ISSN: 1410-8917
Jurnal Kimia Sains & Aplikasi
e-ISSN: 2597-9914

Jurnal Kimia Sains dan Aplikasi 27 (12) (2024): 560-568

Jurnal Kimia Sains dan Aplikasi
Journal of Scientific and Applied Chemistry

Journal homepage: http://ejournal.undip.ac.id/index.php/ksa

An Investigation into the Anti-Aggregation Potential of *Swietenia macrophylla* Triterpenoid on Bovine Serum Albumin: Docking and RMSF

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https://doi.org/10.14710/jksa.27.12.560-568

Article Info

Article history:

Received: 24th October 2024
Revised: 12th December 2024
Accepted: 16th December 2024
Online: 31st December 2024

Keywords:
In silico; *swietenia macrophylla*; anti-aggregation; BSA; triterpenoid

Abstract

Protein aggregation, caused by environmental factors, can lead to neurodegenerative diseases. Hydrophobic compounds like latrepirdine are used in medical treatments like anti-Parkinson's and Huntington's diseases. *Swietenia macrophylla* contains abundant hydrophobic compounds from the triterpenoid group, but their anti-aggregation potential has not been reported. This study investigates the hydrophobic interactions and anti-aggregation potential of triterpenoid compounds, including swietenine, swietenolide, khayasin T, beta-sitosterol, and stigmasterol, against bovine serum albumin (BSA). Latrepirdine is employed as the control compound. *In silico* methods, molecular docking and molecular dynamics showed potential in clusters 1 and 2, with swietenine having a more stable RMSF value than latrepirdine. The study found four clusters with all ligands, with cluster 1 being the earliest protein opening area. Mahogany seed triterpenoid compounds have potential in cluster 1 (51-67%), while cluster 2 has 37-46%. In cluster 2, they have an advantage over latrepirdine (2%). Stigmasterol and beta-sitosterol are spread across the clusters. The swietenine compound has a more stable RMSF value than latrepirdine. This suggests that mahogany seed triterpenoid compounds have potential as anti-aggregation agents.

1. Introduction

The protein aggregation process represents a significant area of investigation within the broader field of biological mechanisms in living organisms. In normal conditions, proteins are in their native or folded conformation. However, under conditions of unstable thermodynamics, proteins can be partially folded or denatured, which initiates protein aggregation [1]. Protein aggregation can be defined as the process of protein unfolding that results in the hydrophobic side of the protein being exposed and forming interactions between proteins, thereby leading to the formation of a protein clump [2]. The aggregation of proteins has been linked to the development of various neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's, as well as other forms of neurodegeneration [3]. Aggregated proteins not only lose their functionality but can also form toxic structures that can damage cells [4]. It is, therefore, essential to investigate methods of preventing protein aggregation.

The identification of compounds that can prevent protein aggregation represents a significant area of interest within the field of neurodegenerative disease therapy. Several compounds, including those with hydrophobic properties, have been shown to possess the ability to inhibit protein aggregation [5]. Hydrophobic compounds, such as latrepirdine, have been employed as therapeutic agents against Parkinson's and Huntington's diseases and other neurodegenerative disorders by modulating protein aggregation [6]. Latrepirdine ($C_{21}H_{25}N$) is a small molecule with a tricyclic diphenyl-methylamine core featuring two benzene rings and a methylamino group, which facilitate its ability to decrease amyloid-β aggregation with a mechanism for blocking the hydrophobic site of amyloid-β [7]. Therefore, it can be concluded that using compounds with

hydrophobic properties effectively prevents protein aggregation.

Mahogany seeds (*Swietenia macrophylla*) are known to contain a plethora of hydrophobic compounds belonging to the triterpenoid group, including swietenine, swietenolide, khayasin T, stigmasterol, beta-sitosterol, and numerous others [8]. Mahogany seeds are commonly known to possess antioxidant, anti-cancer, anti-diabetic, and anti-inflammatory properties [9, 10]. However, research on protein anti-aggregation compounds derived from the triterpenoid group of mahogany seeds has yet to be conducted. Consequently, further investigation is required to ascertain the potential of triterpenoid compounds from mahogany seeds as anti-aggregation protein compounds.

One method to estimate the interaction between the tested compound and the target molecule is molecular docking. This method efficiently examines the activity of numerous anti-aggregation compounds and predicts their binding affinity. In this study, PyRx AutoDock software, LigPlot+, and Chimera were used for molecular docking [11]. PyRx integrates AutoDock and AutoDock Vina, enabling the screening of multiple compounds to predict their binding affinities to target proteins efficiently [12] LigPlot+ was used for generating 2D visualizations of ligand-protein interactions by illustrating hydrogen bonds and hydrophobic [13]. Chimera was employed to prepare molecular structures and 3D visualization [14].

In addition, the current understanding of protein flexibility has been significantly enhanced through utilizing molecular dynamics. In recent decades, molecular dynamics has become an indispensable tool for determining the state of conformationally heterogeneous proteins. This is often achieved through unbiased simulations originating from experimental static structures or combined with experimental data. molecular dynamics simulation data has demonstrated that molecular dynamics trajectories' structural characteristics and dynamics are consistent with those observed in simulations conducted using coarse-grained protein models. One of the tools employed in this process is CABS Flex 2.0 [15].

Root mean square fluctuation (RMSF) is a key measure in molecular dynamics simulations used to assess the flexibility of a protein by tracking deviations in atomic positions from their average locations throughout the simulation. Higher RMSF values indicate increased flexibility, suggesting that the region is more dynamic, while lower values indicate stability and rigidity in that area [16]. This measure is valuable in studying protein behavior, including conformational changes and interactions with ligands. Previous studies have applied RMSF to explore protein dynamics in drug design, helping to identify flexible regions that facilitate binding [17].

Triterpenoid compounds present in mahogany seeds are well recognized for their anti-inflammatory and anticancer properties, as evidenced by Dewanjee *et al.* [18]. Nevertheless, there is no evidence that it can be used as an anti-Parkinson's agent. Parkinson's disease is caused by the formation of protein clumps, or aggregates, due to the accumulation of misfolded proteins. One potential strategy for inhibiting protein aggregation is through ligand interactions with the hydrophobic region of the protein. This mechanism can be evaluated using *in silico* techniques, such as molecular docking and dynamic simulations, which assess binding affinity, the percentage of ligand binding to hydrophobic sites, and the stability of ligand-protein interactions using RMSF values. These parameters are crucial for identifying potential anti-Parkinson agents.

In this study, several compounds derived from mahogany seeds were selected for investigation, including swietenine, swietenolide, khayasin T, swietenine, beta-sitosterol, and stigmasterol. These compounds were chosen because they represent a group of compounds with similar structures—however, there are only slight differences in their functional groups. Latrepirdine was selected because this compound is a hydrophobic compound used as an anti-Parkinson's disease agent. Subsequently, the ligand and bovine serum albumin (BSA) protein are subjected to a docking procedure to elucidate the propensity of the BSA protein to undergo aggregation. This is followed by a molecular dynamics study yielding RMSF results. The outcomes of the docking and molecular dynamics analyses may serve to illustrate the potential of hydrophobic compounds from mahogany seeds as anti-aggregation agents of proteins.

2. Experimental

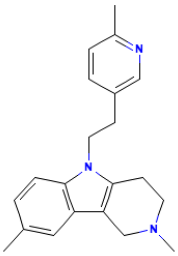
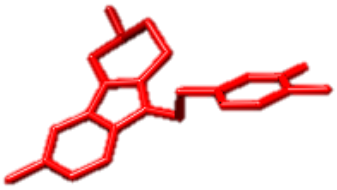
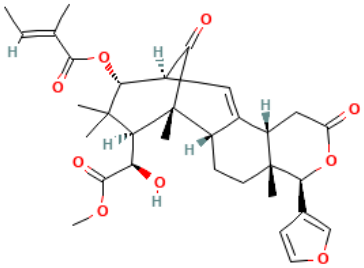
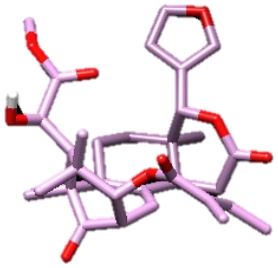
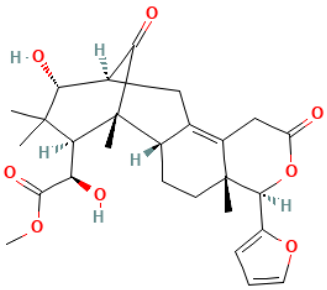
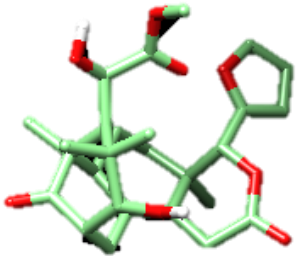
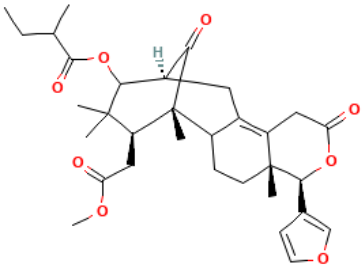
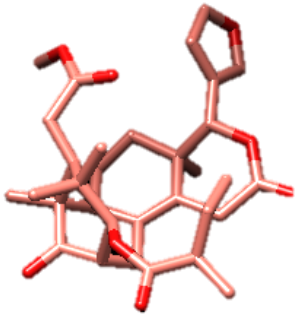
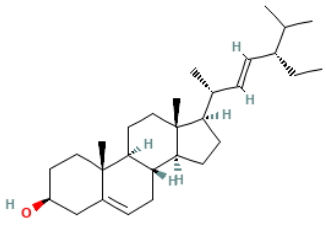
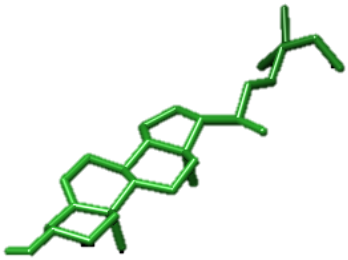
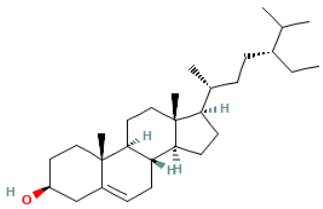
2.1. Materials

The materials used in the molecular docking process included the bovine serum albumin (BSA) protein model (code: 3v03) from the Protein Data Bank (https://www.rcsb.org/) and the chemical structures of compounds from *Swietenia macrophylla*, such as swietenine, swietenolide, khayasin T, stigmasterol and beta-sitosterol, obtained from PubChem (https://pubchem.ncbi.nlm.nih.gov/). The software employed were PyRx, LigPlot+, and Chimera. Additionally, the website (https://biocomp.chem.uw.edu.pl/) was used to obtain Root Mean Square Fluctuation (RMSF) data, and PlayMolecule (https://open.playmolecule.org/landing) was accessed for propensity data.

2.2. Preparation of Metabolites (Ligands)

The metabolite used was downloaded as an SDF file from the PubChem website in the 3D conformer format. The structure was then minimized using the PyRx program. In PyRx, Babel was opened, and a new element was inserted. The downloaded structure was selected, and once it appeared in the tab, it was right-clicked, and "Minimise Selected" was chosen, followed by clicking "OK." After minimization, the structure was right-clicked again, and "Convert Selected to Autodock Ligand (pdbqt)" was selected. The ligand was then ready for docking.

Table 1. The structure of ligands used in docking

Ligand	Chemical formula	2D Structure	3D Structure
Latrepirdine	$C_{21}H_{25}N_3$		
Swietenine	$C_{32}H_{40}O_9$		
Swietenolide	$C_{27}H_{34}O_8$		
Khayasin T	$C_{32}H_{42}O_8$		
Stigmasterol	$C_{29}H_{48}O$		
Beta-sitosterol	$C_{29}H_{50}O$		

2.3. Protein Preparation and Prospensity

The 3D structure of the BSA protein (3V03) was obtained from http://www.rscb.org in .pdb format. The target protein was prepared in Biovia Discovery Studio Visualizer by removing water molecules and ligands, then saved in .pdb format. Next, the protein was optimized using AutoDock Tools by adding hydrogen atoms and saved as a macromolecule in .pdbqt format. Once prepared, the protein file was uploaded to https://open.playmolecule.org/landing and viewed on DeepSite to assess its aggregation propensity based on van der Waals forces.

2.4. Molecular Docking

This method followed the procedure described by Klara *et al.* [19]. Molecular docking was performed using PyRx on the prepared BSA protein and ligands. The docking utilized a blind docking approach, setting the maximum box size to cover the entire protein surface to explore potential binding regions on the protein for each ligand. The resulting data included nine ligand positions that could bind to the protein and their binding affinities, saved as .pdbqt files.

Before molecular dynamics, redocking was conducted at the exact coordinates as for latrepirdine, with the center set to X: 45.5043, Y: 21.6558, Z: 43.2142, and dimensions X: 10 Å, Y: 10 Å, Z: 10 Å. The ligand overlapping with latrepirdine was selected and combined with the BSA protein using AutoDock, then saved as the .pdb file. The combined latrepirdine–BSA protein file was opened in LigPlot+, and the ligand interaction image with amino acid residues was generated to visualize interactions.

2.5. Molecular Dynamics

Molecular dynamics simulations were conducted using CABS Flex 2.0 for 100 cycles, with 100-frame trajectories over 10 ns and additional distance constraints applied with a global weight of 1.0 [15]. The docked BSA protein PDB file was uploaded to the site and configured according to the reference settings. The fluctuations of individual amino acid residues in the top docking hits were assessed based on RMSF values using CABS Flex 2.0 to analyze the conformational stability of the receptor-ligand complex over the nanosecond timescale. Higher RMSF values indicated greater flexibility, while lower values suggested restricted motion within the system during the simulation.

3. Results and Discussion

3.1. Ligand Preparation

The ligands used in this study have hydrophobic properties for anti-aggregation purposes. The compounds in mahogany seeds that were selected were swietenine, swietenolide, and khayasin T; these compounds were chosen because they represent the typical triterpenoid structure of mahogany seeds, these compounds were selected because they represent all the compounds in mahogany seeds, they are easy to isolate using semi-polar solvents, and many reports of these compounds are often isolated for various activities [20]. In addition, beta-sitosterol and stigmasterol from the steroid group were also selected. Pictures of the selected ligands are shown in Table 1.

The ligand presented in Table 1 was obtained by minimizing its 3D structure, and it was downloaded from the PubChem website. This process was conducted using the Open Babel plugin within the PyRx application. Latrepirdine has a compound chemical structure comprising a heptaline ring connected to a piperidine. 3D structure sets exhibit characteristics of both planar and non-planar interactions between the rings and are devoid of steric hindrance [21]. This facilitates the entry of latrepirdine into protein gaps, thereby preventing protein aggregation [7].

The triterpenoid compounds in mahogany seeds, such as swietenine, swietenolide, and khayasin T, exhibit unique 3D structural configurations compared to other secondary metabolites like beta-sitosterol and stigmasterol. These triterpenoids are characterized by a distinctive skeleton structure with continuous cyclization, incorporating furan and lactone rings [22]. Following minimization, the triterpenoid skeleton forms indentations, resulting in a bulkier and larger structure.

In addition to the triterpenoid group, compounds belonging to the steroid group, including beta-sitosterol and stigmasterol, have also been identified in mahogany seeds [10]. Regarding its structural composition, the compound can be defined as a steroid, comprising four rings and a hydroxyl group. This differentiates it from other compounds, such as beta-sitosterol and stigmasterol, which feature a double bond at position C22 and a side chain at C23. The latter distinction contributes to stigmasterol's enhanced flexibility compared to beta-sitosterol.

3.2. Aggregation of BSA Propensity Protein

This study commences with an investigation into the propensity for aggregation to establish the potential for aggregation in BSA proteins based on the side of the protein containing many van der Waals forces. It is hypothesized that van der Waals forces between amino acids represent the point of aggregation for proteins, given that they possess comparatively weak strength compared to other non-covalent bonds, such as those of hydrogen and electrostatic nature. Thus, when the protein is subjected to heat, the initial site to undergo structural changes is the region with the highest concentration of weaker interactions, namely van der Waals forces [23]. This propensity is determined through the utilization of Deepsite (www.playmolecule.org/) data, which is generated in the form of visual van der Waals forces on BSA proteins. This website is also conducive to identifying pockets of known binding sites and delineating atoms, residues, or other features, as evidenced in the ligand-protein interaction database [24]. The visualization of protein sites can be observed in Figure 1.

Table 2. Clustering data of ligands with BSA protein

Ligand		Cluster 1	Cluster 2	Cluster 3	Cluster 4
	∑ (%)	80%	5%	15%	-
Latrepirdine	Mean BA (kcal/mol)	-8.5	-7.6	-8.0	-
	Best BA (kcal/mol)	-9.0	-7.7	-8.4	-
	∑ (%)	63%	37%	-	-
Swietenine	Mean BA (kcal/mol)	-7.5	-7.6	-	-
	Best BA (kcal/mol)	-8.1	-7.8	-	-
	∑ (%)	51%	40%	-	-
Swietenolide	Mean BA (kcal/mol)	-7.6	-7.5	-	-
	Best BA (kcal/mol)	-7.8	-8.0	-	-
	∑ (%)	53%	46%	-	-
Khayasin T	Mean BA (kcal/mol)	-7.5	-7.3	-	-
	Best BA (kcal/mol)	-7.7	-7.9	-	-
	∑ (%)	46%	2%	24%	15%
Beta-sitosterol	Mean BA (kcal/mol)	-8.3	-7.3	-7.5	-7.2
	Best BA (kcal/mol)	-8.6	-7.3	-7.8	-7.5
	∑ (%)	40%	2%	19%	20%
Stigmasterol	Mean BA (kcal/mol)	-8.2	-7.4	-7.6	-7.5
	Best BA (kcal/mol)	-8.4	-7.4	-7.9	-8.0

(Description : BA= Binding afinity; ∑= sum of ligand interactions)

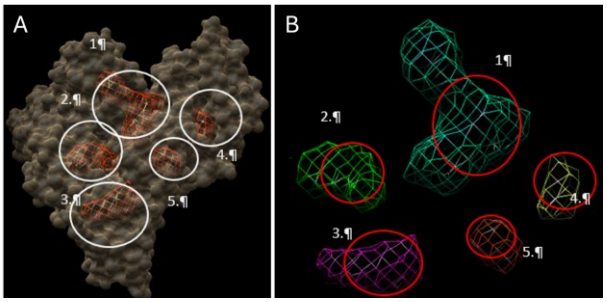


Figure 1. Illustrates the van der Waals forces exerted by the BSA protein surface, with Panel A displaying the protein at 70% transparency and Panel B without transparency

Figure 1 indicates that there are five areas with van der Waals style that may serve as the initial stage of protein aggregation. These areas exhibit distinct characteristics, as outlined in Table 1. Region 1 exhibits a markedly expansive van der Waals radius, thereby increasing the likelihood of protein aggregation at an earlier stage. The Deepsite data corroborates the visual data, indicating that Region 1 has the highest score (0.997), indicating that Region 1 has a greater van der Waals force than the other regions. The visual representation of each cluster surface is presented in Figure 2.

Figure 2 reveals the existence of two distinctive regions: region 1, which exhibits a markedly extensive surface area and a profound depth of excavation, and region 2, which displays a comparatively narrow and expansive surface hole with a considerable depth of excavation. Region 3 is characterized by a hole with a surface area that is narrow but elongated and shallow. In contrast, Region 4 is defined as a narrow and elongated area with a shallow hole.

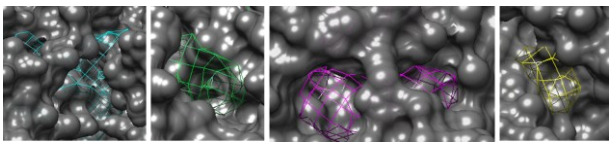


Figure 2. The surface visualization of the protein surface regions is presented herewith. The colour coding is as follows: blue = region 1, green = region 2, purple = region 3, yellow = region 4

3.3. Molecular Docking Ligands with BSA

The objective of the molecular docking method is to ascertain the potential locations where ligands interact with bovine serum albumin (BSA) proteins. Molecular docking is conducted meticulously on the entire surface of the protein to predict the potential for numerous ligands to interact with the surface of the BSA protein [25]. Before commencing the docking process, the grid box is set to its maximum size. The resulting data is a clustering pattern that serves to refine the outcomes of the van der Waals force calculations. Table 2 illustrates the number of ligands that may interact within each cluster and their respective binding affinity values.

As illustrated in Table 2, the greatest percentage of ligand interaction on the BSA protein occurs in cluster 1. This is because cluster 1 exhibits a highly high van der Waals force, thereby facilitating interaction among all ligands at that specific position [26]. Furthermore, cluster 1 is a region with a relatively broad aperture and a depth that is sufficiently pronounced.

Latrepirdine was selected as the control ligand due to its established use as an anti-Parkinson medication by inhibiting protein aggregation [6]. The data table indicates that latrepirdine has the capacity to bind to cluster 1 in 80% of the 45 experimental latrepiridine

ligand positions, exhibiting the lowest binding affinity of -9.0 kcal/mol in cluster 1. This suggests that latrepirdine is most likely to interact with cluster 1 compared to other clusters. This is because latrepirdine has a three-dimensional structure, a planar structure, and no steric hindrance, which allows it to interact with cluster 1 easily (Figure 3). However, in cluster 2, latrepirdine exhibits only 2% potential compared to the other clusters, and the lowest binding affinity is -7.7 kcal/mol. From a visual perspective, cluster 2 (Figure 1) exhibits a considerable area of holes, though not to a considerable depth. This renders cluster 2 less conducive to latrepirdine. However, it is notable that compounds derived from mahogany seeds exhibit a relatively high degree of binding affinity within this cluster compared to latrepirdine.

The data indicates that swietenine has the potential to bind to cluster 1 by 63% and that its lowest binding affinity is -8.1 kcal/mol. This suggests that swietenine is more likely to interact with cluster 1 than cluster 2. A comparison of the binding affinity values of swietenine and latrepirdine reveals that they are not significantly different, indicating that swietenine can also serve as a source of protein anti-aggregation inhibitors in cluster 1. However, swietenine displays a distinct advantage in cluster 2, potentially binding as much as 37%. Its three-dimensional structure is particularly well-suited to the surface of cluster 2, which features a sufficiently large hole with moderate depth. This allows swietenine compounds to interact extensively within cluster 2 compared to latrepirdine. It is also plausible that swietenine can act as an anti-aggregation protein compound by binding to cluster 2.

Meanwhile, stigmasterol and beta-sitosterol tend to disperse across four clusters in relatively equal proportions, with the largest percentage occurring in cluster 1. This is attributable to the planar and elongated structure of stigmasterol and beta-sitosterol, which can enter all clusters, including clusters.

The effectiveness of the interactions across clusters likely depends on each ligand's structural and chemical properties. Clusters with larger and more accessible binding pockets, such as clusters 1 and 2, are expected to produce more significant anti-aggregation effects due to better ligand accessibility and stability. In contrast, smaller or less accessible clusters, like cluster 4, may have lower effectiveness due to steric hindrance or limited interaction surfaces.

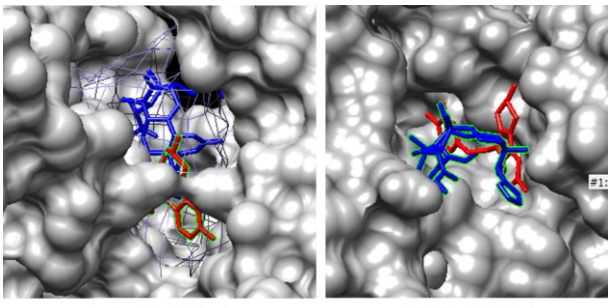


Figure 3. Ligand interactions in clusters 1 and 2 (laterpirdine: blue and swietenine: red)

In the context of molecular docking, the mahogany seed triterpenoid compounds, including swietenine, swietenolide, and khayasin T, demonstrate considerable potential as anti-aggregation agents, exhibiting binding affinity to cluster 1 with approximately 51-63% of ligand positions engaged in interaction. This binding profile is consistent with previous studies on hydrophobic compounds, such as limonoids, which have also demonstrated significant anti-aggregation potential through molecular docking. The aforementioned limonoid compounds exhibited approximately 63.5% inhibition of protein aggregation, with the lowest binding affinity being -6.5 kcal/mol [27]. However, mahogany seed triterpenoid compounds also demonstrate significant potential in cluster 2, with the potential of 37-47% of ligand positions that may interact. Docking results demonstrate their significant potential as anti-protein aggregation agents via clusters 1 and 2. This is evidenced by their ability to inhibit BSA aggregation to a greater extent than latrepirdine, which is used as a control compound.

3.4. Molecular Dynamics

A molecular dynamics analysis was conducted following the docking of the ligand with the BSA protein. A molecular dynamics analysis aims to ascertain the stability of the ligand-protein interaction [28]. This was conducted because molecular docking has not been able to provide information regarding the stability of the ligand-protein interaction in space and time. The analysis was performed by maintaining the ligand in the same position as the control ligand, latrepirdine, in cluster 1. The parameter employed to assess the stability of the ligand-enzyme interaction in molecular dynamics simulation is the RMSF. RMSF is a measure of the structural displacement of an amino acid from its average position over the course of the simulation. The RMSF method effectively assesses local flexibility in protein structures and identifies flexible and rigid areas [16]. The molecular dynamics method employs the CABS Flex 2.0 website, which displays the same data as molecular dynamics using GROMACS software, equivalent to 10 ns [15]. The RMSF fluctuation image is presented in Figure 4.

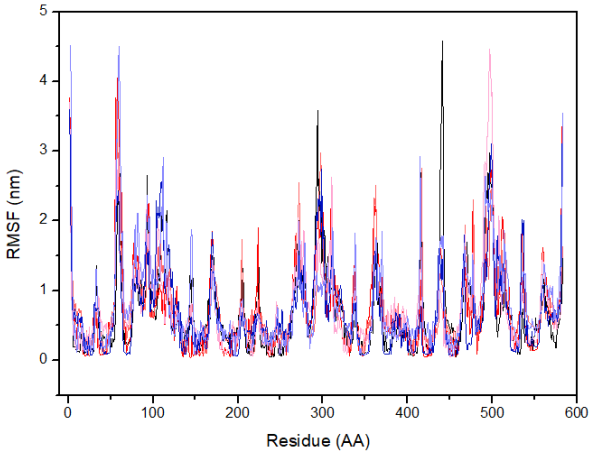


Figure 4. RMSF graph of mahogany seed triterpenoid compounds with latrepirdine (Black = latrepirdine; red=swietenine, pink=swietenolide; pink=khayasin T; dark blue=Stigmasterol; light blue=beta-sitosterol)

Table 3. RMSF values of mahogany seed triterpenoid compounds and latrepirdine against nine amino acids

Amino acids	RMSF value (nm)					
	Latrepirdine (+)	Swietenine	Swietenolide	Khayasin T	Stigmasterol	Beta-sitosterol
LEU 189	0.224	0.131	0.259	0.133	0.368	0.066
SER 192	0.135	0.057	0.394	0.221	0.382	0.065
ALA 193	0.309	0.289	0.291	0.094	0.348	0.067
ARG 196	0.439	0.389	0.462	0.253	0.061	0.136
LYS 431	0.337	0.306	0.373	0.202	0.544	0.21
SER 428	0.341	0.313	0.396	0.081	0.171	0.075
ARG 458	0.067	0.300	0.158	0.158	0.257	0.061
ILE 455	0.069	0.272	0.421	0.165	0.079	0.162
HIS 145	0.815	0.050	0.737	0.581	1.882	0.461

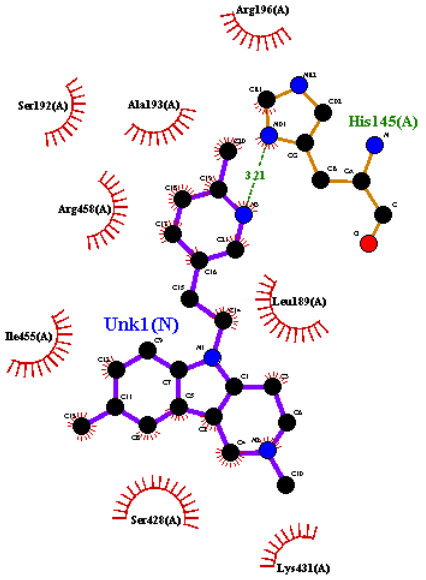


Figure 5. Latrepirdine interaction with BSA amino acid residues

A review of Figure 4 reveals a consistent trend in the RMSF value of the interaction between each ligand. However, it is notable that several ligands exhibit fluctuations that diverge from the overall pattern. Khayasin T is indicated by a yellow line at residue 495-499. The blue line represents beta-sitosterol, which exhibits a notable degree of fluctuation in amino acids 69-73. Latrepirdine, indicated by a black line, exhibits considerable fluctuation in amino acid residue at 435-441. This suggests that the ligands latrepirdine, khayasin T, and beta-sitosterol display an unstable tendency relative to other ligands when conducting molecular dynamics. As latrepirdine serves as a control ligand, exhibiting unstable residues, further examination of the residue interaction with latrepirdine is warranted.

Figure 5 illustrates the amino acid residues of BSA that interact with latrepirdine, comprising nine amino acid residues. Leu 189, Ser 192, Ala 193, Arg 196, Lys 431, Ser 428, Arg 458, and Ile 455 interact hydrophobically with eight residues, while His 145 has a hydrogen interaction. The mean value of RMSF between the ligand and each of the nine amino acids is presented in Table 3.

Table 3 indicates that triterpenoid compounds, including swietenine and khayasin T, exhibit comparatively lower RMSF values when interacting with BSA amino acid residues than latrepirdine. Prior research on anti-aggregation mechanisms, particularly in amyloid beta proteins, has indicated that hydrophobic compounds, such as α-tocopherol, exhibit reduced RMSF values compared to other compounds, including ascorbic acid and malic acid. These hydrophobic compounds are indicative of enhanced stability in ligand-protein complexes. This stability is crucial for preventing aggregation, enabling the ligand to sustain interactions with the target protein [29].

The findings suggest that mahogany seed triterpenoid compounds exhibit greater stability when interacting with amino acid residues than latrepirdine. Conversely, in molecular docking studies, the binding affinity value of mahogany seed triterpenoid compounds is slightly lower than that of latrepirdine. This is due to the rigid molecular structure between BSA and swietenine, which prevents swietenine from penetrating as deeply as latrepirdine. Thus, mahogany seed triterpenoid compounds exhibit considerable potential as anti-aggregation proteins in molecular dynamics, as evidenced by their performance in cluster 1.

Further study is required of triterpenoid compounds to ascertain their potential for use in regulating temperature, thereby enabling the protein to open. Additionally, it would be beneficial to determine the RMSD value, radius of gyration, binding energy, and aggregation score after molecular dynamics utilizing the Aggrescan tool. Further in vitro studies are required.

4. Conclusion

The *in silico* study using molecular docking and RMSF analysis successfully demonstrated the occurrence of hydrophobic interactions between the ligand and the hydrophobic regions of the protein. These hydrophobic

interactions contribute to the ligand's capacity as an anti-aggregation agent. Based on molecular docking results, The study found four clusters with all ligands, cluster 1 being the earliest protein opening region. The molecular docking of triterpenoid compounds in cluster 1 exhibited ligand positions ranging from 51% to 63%, while in cluster 2, the range was 37 to 46%. The triterpenoid compound mahogany seeds exhibited superior performance in cluster 2 compared to the control compound (latrepirdine), indicating a high potential for bioactivity. The triterpenoid compound's stability ligand is more stable than latrepirdine based on RMSF value. This suggests that mahogany seed triterpenoid compounds have potential as anti-aggregation agents.

Acknowledgment

This research is supported by a grant from the DIPA FSM (grant number 1263A/UN7.5.8/PP/2022).

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