to obtain receptors for docking studies. The best protein complex was selected based on the lowest energy score of all clusters or poses.

*Analysis and visualisation of docking results*

PyMOL was used to visualise the generated docking modes from Cluspro, separate protein complexes to obtain Ibalizumab (IBA) as a control and to obtain receptors for docking studies. The best protein complex was selected based on the lowest energy score of all clusters or poses. Finally, PDBsum was used to analyse the best complex by identifying the number and type of bonds between amino acid residues in a specific protein chain (Laskowski *et al*., 2018). Access to the ClusPro tool and its algorithm is available at https://cluspro.bu.edu /publications.php.

***Protein-ligand docking***

*HIV-1 reverse transcriptase receptor determination*

Receptors and existing drugs were searched as positive controls associated with Zidovudine target receptors from Pubmed. The HIV-1 reverse transcriptase protein file with the identifier 1JKH was obtained from the Protein Data Bank (PDB), RCSB. The receptor file with code 1JKH was downloaded in "*.mbd*" format, and its structure was inspected using the Molecular Operating Environment (MOE) program.

*Preparation of receptors with validation*

Protonation at the 1JKH receptor involves adding a proton as a hydrogen cation (H+) to the molecule to correct the partial charge calculation and determine the Gasteiger charge and polar bond for each atom in the molecule. MOE validated the docking approach using two. Calculating the RMSD (Root Mean Square Deviation) value of the target protein and its original ligand validated the docking approach (Hevener *et al*., 2009).

*Docking of the molecules to the receptors*

Using the MOE software, parameters and data are acquired to establish the optimal ligand-receptor interaction, contrasted with positive controls and valid receptors with ligands.

*Analysis and visualisation of docking results*

The docking ligand's conformation (best pose) is determined by choosing conformational ligands with the lowest bond energies. Docking results with pose were best analysed using Discovery Studio. Analysed parameters include amino acid residues, hydrogen bonds, predictive inhibition constant, and free energy bonds. Determination based on bond-free energy is indicated by the docking result with the most negative (S) value.

***Abrusin compound toxicity test***

The toxicity of an *Abrus precatorius* compound called abrucine was evaluated using the Protox Web Server. The Protox Web Server is a website designed for *in silico* prediction of compound toxicity. The following steps were taken to conduct the toxicity test:

I. Access the Protox Web Server database at http://tox.charite.de.

II. Navigate to the menu bar and select "*TOX PREDICTION*".

III. Enter the name of the abrucine compound in the *"search PubChem name"* field and initiate the search.

IV. The 2D shape of the molecule and available toxicity test options will be displayed.

V. Choose any desired toxicity test and click *'Start Tox-Prediction*.' Wait briefly for the toxicity prediction results page to load.

VI. Once the toxicity prediction results page appears, you will find information such as $LD_{50}$ prediction, average similarity, and toxicity predictions.

## Results

Two drugs were used to determine energy-binding activities during the molecular studies – the monoclonal antibody ibalizumab as a control in protein-protein docking and Zidovudine as a control in protein-ligand docking. As explained in the method, protein-protein docking was conducted first to identify an RIP in a plant with better energy binding affinity than Ibalizumab. A search was conducted for various ligand candidates in this plant to find a higher energy binding affinity than Zidovudine in protein-ligand docking.

***Protein-protein docking***

The assessment to verify the 3D was based on the 3D/1D profile, where at least 80% of the amino acids scored ≥ 0.1. A total of 13 plant candidates with different types of RIP were included in the initial docking study, including type 1 and type 2 RIPs: cinnamomin III from *Cinnamomum camphora*, PAP and PAP-S from *Phytolacca americana*, momordin I and MAP30 from *Momordica charantia*, beta-luffin from *Luffa aegyptiaca*, luffaculin I from *Luffa acutangula*, cucurmosin from *Cucurbita moschata*, DAP and dianthin-30 from *Dianthus caryophyllus*, bouganin from *Bougainvillea spectabilis*, maize from *Zea mays*, ricin from *Ricinus communis*, abrin from *Abrus precatorius*, and balsamin from *Momordica balsamina*.

Sixteen RIPs were docked with the CD4 receptor, as shown in Table I. Based on the data, the results showed that abrin from *Abrus precatorius* had the lowest binding energy with the CD4 receptor, with an E-score of -883.9 in cluster 1.

**Table I: Result of TCS CD4 (3O2D chain A) receptor docking with several RIP**

| Source | Protein-ligand | RIP type | PDB ID | Chain | Energy |
|---|---|---|---|---|---|
| Antibody monoclonal | Ibalizumab | - | 3O2D | L | -643.4 |
| *Cinnamomum camphora* | Cinnamomin III | 2 | 2VLC | A | -625.3 |
| | | | | B | -602.8 |
| *Abrus precatorius* | Agglutinin | 2 | 2Q3N | A | -580.5 |
| | | | | B | -973.5 |
| *Phytolacca americana* | PAP | 2 | 1PAF | A | -520.4 |
| | | | | B | -511.3 |
| | PAP-S | 1 | 1GIK | A | -439.1 |
| *Momordica charantia* | Momordin I | 1 | 1MOM | A | -532.2 |
| | MAP30 | 1 | 1D8V | A | -661.9 |
| *Luffa aegyptiaca* | Beta-luffin | 1 | 1NIO | A | -487.0 |
| *Luffa acutangula* | Luffaculin I | 2 | 2OQA | A | -485.6 |
| | | | | B | -472.8 |
| *Cucurbita moschata* | Cucurmosin | 1 | 3BWH | A | -530.9 |
| *Dianthus caryophyllus* | DAP | 1 | 1LP8 | A | -413.6 |
| | Dianthin-30 | 1 | 1RL0 | A | -444.1 |
| *Bougainvillea spectabilis* | Bouganin | 1 | 3CTK | A | -504.5 |
| *Zea mays* | Maize | 2 | 2PQI | A | -609.3 |
| | | | | B | -617.2 |
| *Ricinus communis* | Ricin | 2 | 2AAI | A | -655.5 |
| | | | | B | -855.6 |
| *Abrus precatorius* | Abrin | 2 | 1ABR | A | -668.4 |
| | | | | B | -883.9 |
| *Momordica balsamina* | Balsamin | 1 | 4KMK | A | -558.6 |

The energy value of Chain A was also lower than that of the control. Analysis of PDBsum showed the number of hydrogen bonds formed between the complex and the CD4 receptor. The hydrogen bond between the Ibalizumab complex and the CD4 receptor was formed by 15 bonds, fewer than the 17 hydrogen bonds formed between the abrin complex and the CD4 receptor. The residues contacts of the complexes, abrin and CD4 receptor interactions, were Gln139-Lys6, Gln129-Lys6, Asn137-Lys6, Glu169-Arg11, Gly135-Cys8, Asp173-Asn140, Gln152-Asp99, Arg131-Tyr12, Arg131-Ser9, Arg131-Ser10, Gln148-Asn225, Ser154-Thr138, Gln112-Thr265, His107-Pro144, and Gln110-Phe223 as shown in Figure 1, 2 and 3.

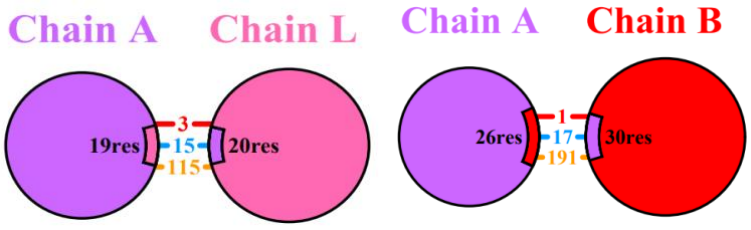



**Figure 1: IBA (chain L)-TCS CD4 (chain A) (left) and ABR (chain B)-TCS CD4 (chain A) (right) Interactions (salt bridge: red, Hydrogen bond: blue, non-bonded contact: orange).**

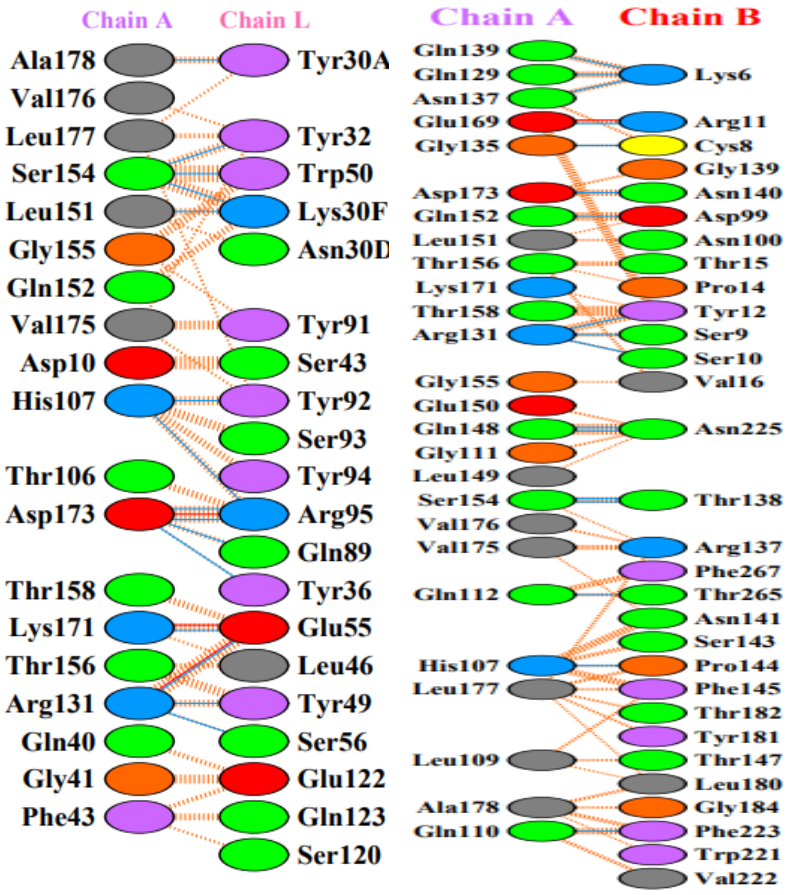



**Figure 2: Analysing various interactions in IBA (chain L)-TCS CD4 (Chain A) (left) and ABR (Chain B)-TCS CD4 (Chain A) (right) using PDBsum**

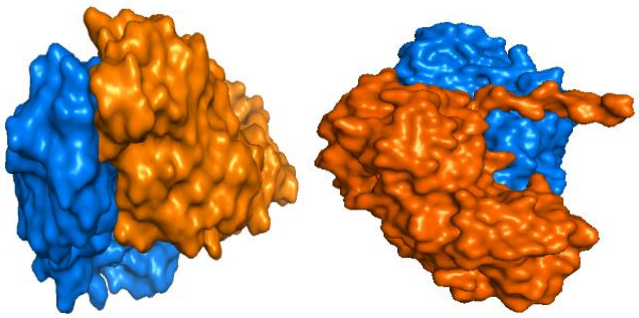


**Figure 3: IBA(chain L)-TCS CD4 (chain A) (left) and ABR (chain B)-TCS CD4 (chain A) (right) docked complex. The receptor is shown as marine blue, and the protein-ligand is shown as orange**

***Protein-ligand docking***

The docking resulted in predicting the activity of the interaction between the ligand and the receptor. Six compounds were selected as candidates for docking to investigate their interaction with the HIV-1 Reverse Transcriptase receptor (HRTR). The interaction between AZT-HRTR and AZT-ABS with amino acid residues is shown in Figure 4. Based on the docking results, the free energy values of the six compounds abrusin, abrusogenin, eicosadienoic acid, heneicosane, precatorine, and trigonellin were -19.2158; -16.7057; -15.5155; -13.9632; -15.6119; -9.2620 respectively as shown in Table II.

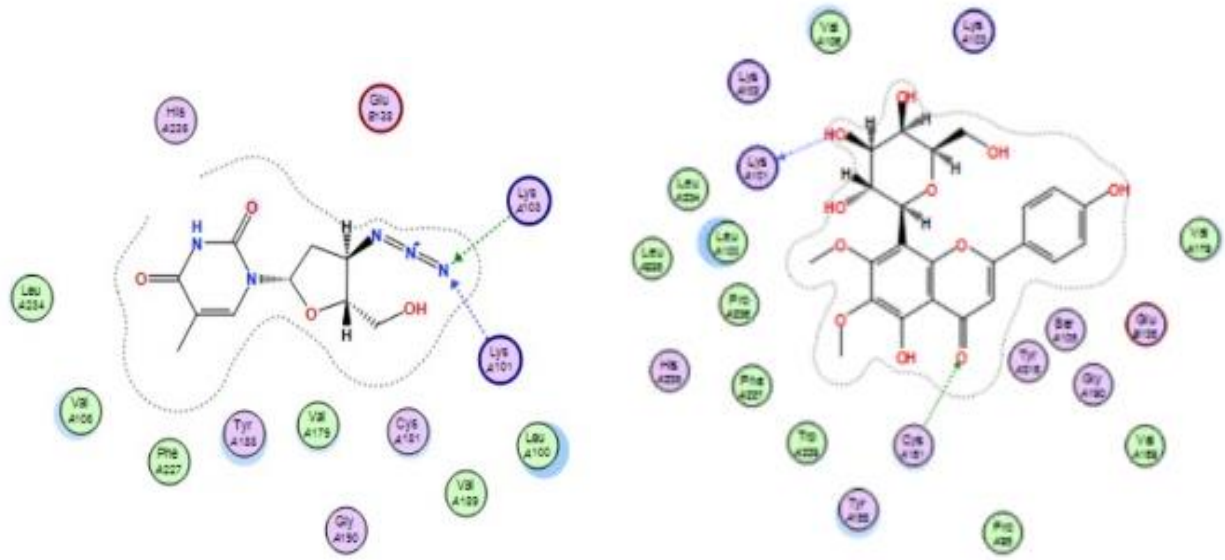
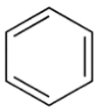


**Figure 4: Interaction AZT-HRTR and AZT-ABS with amino acid residues**

**Table II: The result of HIV-1 Reverse Transcriptase and the (1JKH) receptor docking with several ligands**

| Ligand | ΔS (Joules/kg.mol) | Ligand and receptor interaction |
|---|---|---|
| Abrusin | -19.2158 | R-OH → Lys A101<br>R = O → Cys A181 |
| Abrusogenin | -16.7057 | There is only ligand exposure and receptor exposure |
| Eicosadienoic acid | - 15.5155 | There is only ligand exposure and receptor exposure |
| Heneicosane | -13.9632 | There is only ligand exposure and receptor exposure |
| Precatorine | -15.6119 |  → Leu A100 |
| Trigonelline | -9.2620 |  → Leu 100 |
| Zidovudine (Positive control) | -12.5068 | |

This study tested six ligands for their ability to bind to the 1JKH receptor, and Abrusin (ABS) had the strongest interaction. ABS's Gibbs S free energy value was -19.2158 Joule/kg.mol, higher than the other five ligands tested.

***Toxicity test***

Abrusin showed an $LD_{50}$ value of 832 mg/kg *in silico*. This toxicity is classified in class four with the warning "*harmful if swallowed*". The toxicity test result is shown in Table III.

**Table III: Toxicity test results of Abrusin compound**

| Classification | Target | Prediction |
|---|---|---|
| Organ toxicity | Hepatotoxicity | Inactive |
| Toxicity endpoints | Carcinogenicity | Inactive |
| Toxicity endpoints | Immunotoxicity | Active |
| Toxicity endpoints | Mutagenicity | Inactive |
| Toxicity endpoints | Cytotoxicity | Inactive |
| Tox21-Nuclear receptor signalling pathways | Aryl hydrocarbon Receptor (AhR) | Active |
| Tox21-Nuclear receptor signalling pathways | Androgen Receptor (AR) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Androgen Receptor Ligand Binding Domain (AR-LBD) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Aromatase | Inactive |
| Tox21-Nuclear receptor signalling pathways | Estrogen Receptor Alpha (ER) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Estrogen Receptor Ligand Binding Domain (ER-LBD) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Peroxisome Proliferator-Activated Receptor Gamma (PPAR-Gamma) | Inactive |
| Tox21-Stress response pathways | Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE) | Inactive |
| Tox21-Stress response pathways | Heat shock factor response element (HSE) | Inactive |
| Tox21-Stress response pathways | Mitochondrial Membrane Potential (MMP) | Inactive |
| Tox21-Stress response pathways | Phosphoprotein (Tumour Suppressor) p53 | Inactive |
| Tox21-Stress response pathways | ATPase family AAA domain-containing protein 5 (ATAD5) | Inactive |

## Discussion

Ribosome-inactivating proteins (RIPs) are a class of toxic enzymes that catalyse the depurination of the universally conserved alpha-sarcin loop of large ribosomal ribonucleic acid (rRNA), a critical component of the protein synthesis machinery. This depurination irreversibly inactivates the ribosome, leading to a block in protein synthesis. Although initially believed to target only ribosomal substrates, it has become clear that RIPs can also inactivate a variety of nonribosomal nucleic acid substrates, including DNA and RNA. This property has led to their classification as polynucleotide: adenosine glycosidases (Walsh *et al*., 2013). To achieve this, molecular studies such as protein-protein docking and protein-ligand docking examine energy-binding activity compared to controls. The control was established using drugs that are widely used and believed to have the best efficacy in anti-HIV therapy, particularly for first-line treatment that permits resistance.

Good high-resolution structures usually produce values around 95% or higher. For lower resolutions ranging from 2.5 to 3A, the average overall quality factor is around 91%. According to Ramachandran plot analysis, it is expected that only up to 2% of residues should belong to the allowed region. In contrast, no residue should reside in the disallowed or outlier region. Chain B in Abrin was responsible for the best docking score compared to Chain A (-668.4). The value difference was significant compared to the control (ibalizumab), which only had an energy score of -648.2 in cluster 3. The energy value of Chain A was lower than that of the control, indicating abrin as a potential candidate drug for anti-HIV therapy in the docking study.

### *Abrin*

Abrin is a type 2 ribosome-inactivating protein (RIP) derived from the seeds of *Abrus precatorius*, also known as the "*jequirity seed*", "*rosary pea*", and "*crab's eye*" (Sedov *et al*., 2011). Various natural compounds within its seeds were investigated to further explore the potential of the Abrus precatorius plant. This was conducted to find additional compounds with HIV-1 antiviral activity and to ease the isolation of compounds and proteins for the development of drugs.

A literature search was conducted using PubMed and Google Scholar to explore the natural compound content in *Abrus precatorius* seeds, the source of abrin. The search focused on articles and studies from an unspecified year using the terms *Abrus precatorius*, Seed, and natural compound. Relevant data was gathered from all English-language articles, accepted types of articles, and the manufacturer's website. While not all results were molecular docking studies, the search ended when a ligand with better binding energy activity than zidovudine in HIV-1 reverse transcriptase protein was found.

CD4 is a protein predominantly found on the surface of T cells, serving as a co-receptor for the T cell receptor. The human immunodeficiency virus (HIV) also uses CD4 as a receptor to enter and infect T cells. After binding to CD4, HIV binds to a co-receptor called CXCR4 or CCR5, leading to virus entry and replication. In the case of abrin, it is thought to bind to CD4 on the surface of T cells and prevent HIV from binding to and entering those cells. Abrin also appears to block the fusion of HIV with the T cell membrane, further preventing virus entry.

The exact mechanism by which abrin inhibits HIV entry is not completely understood (Limmatvapirat, 2004). However, research has shown that abrin binds to a specific site on CD4, which is distinct from the binding site used by HIV (Reference). This suggests that abrin may compete with the virus for binding to CD4, effectively blocking the virus from entering T cells. Overall, abrin acts as a CD4-directed postattachment inhibitor by preventing HIV from binding to and entering T cells. This mechanism of action makes Abrin a promising target for the development of new HIV therapies.

***Abrusin***

The exact mechanism of action of abrusin as a reverse transcriptase inhibitor is not fully understood, but several mechanisms have been proposed (Victoria & Mrsc, 2020). One possible mechanism is that abrusin binds to the active site of reverse transcriptase, preventing the enzyme from synthesising new DNA strands. Reverse transcriptase requires a nucleic acid template to synthesise a complementary DNA strand. Abrusin may interfere with this process by binding to the enzyme's active site, disrupting the formation of the enzyme-substrate complex needed to synthesise the DNA strand.

Another possible mechanism is that abrusin inhibits reverse transcriptase by directly interacting with the RNA template, interfering with its ability to bind to the enzyme. Reverse transcriptase requires an RNA template to synthesise a complementary DNA strand. Abrusin may block the interaction between the RNA template and the enzyme, making it impossible for the enzyme to start the process of DNA synthesis. Additionally, abrusin may inhibit reverse transcriptase by interfering with the process of reverse transcription in some other way. For instance, it may inhibit the correct folding of the RNA template, which is necessary for reverse transcription.

Following the test to determine the binding ability of the six ligands to the 1JKH receptor, Abrusin had the strongest interaction, and this was due to its several interactions with receptors, including the R-OH (Alkyl alcohol) bond with Lys A101 and the R=O (Ester) bond with Cys A181In addition, the Gibbs S free energy value of berberine was found to be lower than that of devazepide, indicating that berberine had weaker hydrogen bonds than devazepide. Overall, the more negative the Gibbs energy value, the stronger the hydrogen bonds (Beccari *et al*., 2019).

In the toxicity test, 18 specific targets were identified as objects of toxicity evaluation. Two of these targets displayed toxic activities when exposed to the abrusin compound. The presence of active immunotoxicity indicates that abrusin compounds have the potential to cause gene mutations or influence the regulation of genes responsible for immunoregulation (Bou Zerdan, 2021). These changes can disrupt the normal functioning of the immune system. Generally, chemicals can modify immune tolerance and regulation, leading to inappropriate immune stimulation or suppression. The aryl hydrocarbon receptor (AHR) is a transcription factor in the cytoplasm that significantly regulates xenobiotic metabolism. If toxicity occurs with the aryl hydrocarbon receptor (AHR), it can impact the cellular processes involved in managing xenobiotics (Shivanna et al., 2022).

***Future challenge***

Abrin, an extremely toxic protein extracted from Abrus precatorius seeds, consists of two protein chains, A and B, connected by a disulfide bond. While the B chain is responsible for the attachment of abrin to cells, the A chain is toxic. Abrin is one of the most potent plant toxins, with an IC50 of 0.4 ng/mL for protein synthesis in cultured cell lines and an $LD_{50}$ of 0.04 g/kg for mice. Several studies have successfully reduced abrin toxicity by removing the A chain, resulting in the recombinant abrin B chain. This recombinant protein retains the ability to bind to cell surfaces while being non-toxic and can be produced in significant quantities using bacterial expression systems (Surendranath & Karande, 2008).

## Conclusion

This research focused on investigating the interaction between several plant proteins, including Cinnamomin III, Agglutinin, PAP, PAP-S, Momordin I, MAP30, Beta-luffin, Luffaculin I, Cucurmosin, DAP, Dianthin-30, Bouganin, Maize, Ricin, Abrin, and Balsamin, with CD4 receptors, using Ibalizumab as a control. The ligand abrin from Abrus precatorius exhibited the strongest binding affinity with the CD4 receptor, with an E score of -883.9 Joules/kg.mol in cluster 1. The bond energy value was primarily observed through the bonds to the B chain. Furthermore, the abrin complex formed more hydrogen bonds with the CD4 receptor than the Ibalizumab complex, with 17 and 15 hydrogen bonds, respectively.

The study presents findings on identifying potential compounds in Abrus precatorius and their interactions with the HIV-1 Reverse Transcriptase Receptor (HRTR). The identified compounds include abrusin, abrusogenin, eicosadienoic acid, heneicosane, precatorine, and trigonelline. Molecular docking analysis of these compounds with HRTR showed that abrucin had the strongest binding affinity. The bond energy for abrucin was -19.2158 Joules/kg.mol, which was higher than the positive control, Zidovudine (-12.5068 Joules/kg.mol). The study also found that abrucin interacted with specific amino acid residues in HRTR, specifically the R-OH (Alkyl alcohol) bond with Lys A101 and the R=O (Ester) bond with Cys A181.

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## Conflicts of Interest

The authors declare no conflict of interest.

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