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Molecular docking: Bioactive compounds of *Mimosa pudica* as an inhibitor of *Candida albicans* Sap 3

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ABSTRACT

Candida albicans (C. albicans) is a commensal microbiota that resides in humans. However, in certain cases, C. albicans can infect and cause several diseases to humans. This study aimed to investigate the interaction between Mimosa pudica (M. pudica) bioactive compounds and C. albicans Sap 3. Molecular docking analysis was carried out using YASARA structure. The procedures involved preparation of ligands and target receptor, molecular docking, data analysis and visualization. The seven ligands were 3D downloaded from PubChem, while target receptor was downloaded from RCSB PDB. The interaction between M. pudica bioactive compounds against Sap 3 resulted in a binding energies ranges from 5,168 – 7,480 kcal/mol and most of the interactions formed were relatively strong. Furthermore, the test ligands had contact with the catalytic residues and substrate binding site pockets S1/S2/S3/S4 on the target receptor. The bioactive compounds of M. pudica have a relatively good interaction, approaching standard ligand, in inhibiting of C. albicans 3.

Keywords: *Candida albicans, Mimosa pudica*, *Molecular docking, Secreted aspartic proteinase (Sap) 3, YASARA Structure*

ABSTRAK

Candida albicans (C. albicans) merupakan mikrobiota komensal yang berada didalam manusia. Namun, dalam beberapa kasus tertentu, C. albicans dapat menginfeksi dan menimbulkan beberapa penyakit bagi manusia. Penelitian ini bertujuan untuk investigasi adanya interaksi antara senyawa bioaktif Mimosa pudica (M. pudica) dengan Sap 3 C. albicans. Metode penambatan molekuler dilakukan menggunakan YASARA stucture. Prosedur yang dikerjakan meliputi preparasi ligan dan reseptor target, penambatan molekuler, analisis data dan visualisasi. Ketujuh 3D ligan diunduh dari PubChem NCBI, sedangkan reseptor target diunduh dari RCSB PDB. Interaksi senyawa bioaktif Mimosa pudica dengan Sap 3 menghasilkan energi ikatan berkisar antara 5.168 – 7.480 kkal/mol dan interaksi yang terbentuk dominan tergolong kuat. Selebihnya, ligan uji mempunyai kontak dengan residu katalitik dan kantong situs pengikatan substrat pada S1/S2/S3/S4 reseptor target. Senyawa bioaktif M. pudica mempunyai interaksi yang cukup baik, mendekati standar ligan, dalam menghambat Sap 3 C. albicans.

Kata kunci: *Candida albicans, Mimosa pudica, Penambatan molekul, Secreted aspartic proteinase (Sap) 3, Struktur YASARA*

1. INTRODUCTION

Most of the human pathogenic fungi of the genus *Candida* reside in animals and humans (Kumamoto *et al.* 2020). Invasive *Candida* infection is one of the most common fungal infections globally (Pfaller dan Diekema 2007; Bhattacharya *et al.* 2020). In western countries, individuals generally have *Candida* as a commensal microbiota in their gut (Kumamoto *et al.* 2020). In the United States, *Candida* spp. is reported to be one of the leading causes of healthcareassociated infections (Pfaller dan Diekema 2007; Bhattacharya *et al.* 2020). *Candida* infection is also often associated with medical devices such as central venous catheters, cardiovascular machines, and urinary catheters (Kojic dan Darouiche 2004; Bhattacharya *et al.* 2020). Among the species of *Candida* sp., *Candida albicans* (*C. albicans*) (37%) is the most commonly found in the clinical species (Bhattacharya *et al.* 2020) [2]. Invasive candidiasis is associated with a high mortality rate, ranging from 20 to 49%. *C. albicans* can be found to colonize various mucosal surfaces such as skin, mouth, and vagina; most studies consider the gastrointestinal tract as the main entry point for *C. albicans* to enter the bloodstream (Zhu dan Filler 2010; Sheppard dan Filler 2015; Meenambiga *et al.* 2018; Basmaciyan *et al.* 2019; Lapaquette *et al.* 2022).

On the other hand, *C. albicans* is the most common causative agent of oral, vaginal, and disseminated candidiasis. Oral candidiasis is one of the most common opportunistic infectious diseases among patients suffering from HIV infection. *C. albicans* can multiply rapidly, invade tissues, and cause symptomatic mucosal lesions in people with immune systems disorder (Barchiesi *et al.* 2002; Selmecki *et al.* 2010; Santos *et al.* 2021). Therefore, good immune systems are important to maintain the fungus in a commensal state, preventing invasion, epithelial damage, and mucosal infection (Kumamoto *et al.* 2020; Westman *et al.* 2022). It is estimated that more than 7.5 million people globally have been infected by invasive candidiasis. There are unwanted side effects, ineffectiveness, and the rapid development of resistance by fungi, therefore there is a need for the development of new antifungals (Meenambiga *et al.* 2018). Many factors and activities have been identified as the cause of the pathogenicity of *C. albicans* (Prieto *et al.* 2016; Kumamoto *et al.* 2020), secreted aspartic proteinases (Sap) 1-3 have been observed to play an important role in adhesion and tissue damage in local infections (Borelli *et al.* 2007; Calugi *et al.* 2013). In-depth understanding of the contribution of the Sap family to the pathogenicity of *C. albicans*, obtained by apprehending the *C. albicans* strains; Sap 1-3 are involved in mucosal infections, and Sap 4-6 are involved in systemic infections (Borelli *et al.* 2007). *C. albicans* Sap plays a multimodal role in the infection process, therefore the development of inhibiting Sap as targets for a wide variety of infections caused by *C. albicans* appears to be a good strategy (Santos *et al.* 2021). Thus, in this study we used Sap 3, as it is closely related to mucosal infection.

Mimosa pudica Linn (*M. pudica*) is a medicinal plant with pharmaceutical and nutraceutical potential; this plant is also popular among traditional healers to treat various diseases (Vijayalakshmi *et al.* 2023). Herbal plants have been widely used to treat several diseases and are used as traditional medicine (Zahra *et al.* 2022). This plant was observed because of its thigmotactic and seismonastic movements. *M. pudica* is known for its analgesic, anti-inflammatory, diuretic activity, insomnia, and urogenital infections (Kaur *et al.* 2016; Muhammad *et al.* 2016; Vijayalakshmi *et al.* 2023).

The molecular docking method is one of the *in silico* research methods and is one of the most powerful techniques to help discover new ligands for proteins with known structures, thus playing a pivotal role in structure-based drug design (Chopade *et al.* 2015; Gholam dan Artika 2023). Therefore, in this study we investigated the possibility of an interaction between bioactive compounds from *M. pudica* and the Sap 3 *C. albicans* to find new inhibitor candidates.

2. METHODOLOGY

Receptor preparation

Sap 3 with the code “2H6T” with

resolution 1.90 Å, was downloaded from the RCSB PDB website (https://www.rcsb.org/structure/2H6T, accessed on 13 July 2022). Preparation was carried out using YASARA structure (Bioinformatics 30.2981-2982 Version 19.9.17) (Krieger dan Vriend 2014; Krieger dan Vriend 2015) by adding hydrogen atoms and removing water molecules around the receptor (Gan *et al.* 2018).

Ligand preparation

Seven bioactive compounds of *M. pudica* was obtained from Vijayalakshmi *et al.* (2023) and pepstatin as standard ligand, then the 3D structure was downloaded from the NCBI PubChem page (https://pubchem.ncbi.nlm.nih.gov/, accessed on 13 July 2022) with (.sdf) format (Figure 1) (Kim *et al.* 2019). The preparation also used YASARA structure to add hydrogen atoms and energy minimization (Krieger dan Vriend 2014; Krieger dan Vriend 2015; Gan *et al.* 2018; Gholam 2022).

Molecular docking

To explore the possibility of ligand binding into the pocket area of the substrate binding site or receptor catalytic residue, molecular docking was carried out using YASARA structure software (Krieger dan Vriend 2014; Krieger dan Vriend 2015; Gan *et al.* 2018; Gholam 2022; Gholam dan Firdausy 2022) [26]. YASARA structure was set to AutoDock Vina settings, AMBER03 force field, and 25 runs (dock_run). The docking area was set to around all atoms to expand the docking area. Then the other parameters remained unchanged. Finally, the resulting conformers were analyzed to determine hydrogen bonding, hydrophobic interactions, electrostatic interactions, and other interactions (Ding *et al.* 2018; Gan *et al.* 2018; Gholam *et al.* 2022).

Data analysis and visualization

After docking, the receptor-ligand complex interactions were analyzed using BIOVIA Discovery Studio Visualizer v21.1.0.20298. The results of the analysis were in the form of 2D and 3D structures to help visualize and analyze the interaction pattern of the ligand-protein complex (Meenambiga *et al.* 2018; Zahra *et al.* 2023).

3. RESULTS

Based on the results of this study, interestingly, pepstatin (standard ligand) had the highest binding energy of 8.857 kcal/mol and Kd 321908.8438 pM. The test ligands that have binding energy close to pepstatin are

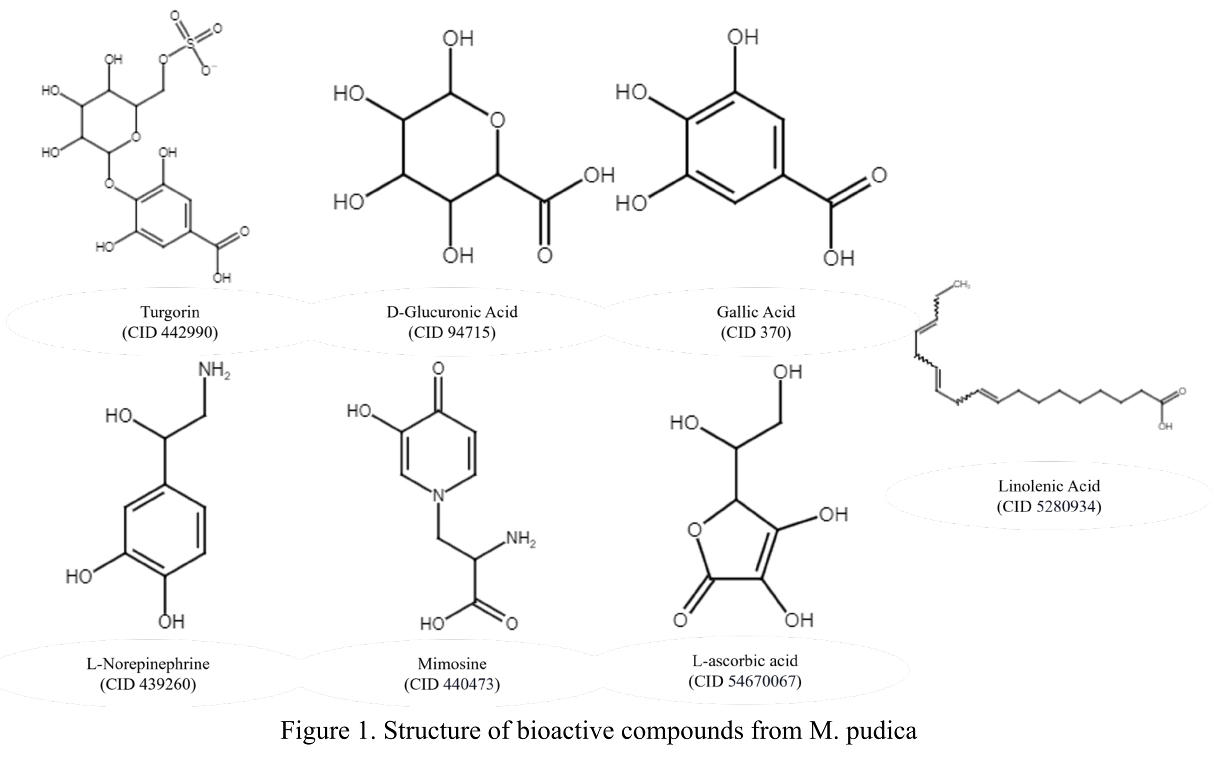

Figure 1. Structure of bioactive compounds from M. pudica

turgorin with a binding energy of 7,480 kcal/mol and K_d 3289177.500 pM, then based on the binding energy respectively, D-glucuronic acid with a binding energy of 6.219 kcal/mol and Kd 27632016.000 pM, gallic acid with a binding energy of 6.053 kcal/mol and Kd 36567240.000 pM, L-norepinephrine with a binding energy of 5.770 kcal/mol and Kd 58956804.000 pM, mimosine with a binding energy of 5.599 kcal/mol and Kd 78682576.000 pM, L-ascorbic acid with a binding energy of 5.390 kcal/mol and Kd 111963792.000 pM, and the lowest binding energy is linolenic acid with a binding energy of 5.168 kcal/mol and Kd 162856752.000. The results of the binding energies are presented in Figure 2.

Through the help of the Discovery Studio software, the patterns of interactions that are formed within the complex can be seen. The results of the analysis are presented in Table 2. Pepstatin tends to make hydrogen bonds with the target receptor (Figure 3). Hydrogen bonds have a distance ranging between 1.99 - 3.0 Å. The category of hydrogen bonds formed in the Sap3-Pepstain complex has from chemistry H-donor and to chemistry H-acceptor. SER13, GLY85, ASP86, and THR222 bind with the O atom in pepstatin. GLY220 and THR222 bind with the H atom of pepstatin. Pepstatin also has hydrophobic and unfavorable interactions. The hydrophobic interaction between A:TYR84 - A:UNK1:C was Pi-Alkyl type. Other

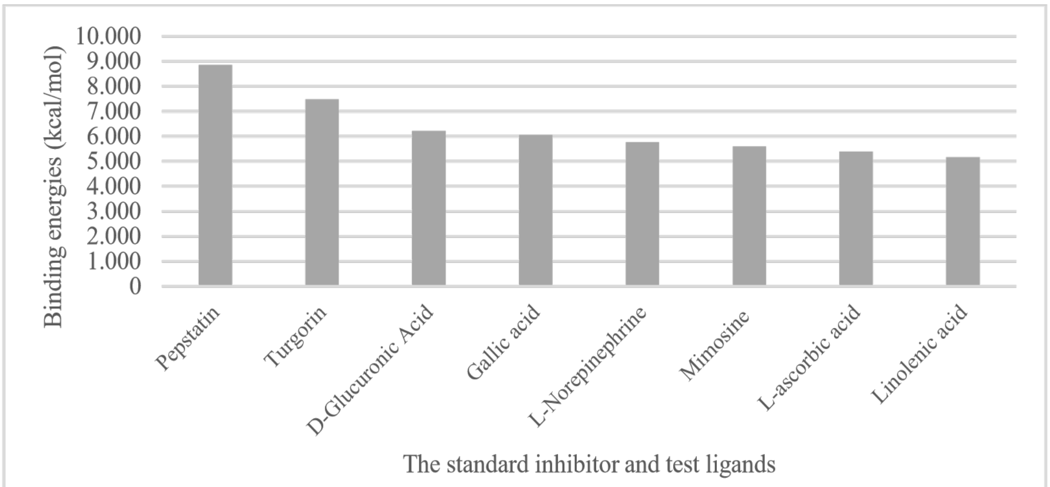

Figure 2. The binding energies of M. pudica bioactive compounds against Sap 3 determined using YASARA structure

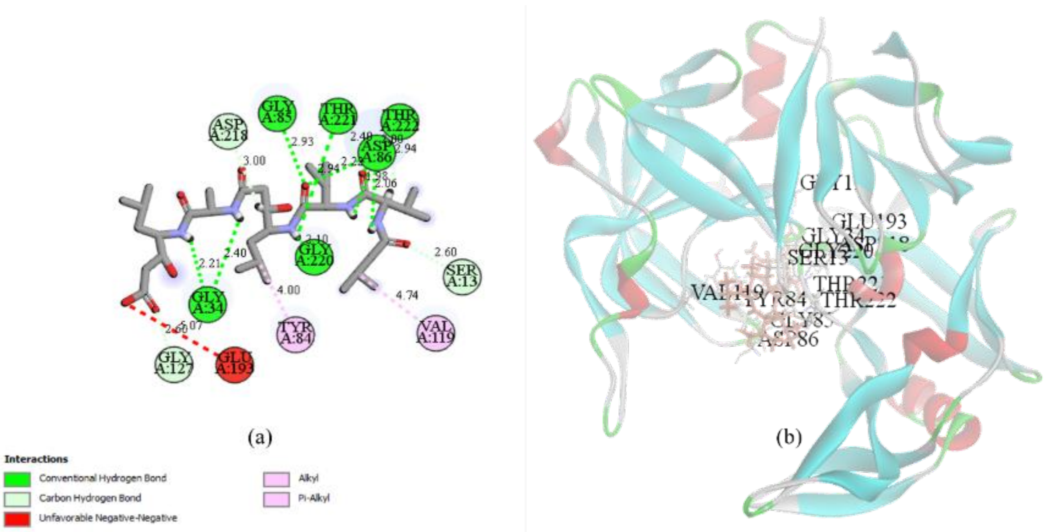

Figure 3. Visualization using BIOVIA Discovery Studio shows the interaction formed on the pepstatin complex with Sap 3 (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows the semi-transparent complex

hydrophobic interactions also formed in Alkyl type between A:UNK1:C - A:VAL119. This study found an unfavorable interaction in the Sap 3-Pepstatin complex at A:GLU193:OE1 - A:UNK1:O under the negative-negative unfavorable type.

Turgorin formed ten interactions with the target receptor; out of ten interactions, only one was hydrophobic (Figure 4). The hydrogen bonds formed have a distance between 1.92 - 2.81 Å. This ligand had contact with the ASP218 catalytic residue formed the OH group. Amino acid residues that interact with the ligand O atom were ASP85 and ASP86 by forming hydrogen bonds. TYR84 interaced with the ligand aromatic ring with a distance of 4.68817 Å, with from chemistry Pi-Orbitals and to chemistry Pi-Orbitals. The strongest hydrogen bond was found on the ASP218 catalytic residue and the ligand OH group with a distance of 1.92 Å. These ligands interacted with amino acid residues in S1/S2 and catalytic residues.

D-glucuronic acid, gallic acid, and L-ascorbic acid had no interaction with the substrate binding site pocket. They did not even interact with the Sap 3 target receptor's catalytic residue (Table 2).

D-glucuronic acid had ten interactions, with details of nine hydrogen bonds and one unfavorable interaction (Figure 5). Amino acid residues that formed OH groups with ligands are ASN9, GLN11, ARG162, GLN163, and ARG312. The distance created due to the presence of hydrogen bonds ranged from 2.10 - 2.94 Å. Unfavorable bonds were formed on the

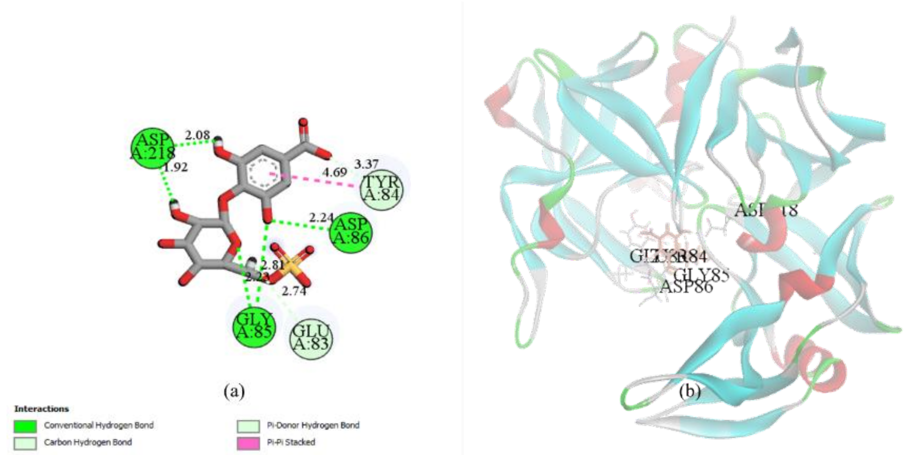

Figure 4. Visualization using BIOVIA Discovery Studio shows the interaction formed in the turgorine-Sap 3 complex (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows the complex in a semi-transparent manner

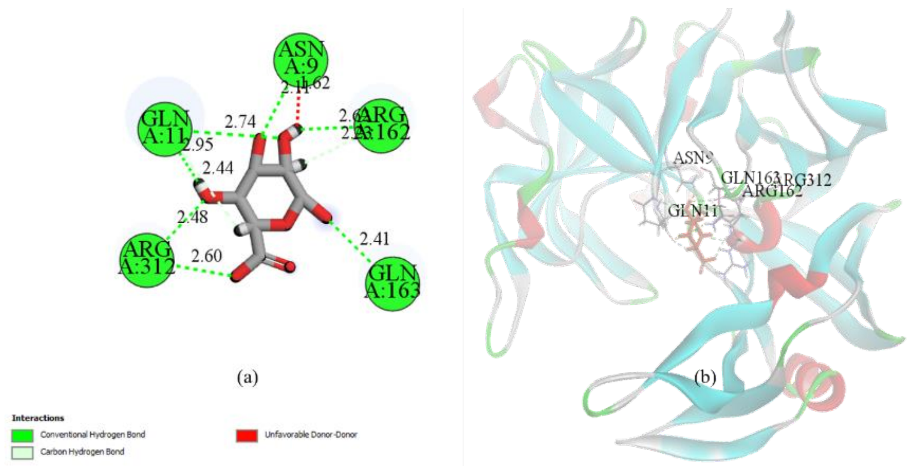

Figure 5. Visualization using BIOVIA Discovery Studio shows the interaction formed on the Dglucuronic acid-Sap 3 complex (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows the semi-transparent complex

ASN9 amino acid residues with ligand H atoms, from chemistry H-donor and to chemistry Hdonor, and the distance is 1.61 Å.

ARG162 formed a hydrogen bond by interacting with the aromatic ring of the gallic acid ligand with a distance of 3.21 Å (Figure 6), and from chemistry H-donor, to chemistry Piorbitals. The distance produced by the presence of hydrogen bonds ranges from 2.11 - 3.21 Å, while the hydrophobic interaction has a distance of 4.60 Å.

L-norepinephrine with the target receptor formed three electrostatic bonds, two of which have the same amino acid residue and ligand atom (Figure 7), which also formd hydrogen bonds, namely A:UNK1:H1 - A:ASP218:OD2 and A:UNK1:H3 - A: ASP218:OD2, while A:UNK1:N - A:ASP32:OD1 only formed electrostatic bonds. The distance created by the presence of hydrogen bonds ranges from 2.16- 5.09 Å. The two catalytic residues formed hydrogen and electrostatic bonds with the ligands in this complex. The hydrophobic interactions formed in this complex are known to form in the amino acid residues VAL30 and ILE123, which had contact with the aromatic ring of the ligand. This ligand had contact with amino acid residues located at S1/S2/S3 and the catalytic residues.

Mimosine also formed hydrogen bonds and electrostatic bonds on the identical amino acid residues and ligand atom (Figure 7), namely at A:UNK1:H1 - A:ASP218:OD2 and A:UNK1:H2 - A:ASP32:OD2. An electrostatic bond was also formed at A:UNK1:N - A:ASP32:OD1. Both receptor catalytic residues

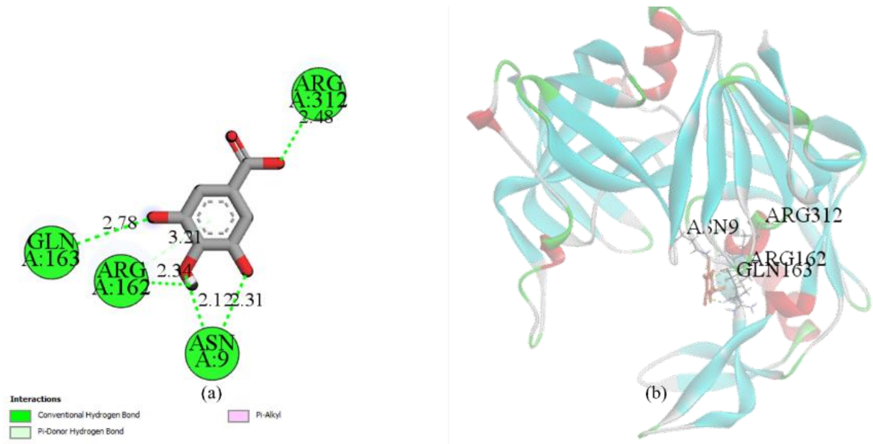

Figure 6. Visualization using BIOVIA Discovery Studio shows the interaction formed on the gallic acid-Sap 3 complex (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows semi-transparent complex

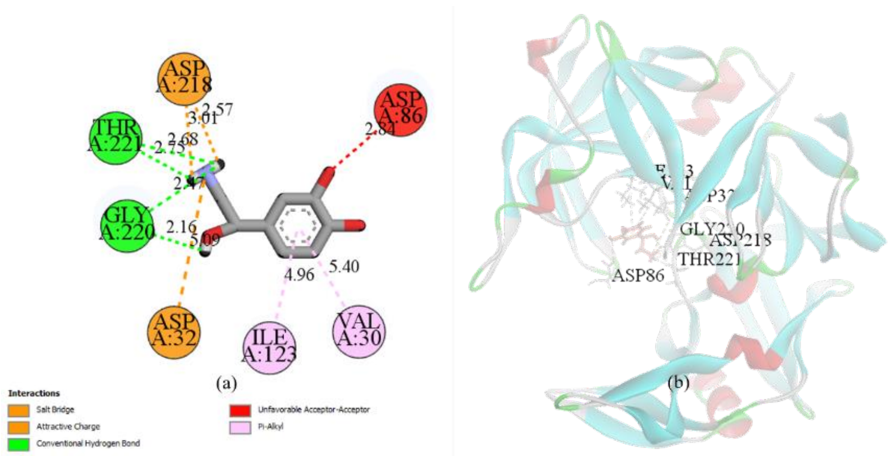

Figure 7. Visualization using BIOVIA Discovery Studio shows the interaction formed in the LNorepinephrine-Sap 3 complex (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows semi-transparent complex

are formed in the two interactions. The distance created due to the presence of hydrogen bonds ranges from 1.99 - 3.34 Å. In this complex, the interactions formed at the VAL30, TYR84, and ILE123 amino acid residues had contact with the aromatic ring of the ligand.

Dominantly, L-ascorbic acid has hydrogen bond and one unfavorable bond with the target receptor (Figure 9). The distance generated by the presence of hydrogen bonds ranges from 2.12 - 2.97 Å. The O atom of the ligand binds with the amino acid residues GLY127, GLU193, and LEU194, while TYR128 forms the OH group. An unfavorable bond is formed between the amino acid residue ASN192 and the O atom of the ligand. The bond distance is 2.69 Å with an unfavorable acceptor-acceptor type.

Linolenic acid has five hydrogen bonds and four hydrophobic interactions (Figure 10). The hydrogen bond distance formed ranges from 1.98 - 3.19 Å. The hydrogen bond in this ligand is also caused by the presence of from chemistry H-donor and to chemistry H-acceptor. THR222 and ILE223 bind with the ligand O atom.

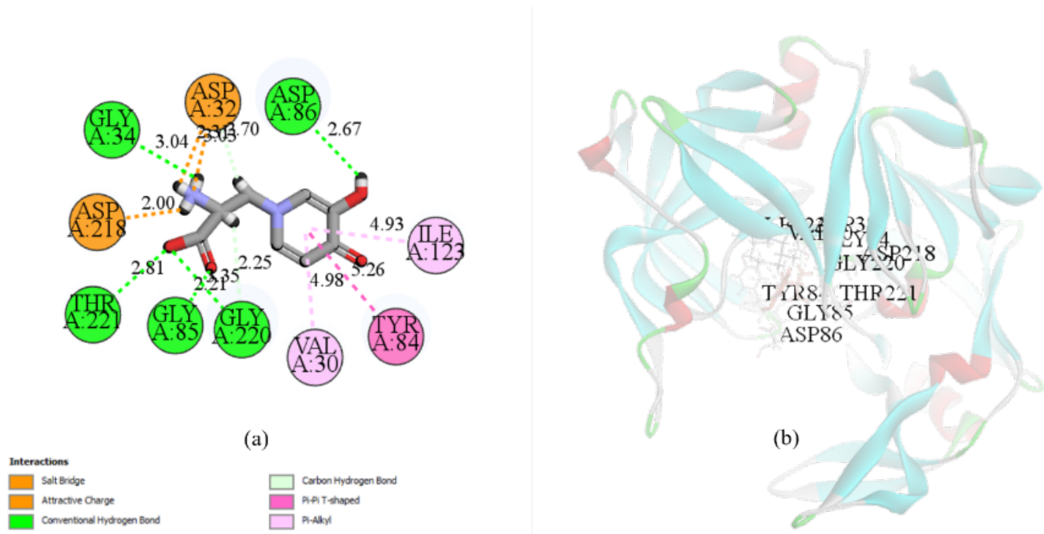

Figure 8. Visualization using BIOVIA Discovery Studio shows the interaction formed on the mimosine-Sap 3 complex (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows semi-transparent complex

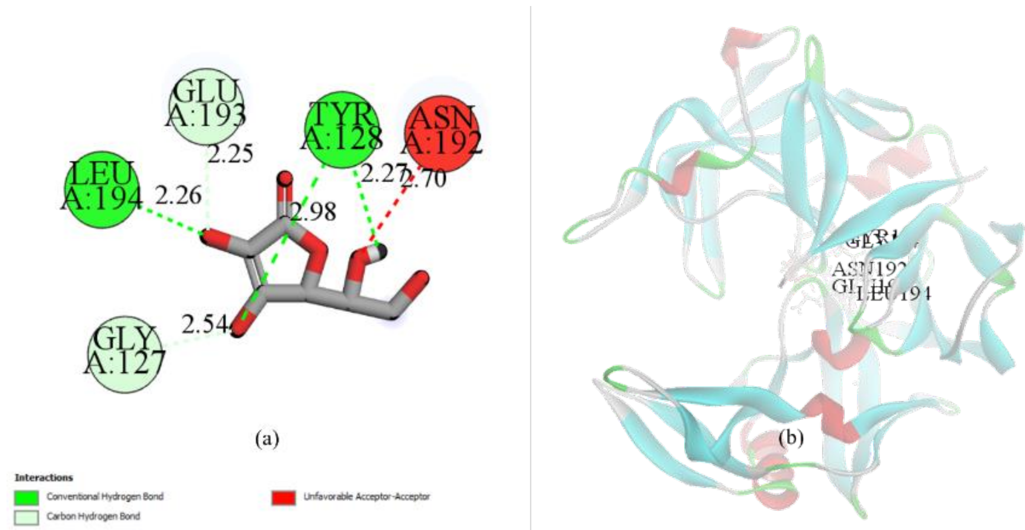

Figure 9. Visualization using BIOVIA Discovery Studio shows the interaction formed on the Lascorbic acid-Sap 3 complex (a) 2D visualization shows bond distance, amino acid residues, and interaction type (b) 3D visualization shows semi-transparent complex

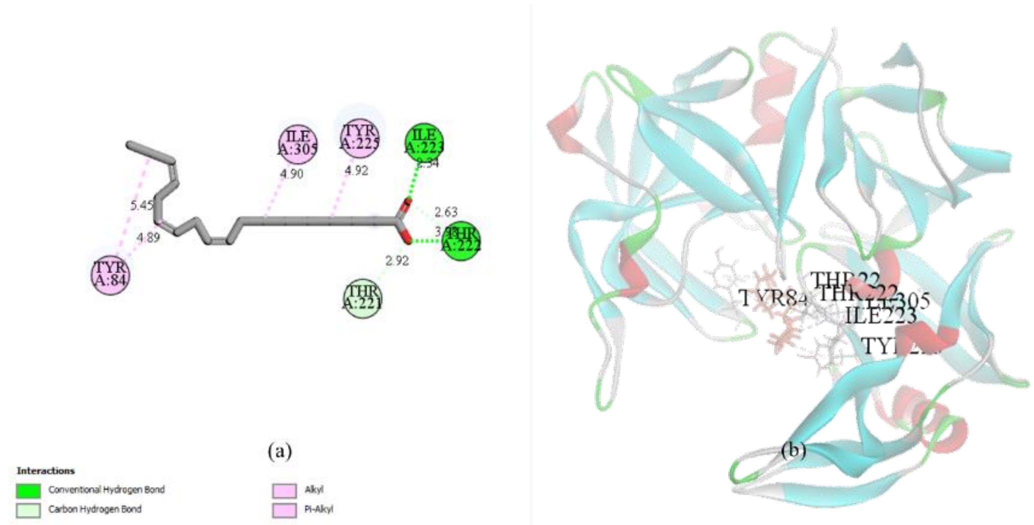

Figure 10. Visualization using BIOVIA Discovery Studio shows the interaction formed on the linolenic acid-Sap3 complex (a) 2D visualization shows bond distance, amino acid residues, and type of interaction (b) 3D visualization shows semi-transparent complex

4. DISCUSSION

This research used the molecular docking method to bind compounds (test ligands) from *Mimosa pudica* (*M. pudica*) to Sap 3 *Candida albicans* (*C. albicans*). The docking process does not target specific residues or limit the docking area, allowing all amino acid residues to potentially interact with the ligand.

It is widely known that *C. albicans* has Sap 1 to Sap 10 genes. Sap is one of the classic virulent factors whose expression is modulated by several conditions such as the influence of pH, temperature, site of infection, and physicochemical environmental conditions (Naglik *et al.* 2003; Santos *et al.* 2021). The pepstatin used as the standard ligand to refer to the standard binding energy, dissociation constant (Kd), and amino acid residues (Santos *et al.* 2021).

The more positive value of the binding energy indicates stronger bond between the ligand and the target receptor whereas (Pandey *et al.* 2019; Uma Maheshwari Nallal *et al.* 2021) (Figure 1). The smaller value of Kd indicates that ligand binding affinity againts the receptor is stronger (Forlemu *et al.* 2017; Aamir *et al.* 2018; Masomian *et al.* 2018). The dissociation constant (Kd) is a quantitative measure of how tightly a ligand binds to a receptor. It is defined as the concentration of the ligand at which half of the receptor sites are occupied (Kalra *et al.* 2018; Abdel *et al.* 2019). We also show the Kd and overall residual contacts in Table 1.

It is important to note that through Borelli *et al.* (2007) research, Sap 3 was known to be divided into several pockets of substrate binding sites on S1, S2, S3, and S4. S1 consists of VAL30, TYR84, ASP86, THR88, VAL119, and ILE123 amino acid residues. The S2 consists of GLY85, ASP86, THR221, TYR225, SER301, TYR303, and ILE305 amino acid residues. S3 consists of VAL12, SER13, ASP86, THR88, SER188, ASP120, and GLY220 amino acid residues. S4 consists of VAL12, THR222, ILE223, TYR225, GLN295, LEU297, and GLY299 amino acid residues, while the catalytic residues are located in ASP32 and ASP218. This study usedthese important residues as a criterion.

Pepstatin interacts with amino acid residues at S1/S2/S3/S4 and catalytic residues. In Borelli *et al.* (2007) research, pepstatin interacted with amino acid residues located at S1/S2/S3/S4. However, pepstatin suboptimally filled several binding sites, mainly at S3/S4 and his research also explained that pepstatin is a pentapeptide produced by the *Streptomyces*.

Abu-Izneid *et al.* (2018) explained that glucuronide or glucuronoside, which are D-glucuronic acid and glucuronide derivatives, is an important class of active pharmaceutical compounds known to have antiviral activity against viruses, such as A/H1N1 and A/H3N2 strains of influenza virus.

Table 1. Molecular docking results of M. pudica bioactive compounds against Sap 3 using YASARA structure

Ligand	Dissoc. Constant (pM)	Contacting receptor residues
Pepstatin (standard ligand)	321908.8438	A VAL 12 A SER 13 A VAL 30 A ASP 32 A THR 33 A GLY 34 A SER 35 A SER 36 A ILE 82 A GLU 83 A TYR 84 A GLY 85 A ASP 86 A VAL 119 A ASP 120 A GLN 121 A ILE 123 A GLY 127 A TYR 128 A ASN 192 A GLU 193 A LEU 194 A ARG 195 A LEU 216 A ASP 218 A GLY 220 A THR 221 A THR 222 A ILE 223 A TYR 225 A TYR 303 A ILE 305
Turgorin	3289177.500	A VAL 30 A ASP 32 A GLY 34 A GLU 83 A TYR 84 A GLY 85 A ASP 86 A THR 88 A VAL 119 A ILE 123 A ARG 195 A LEU 216 A ASP 218 A GLY 220 A THR 221 A TYR 303 A ILE 305
D-Glucuronic Acid	27632016.000	A ASN 9 A GLN 11 A VAL 12 A TYR 14 A ARG 162 A GLN 163 A THR 222 A ALA 281 A LEU 297 A ASN 309 A ARG 312
Gallic acid	36567240.000	A ASN 9 A GLN 11 A TYR 14 A ARG 162 A GLN 163 A THR 222 A LEU 297 A ASN 309 A ARG 312
L-Norepinephrine	58956804.000	A VAL 30 A ASP 32 A GLY 34 A TYR 84 A GLY 85 A ASP 86 A THR 88 A VAL 119 A ILE 123 A ASP 218 A GLY 220 A THR 221 A ILE 305
Mimosine	78682576.000	A SER 13 A VAL 30 A ASP 32 A GLY 34 A SER 35 A TYR 84 A GLY 85 A ASP 86 A THR 88 A VAL 119 A ILE 123 A ASP 218 A GLY 220 A THR 221
L-ascorbic acid	111963792.000	A THR 33 A GLY 34 A SER 35 A SER 36 A GLY 127 A TYR 128 A LYS 129 A ASN 192 A GLU 193 A LEU 194 A LEU 216
Linolenic acid	162856752.000	A ASP 32 A GLY 34 A SER 35 A TYR 84 A GLY 85 A ASP 86 A LEU 216 A ASP 218 A GLY 220 A THR 221 A THR 222 A ILE 223 A TYR 225 A ILE 305

Table 2. The interactions of *M. pudica* bioactive compounds against *C. albicans* Sap 3

Ligand	Name	Distance (Å)	Category	From chemistry	To chemistry
	A:GLY85:H - A:UNK1:O	2,93	Hydrogen Bond	H-Donor	H-Acceptor
	A:ASP86:H - A:UNK1:O	2,22	Hydrogen Bond	H-Donor	H-Acceptor
	A:THR222:H - A:UNK1:O	1,99	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ASP86:OD2	2,06	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ASP86:OD2	1,98	Hydrogen Bond	H-Donor	H-Acceptor
Pepstatin	A:UNK1:H - A:GLY220:O	2,09	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:THR221:OG1	2,93	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:GLY34:O	2,40	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:GLY34:O	2,20	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:UNK1:O	2,72	Hydrogen Bond	H-Donor	H-Acceptor
	A:SER13:HB2 - A:UNK1:O	2,60	Hydrogen Bond	H-Donor	H-Acceptor
	A:GLY127:HA2 - A:UNK1:O	2,59	Hydrogen Bond	H-Donor	H-Acceptor
	A:THR221:HA - A:UNK1:O	2,39	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:THR222:OG1	2,93	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ASP218:OD2	3	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:C - A:VAL119	4,74	Hydrophobic	Alkyl	Alkyl
	A:TYR84 - A:UNK1:C	3,99	Hydrophobic	Pi-Orbitals	Alkyl
	A:GLU193:OE1 - A:UNK1:O	5,07	Unfavorable	Negative	Negative
	A:GLY85:HN - A:UNK1:O	2,23	Hydrogen Bond	H-Donor	H-Acceptor

Table 2. The interactions of *M. pudica* bioactive compounds against *C. albicans* Sap 3 (continued)

Ligand	Name	Distance (Å)	Category	From chemistry	To chemistry
	A:GLY85:HN - A:UNK1:O	2,81	Hydrogen Bond	H-Donor	H-Acceptor
	A:ASP86:HN - A:UNK1:O	2,24	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ASP218:OD2	1,92	Hydrogen Bond	H-Donor	H-Acceptor
Turgorin	A:UNK1:H - A:ASP218:OD2	2,08	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:UNK1:O	2,16	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H1 - A:GLU83:O	2,74	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H2 - A:UNK1:O	1,98	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:O - A:TYR84	3,36	Hydrogen Bond	H-Donor	Pi-Orbitals
	A:TYR84 - A:UNK1	4,68	Hydrophobic	Pi-Orbitals	Pi-Orbitals
	A:ASN9:HD21 - A:UNK1:O	2,1	Hydrogen Bond	H-Donor	H-Acceptor
	A:GLN11:HE22 - A:UNK1:O	2,74	Hydrogen Bond	H-Donor	H-Acceptor
	A:GLN163:HE22 - A:UNK1:O	2,4	Hydrogen Bond	H-Donor	H-Acceptor
	A:ARG312:HH22 - A:UNK1:O	2,47	Hydrogen Bond	H-Donor	H-Acceptor
	A:ARG312:HH22 - A:UNK1:O	2,6	Hydrogen Bond	H-Donor	H-Acceptor
D-Glucuronic Acid	A:UNK1:H - A:GLN11:O	2,94	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ARG162:O	2,61	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ARG162:O	2,23	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:GLN11:O	2,44	Hydrogen Bond	H-Donor	H-Acceptor
	A:ASN9:HD21 - A:UNK1:H	1,61	Unfavorable	H-Donor	H-Donor
	A:ASN9:HD21 - A:UNK1:O	2,11	Hydrogen Bond	H-Donor	H-Acceptor
	A:ASN9:HD21 - A:UNK1:O	2,31	Hydrogen Bond	H-Donor	H-Acceptor
Gallic acid	A:GLN163:HE22 - A:UNK1:O	2,77	Hydrogen Bond	H-Donor	H-Acceptor
	A:ARG312:HH22 - A:UNK1:O	2,47	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ARG162:O	2,33	Hydrogen Bond	H-Donor	H-Acceptor
	A:ARG162:HE - A:UNK1	3,21	Hydrogen Bond	H-Donor	Pi-Orbitals
	A:UNK1 - A:ARG162	4,6	Hydrophobic	Pi-Orbitals	Alkyl
	A:UNK1:H1 - A:ASP218:OD2	3,01	Hydrogen Bond;Electrostatic	H-Donor;Positive	H-Acceptor; Negative
	A:UNK1:H3 - A:ASP218:OD2	2,56	Hydrogen Bond;Electrostatic	H-Donor; Positive	H-Acceptor; Negative
	A:UNK1:N - A:ASP32:OD1	5,09	Electrostatic	Positive	Negative
	A:UNK1:H - A:GLY220:O	2,16	Hydrogen Bond	H-Donor	H-Acceptor
L-Norepinephrine	A:UNK1:H1 - A:THR221:OG1	2,74	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H3 - A:GLY220:O	2,47	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H3 - A:THR221:OG1	2,67	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1 - A:VAL30	5,39	Hydrophobic	Pi-Orbitals	Alkyl
	A:UNK1 - A:ILE123	4,96	Hydrophobic	Pi-Orbitals	Alkyl
	A:UNK1:H1 - A:ASP218:OD2	1,99	Hydrogen Bond;Electrostatic	H-Donor; Positive	H-Acceptor; Negative
	A:UNK1:H2 - A:ASP32:OD2	2,3	Hydrogen Bond;Electrostatic	H-Donor; Positive	H-Acceptor; Negative
	A:UNK1:N - A:ASP32:OD1	3,03	Electrostatic	Positive	Negative
	A:GLY85:HN - A:UNK1:O	2,21	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:O - A:GLY220:O	3,34	Hydrogen Bond	H-Donor	H-Acceptor
Mimosine	A:UNK1:O - A:THR221:OG1	2,8	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:ASP86:OD2	2,66	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H3 - A:GLY34:O	3,03	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H1 - A:ASP32:OD2	2,69	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:GLY220:O	2,24	Hydrogen Bond	H-Donor	H-Acceptor

Table 2. The interactions of *M. pudica* bioactive compounds against *C. albicans* Sap 3 (continued)

Ligand	Name	Distance (Å)	Category	From chemistry	To chemistry
	A:TYR84 - A:UNK1	5,25	Hydrophobic	Pi-Orbitals	Pi-Orbitals
	A:UNK1 - A:VAL30	4,97	Hydrophobic	Pi-Orbitals	Alkyl
	A:UNK1 - A:ILE123	4,93	Hydrophobic	Pi-Orbitals	Alkyl
	A:TYR128:HN - A:UNK1:O	2,97	Hydrogen Bond	H-Donor	H-Acceptor
	A:LEU194:HN - A:UNK1:O	2,25	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H - A:TYR128:O	2,26	Hydrogen Bond	H-Donor	H-Acceptor
L-ascorbic acid	A:GLY127:HA2 - A:UNK1:O	2,54	Hydrogen Bond	H-Donor	H-Acceptor
	A:GLU193:HA - A:UNK1:O	2,24	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:H1 - A:UNK1:O	2,12	Hydrogen Bond	H-Donor	H-Acceptor
	A:ASN192:O - A:UNK1:O	2,69	Unfavorable	H-Acceptor	H-Acceptor
	A:THR222:HN - A:UNK1:O	1,98	Hydrogen Bond	H-Donor	H-Acceptor
	A:ILE223:HN - A:UNK1:O	2,33	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1:O - A:THR222:OG1	3,19	Hydrogen Bond	H-Donor	H-Acceptor
Linolenic acid	A:THR221:HA - A:UNK1:O	2,92	Hydrogen Bond	H-Donor	H-Acceptor
	A:THR222:HB - A:UNK1:O	2,62	Hydrogen Bond	H-Donor	H-Acceptor
	A:UNK1 - A:ILE305	4,89	Hydrophobic	Alkyl	Alkyl
	A:TYR84 - A:UNK1	4,88	Hydrophobic	Pi-Orbitals	Alkyl
	A:TYR84 - A:UNK1:C	5,44	Hydrophobic	Pi-Orbitals	Alkyl
	A:TYR225 - A:UNK1	4,91	Hydrophobic	Pi-Orbitals	Alkyl

Through docking simulations, we looked for whether there was a possibility that D-glucuronic acid ligand has antifungal activity. From the results of the analysis of D-glucuronic acid ligand targeting Sap 3, which showed that nine hydrogen bonds were formed in the receptor-ligand complex, although this ligand had no contact with the catalytic residue or the pocket of the substrate binding site, we predicted this ligand was quite good at inhibiting the *C. albicans* Sap 3.

Liberato *et al.* (2022) through an in vitro study, explained that gallic acid has potential as antifungal activity against *Candida* spp. Another study also reported, through *in vitro* and *in silico* studies by Uma Maheshwari Nallal *et al.* (2021), that gallic acid, which is classified as an active phytochemical compound, is predicted to be an effective inhibitory agent of Sap from *Candida* species. Therefore, even though in this research gallic acid did not interact with the substrate binding site pocket or the catalytic residue of the target receptor, gallic acid was predicted to have a reasonably good interaction in inhibiting Sap 3.

Mimosine had contact with amino acid residues located at S1/S2/S3 and catalytic residues. It was reported that mimosine proved to be more efficient for controlling dermatophyte fungi in a previous study Nguyen dan Tawata (2016). Mimosine also has antimicrobial and antiviral activity (Nguyen dan Tawata 2016).

The number of hydrogen bonds formed is known to determine binding strength in the receptor-ligand complexes. In addition, the efficiency of ligand binding to enzymes is also influenced by the binding energy (Uma Maheshwari Nallal *et al.* 2021; Gholam dan Firdausy 2022). The phytochemicals present in medicinal plants are known to have the potential as antimicrobial and various other biological activities (Selvaraj *et al.* 2022). All analysis data were summarized in Table 2.

We found in this study a type of unfavorable bond. We hypothesized that the presence of such contacts in this study conferred instability in the receptor-ligand complex (Dhorajiwala *et al.* 2019).

Based on the results of the present study, by utilizing the binding energy and interactions formed in the receptor-ligand complex and based on several other analytical parameters, we predict that the bioactive compounds of

Mimosa pudica have a significantly good interaction with Sap 3, when compared with standard ligand. These data were completely structure-based prediction results, therefore further research are needed to strengthen and confirm the results of this study.

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