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

HIV-1 reverse transcriptase is the receptor HIV (human immunodeficiency virus) uses to convert RNA into viral DNA. When the virus binds to this receptor, this enzyme will catalyze the reverse transcription of RNA into double-stranded DNA in infected cells and start the viral development cycle. In addition, the CD4 receptor is also used by the virus to enter CD4+ T cells and replicate. In this study, several proteins in Indonesian plants were identified that have the potential to bind to the CD4 receptor. The process of molecular docking was carried out with the use of Cluspro 2.0 specifically for the docking of protein to protein, and MOE for the docking of protein to ligand. The protein ligands are Cinnamomin III, Agglutinin, PAP, PAP-S, Momordin I, MAP30, Beta-luffin, Luffaculin I, Cucurmosin, DAP, Dianthin-30, Bouganin, Maize, Ricin, Abrin, and Balsamin. Bond energy values in (Joules/kg.mol) are -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. After that, plants with proteins with the best binding energy with CD4 are selected to identify the compound's molecule in them. These compounds are abrusin, abrusogenin, eicosadienoic acid, heneicosane, precatorine, and trigonelline. The internal bond energy values (Joules/kg.mol) are -19.2158, -16.7057, -15.5155, -13.9632, -15.6119, and -9.2620, respectively. The toxicity test of the abrusin compound was carried out against 18 targets, and only 2 targets showed toxic activity. The content of RIP and natural chemical compounds in Abrus precatorius seeds make them the best candidate for antiretroviral therapy against HIV-1.

Keywords: *CD4, HIV-1 reverse transcriptase, Ibalizumab, molecular docking, Zidovudine*

1. INTRODUCTION

HIV-1 reverse transcriptase (RT) is a complex enzyme composed of two related subunits, p66 and p51, forming an asymmetric heterodimer together. These subunits are derived from a more significant precursor protein. This Gag-Pol polyprotein is synthesized from unspliced viral RNA and cleaved by the viral protease (PR) into its constituent parts [1].

Zidovudine 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 synthesized 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 [2].

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 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. Two additional mutations, M41L and L210W, were subsequently identified that could confer resistance to AZT. The term "thymidine analog mutations" (TAM) was coined to describe these mutations, as they were also found to mediate resistance to other thymidine analogs, such as d4T. Each TAM mutation can confer modest resistance to AZT, ranging from 1.5- to 4-fold, with high-level resistance requiring the presence of multiple mutations [3].

A multitude of MAbs have been created and are being studied to address different illnesses, including malignancies, autoimmune disorders, and infectious diseases. 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 i.v. MAb for treating HIV-1 infection and a novel agent for managing the disease in over a decade. Following FDA approval in March 2018, ibalizumab can now be used in conjunction with other ARTs to treat MDR HIV-1 infection in severely treatment-experienced adults who are failing their current antiretroviral regimen [12].

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 [4].

The quest to find better and safer antivirals remains a highly researched field, with plants being a commonly utilized source due to their various protein-based defense 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 [15].

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.

RESEARCH METHOD

A. Protein-Protein Docking

1. 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 are drawn on the error axis to indicate the level of confidence in rejecting

regions that surpass the error value. This is expressed as a percentage of the protein for which the calculated error value falls below the 95% rejection limit. 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%. The assessment of verify3D is based on the 3D/1D profile, where at least 80% of the amino acids scored >= 0.1. According to Ramachandran plot analysis, it is expected that only up to 2% of residues should belong to the allowed region, while no residue should reside in the disallowed or outlier region.

2. 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 have been evaluated was investigated through molecular docking using the auto-docking tool, ClusPro 2.0 webserver. This tool utilizes various protein parameters to screen docked complexes and their cluster memberships [6]. 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 visualize the generated docking modes from Cluspro [5], 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.

3. Analysis and visualization of docking results

PyMOL was used to visualize 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 analyze the best complex by identifying the number and type of bonds between amino acid residues in a specific protein chain [7]. Access to the ClusPro tool and its algorithm are available at https://cluspro.bu.edu/publications.php.

B. Protein-Ligand Docking

1. HIV 1 Reverse Transcriptase receptor determination.

Receptors and existing drugs are searched as positive controls associated with Zidovudin target receptor 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 is downloaded in ".mbd" format, and its structure is inspected using the Molecular Operating Environment (MOE) program.

2. Preparation of receptors with validation

Protonation at the 1JKH receptor by adding a proton in the form of a hydrogen cation (H+ ion) to the molecule to correct the partial charge calculation, and determining the gasteiger charge and polar bond for each atom in the molecule. MOE conducted validation of the docking approach utilizing two Calculating the RMSD (Root Mean Square Deviation) value of the target protein and its original ligand was used to validate the docking approach. RMSD is a measure used to determine the similarity between flexible and stiff crystallographic result interaction techniques and docking ligands [8]. The target protein is considered legitimate if the RMSD value is less than 2 [9]

3. Docking of the molecules to the receptors

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

4. Analysis and visualization of docking results

Determination of the conformation of the docking ligand (best pose) is done by choosing conformational ligands that have bond energies the lowest. Docking results with pose best then analyzed using Discovery Studio. Analyzed parameters include amino acid residues, hydrogen bonds, predictive inhibition constant, and free energy bond. Determination based on bond-free energy is indicated by the docking result which has the most negative (S) value.

C. 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:

1. Access the Protox Web Server database at http://tox.charite.de.
2. Navigate to the menu bar and select 'TOX PREDICTION.'
3. Enter the name of the abrucine compound in the 'search pubchem name' field and initiate the search.
4. The 2D shape of the molecule and available toxicity test options will be displayed.
5. Choose any desired toxicity test and click 'Start Tox-Prediction.' Wait briefly for the toxicity prediction results page to load.
6. Once the toxicity prediction results page appears, you will find information such as LD50 prediction, average similarity, and toxicity predictions.

RESULTS AND DISCUSSION

Ribosome-inactivating proteins (RIPs) are a class of toxic enzymes that catalyze 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 [10].

This study aims to identify various chemical compounds and proteins in a plant that contains RIP as a potential candidate for anti-HIV therapy. To achieve this, we employed molecular studies such as protein-protein docking and protein-ligand docking to examine energy binding activity compared to controls. 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. Two drugs were used – the monoclonal antibody ibalizumab as control in protein-protein docking and Zidovudine as 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. We then searched for various ligand candidates in this plant to find better energy binding affinity than Zidovudine in protein-ligand docking.

1. Protein-Protein Docking

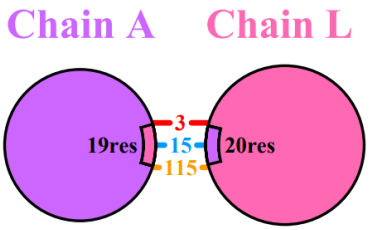
Table 1. Result of TCS CD4 (3O2D chain A) receptor docking with several RIP

Source	Protein Ligand	RIP Type	PDB ID	Chain	Energy	Cluster
Antibody Monoclonal	Ibalizumab	-	3O2D	L	-643.4	3
Cinnamomum camphora	Cinnamomin III	2	2VLC	A	-625.3	0
				B	-602.8	2
Abrus precatorius	Agglutinin	2	2Q3N	A	-580.5	5
				B	-973.5	0
Phytolacca americana	PAP	2	1PAF	A	-520.4	0
				B	-511.3	0
	PAP-S	1	1GIK	A	-439.1	1
Momordica charantia	Momordin I	1	1MOM	A	-532.2	6
	MAP30	1	1D8V	A	-661.9	0
Luffa aegyptiaca	Beta-luffin	1	1NIO	A	-487.0	1
Luffa acutangula	Luffaculin I	2	2OQA	A	-485.6	0
				B	-472.8	0
Cucurbita moschata	Cucurmosin	1	3BWH	A	-530.9	0
Dianthus caryophyllus	DAP	1	1LP8	A	-413.6	23
	Dianthin-30	1	1RL0	A	-444.1	0
Bougainvillea spectabilis	Bouganin	1	3CTK	A	-504.5	10
Zea mays	Maize	2	2PQI	A	-609.3	3
				B	-617.2	4
Ricinus communis	Ricin	2	2AAI	A	-655.5	8
				B	-855.6	0

Abrus precatorius	Abrin	2	1ABR	A	-668.4	1
				B	-883.9	3
Momordica balsamina	Balsamin	1	4KMK	A	-558.6	0

Thirteen 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 1. 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. Chain B in abrin was responsible for the best docking score compared to Chain A (-668.4). The difference in values 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 also lower than the control, indicating that abrin is a potential candidate drug for anti-HIV therapy in the docking study. 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, which was 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.



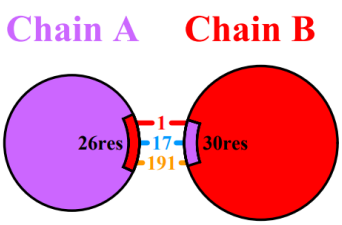


Fig. 1 IBA (chain L)-TCS CD4 (chain A) (left) and ABR (chain B)-TCS CD4 (chain A) (right) Interactions (salt bridge: red, Hydrogen bond: blue, non-bonded contact: orange).

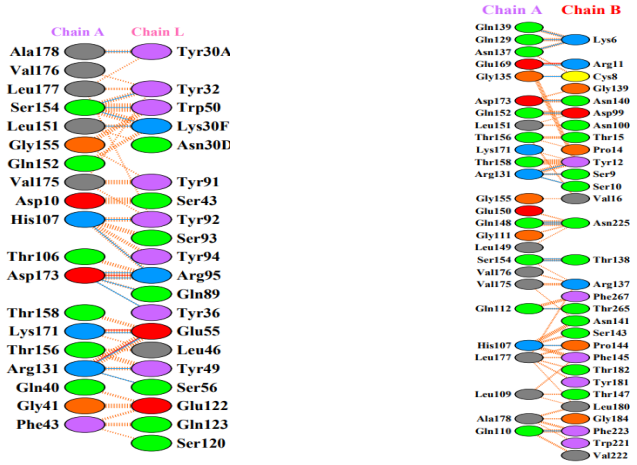


Fig. 2 Analyzing various interactions in IBA (chain L)-TCS CD4 (chain A) (left) and ABR (chain B)-TCS CD4 (chain A) (right) using PDBsum

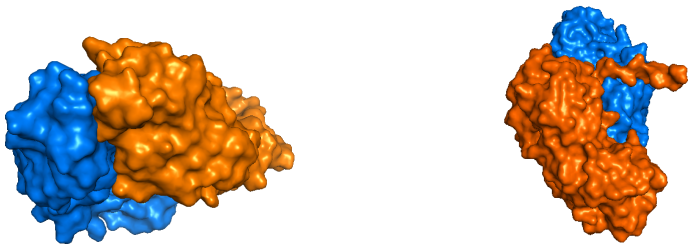


Fig. 3 IBA(chain L)-TCS CD4 (chain A) (left) and ABR (chain B)-TCS CD4 (chain A) (right) docked complex. Receptor is shown blue marine, and protein ligand is shown orange

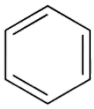
2. Protein-Ligand Docking

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 [11]. To further explore the potential of the abrus precatorius plant, we have chosen to investigate various natural compounds contained within its seeds. It is hoped that if other compounds in addition to abrin possess HIV-1 antiviral activity, development of drugs for the isolation of compounds and proteins will be easier.

A literature search was conducted using PubMed and Google Scholar to explore 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 and accepted types of articles as well as from the manufacturer's website. While not all of the

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.

Table 2. Result of HIV-1 REVERSE TRANSCRIPTASE (1JKH) receptor docking with several ligands

Ligand	ΔS (Joules/kg.mol)	Ligand and receptor interaction
ABRUSIN	-19,2158	R-OH → Lys A101 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 Cysteine 94
PRECATORINE	-15,6119	 → Leu A100 O^- Lys A101 Lys A102 N^+ → Glu 2125
TRIGONELLIN	-9,2620	 → Leu 100
ZIDOFUDINE (POSITIVE CONTROL)		-12,5068

The result of the docking method is the prediction of the activity of the interaction between the ligand and the receptor. Six compounds were selected as candidates for docking to evaluate whether they interact with the HIV-1 Reverse Transcriptase receptor (HRTR).

Based on the docking results, the free energy values of the 6 compounds Abrusin, abrusogenin, eicosadienoic acid, Heneicosane, Precatorine, and Trigonellin were -19.2158 respectively; -16.7057; - 15.5155; -13.9632; -15.6119; -9.2620.

In this study, six ligands were tested for their ability to bind to the 1JKH receptor, and it was found that Abrusin (ABS) had the strongest interaction. This was due to several interactions with receptors, including the R-OH (Alkyl alcohol) bond with Lys A101 and the R=O (Ester) bond with Cys A181. The Gibbs S free energy value of ABS was -19.2158 Joule/kg.mol, which is higher than that of the other five ligands tested. In 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 [12].

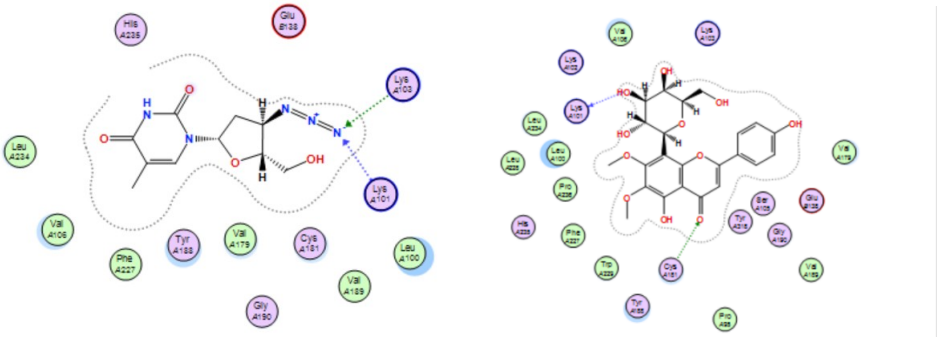


Fig 4. Interaction AZT-HRTR and AZT-ABS with amino acid residues

3. Toxicity Test

Abrusin showed an LD50 value of 832 mg/kg in silico. This toxicity is classified in class 4 with the warning “harmful if swallowed”. In this toxicity test, 18 specific targets were identified as objects of toxicity evaluation. Among these targets, 2 displayed toxic activity 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. These changes can disrupt the normal functioning of the immune system. Specifically, 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 [17,18].

Table 3. Toxicity Test Results of Abrusin Compound

Classification	Target	Prediction
Organ toxicity	Hepatotoxicity	Inactive
Toxicity end points	Carcinogenicity	Inactive
Toxicity end points	Immunotoxicity	Active
Toxicity end points	Mutagenicity	Inactive
Toxicity end points	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 (Tumor Supressor) p53	Inactive
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	Inactive

4. Mechanism of Action

1. Abrin

CD4 is a protein that is predominantly found on the surface of T cells, where it serves 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 then 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. Additionally, 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 [13]. However, research has shown that abrin binds to a specific site on CD4, which is distinct from the binding site used by HIV. 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.

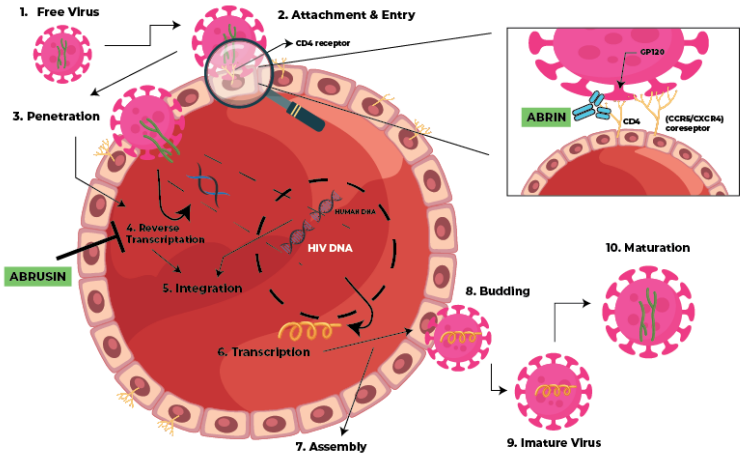


Fig. 5 Mechanism of action Abrin and Abrusin against HIV-1

2. Abrusin

The exact mechanism of action of abrusin as an inhibitor of reverse transcriptase is not fully understood, but several mechanisms have been proposed [14]. One possible mechanism is that abrusin binds to the active site of reverse transcriptase, preventing the enzyme from synthesizing new DNA strands. Reverse transcriptase requires a nucleic acid template to synthesize a complementary DNA strand. Abrusin may interfere with this process by binding to the active site of the enzyme, disrupting the formation of the enzyme-substrate complex needed for the synthesis of 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 synthesize a complementary DNA strand. Abrusin may block the interaction between 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 to occur.

5. 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 known as one of the most potent plant toxins, with an IC50 of 0.4 ng/mL for protein synthesis in cultured cell lines, and an LD50 of 0.04 g/kg for mice. Several studies have successfully reduced the toxicity of abrin 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 [16].

CONCLUSION

This research focuses 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 study provides valuable insights into the molecular mechanisms underlying these interactions. The ligand abrin

from Abrus precatorius was found to exhibit 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 hydrogen bonds and 15 hydrogen bonds, respectively.

The study presents findings on the identification of 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, Zidofudine (-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.

The seeds of Abrus precatorius containing the RIP compounds abrin and abrusin have been identified as the best candidate therapy against HIV-1 through molecular docking studies.

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