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In silico analysis of plant phytochemicals against secreted aspartic proteinase enzyme of *Candida albicans*

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ABSTRACT

Candida albicans, a polymorphic fungal species of human microflora, is pathogenic and known to cause immense damage to the host organism which includes biofilm formation, oral and skin infections in immune deficient individuals. Secreted aspartic proteinase (SAP) enzyme plays a major role in promoting virulence to *C. albicans*, and thus could be established as a drug target for *Candida* infections. As a result, inhibiting the enzyme's active center using phytochemicals would reduce the severity of the enzyme's virulence. The present work focuses on the *in silico* analysis of about 15 plant phytochemicals against the SAP enzyme using the AutoDock 4.2.6 software. The docking results were found to be promising with emodin having the highest binding score of −6.44 kCal/mol followed by the isoflavonoid equol with the binding score of −6.29 kCal/mol. Thus, these bioactive compounds could be used as leads for drugs targeting SAP enzymes in treating resistant *Candida* infections.

INTRODUCTION

Candida are group opportunistic pathogenic yeast. *Candida* sp. is found in the diverse ecological niche throughout the earth. Because of their significant adaptive evolutionary biochemical mechanism, they also survive as endophytic fungi in several plants and also in the human gut microflora (Moore *et al*., 2011*)*. On an average, 40%–50% of these species are found in the gut and the oral microflora of a normal human being. These fungal species occur as commensal that depend on the host for shelter and nutrition and does not cause any damage to them and are capable of causing irreversible pathogenic effects in immunocompromised host organism such as candidiasis. The fungal kingdom is often characterized by their biochemical pathways secreted by them (Keller *et al*., 2005). These fungi are often ranked at the top for their ability to cause nosocomial infections (Sydnor and Perl, 2011). More often, these fungi are much known to cause skin infections and oral infections and are capable of forming biofilms that cause severe effects on the host. This biofilm forming ability of the organism is due to the biochemical pathway that involves the secretion of virulence enzyme called secreted aspartic proteinases (SAP). The biofilm formation occurs in the following ways: (1) yeast-forms cells that attach to the substrate, (2) the intermediate step, which involves the formation of microcolonies to produce hyphae and mycelium, (3) the maturation step, which involves the accumulation of extracellular matrix from the organism like proteoglycans, and (4) biofilm formation by colonization of yeast-form cells.

The important factor responsible for virulence caused by microorganism is the secretion of the hydrolytic enzyme. These enzymes play a major role in the pathogenesis (Barth and Gaillardin, 1997). Even though there are several enzymes, the proteinase is the most responsible for virulence factor. The proteinases are protein or peptide bond degrading enzymes and cleave the important proteins. These enzymes catalyze the hydrolysis process, thus breaking the peptide bonds. Proteinases are classified into four categories, based on their mechanism of the catalytic reaction, namely (1) serine proteinase, (2) cysteine proteinase, (3) aspartyl proteinase, and (4) metalloproteinase.

Candida albicans secretes three different hydrolytic enzymes namely secreted aspartyl proteinase, lipases, and

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phospholipase B (Monod *et al*., 1994). The secretion of aspartic proteinases by C. albicans was determined to be one of the virulence determinants for different types of candidiasis. SAPs enable hyphae formation, adhesion, and phenotypic switching; digestion of the host cell membranes and evading host immune responses by degrading and inactivating the central human complement system. Therefore, an agent capable of inhibiting production of *C. albicans* SAPs will be useful in treating *Candida* infections. Diverse *Candida* species apart from *C. albicans* have shown the potential to produce the SAP proteins such as *Candida dubliniensis, Candida tropicalis, and Candida parapsilosis. Candida tropicalis contains four SAP genes, C. parapsilosis* contains two SAP genes, and *C. dubliniensis* possesses nine SAP genes in their genome (De Viragh *et al*., 1993; Gilfillan *et al*., 1998; Naglik *et al*., 2003). *Candida albicans* secretes an extracellular proteolytic enzyme called SAP. The SAP is the constitution of 10 enzymes ranging from SAP1 to SAP10 (Borelli *et al*., 2008). Each of these enzymes possesses the virulence activity. The SAPs are used to degrade foreign tissue and evade the host defence mechanism (Lan *et al*., 2004). Strains of *C. albicans* with deleted SAP1, SAP2, and SAP3 are less virulent and caused little damage to the *in vitro* model (Schaller *et al*., 1999).

The SAP5 enzyme of the SAP family is more prone to cause virulence. SAP enzyme performs the role of digesting molecules in order for the acquisition of nutrients, disrupting the host cell membrane for invasion and tissue damage, and attack the immune system in order to escape the antimicrobial attack from the host organism (Zaugg *et al*., 2011). The current study was aimed to study the drug-likeness and molecular docking of natural plant phytochemicals against the active site of *C. albicans* SAP enzyme by *in silico* approach. This work would be an initiative for developing plant phytochemicals as leads for *C. albicans* treatment.

The active center of the virulent enzyme SAP can be inhibited by natural plant phytochemicals. The phytochemicals are plant's secondary metabolites that are not directly involved in the growth and development of the plant but instead they have several medicinal properties such as antimicrobial, anticancer, antitoxic, and anti-diabetic properties (Raut and Karuppayil, 2016). Plant phytochemicals act as a potential inhibitor for inhibiting the active site of the enzyme by competing with the substrate, thereby neutralizing the effects of the virulence responsible enzyme. Several plant extracts such as methanol in hydroalcoholic and ethyl acetate-methanol leaf extracts from the plant *Schinus terebinthifolius* have shown the potential to inhibit *Candida* biofilm formation. Thin layer chromatography analysis revealed the presence of alkaloids, terpenoids, phenols, and anthraquinones (Alves *et al*., 2013). Ethyl-acetate and methanol extracts of stem bark from *Croton urucurana* have shown to inhibit *C. albicans* biofilm formation. Similarly, ethyl-acetate extracts of flower buds from *Syzygium aromaticum* are good potential inhibitors of *Candida* biofilms . In addition to the crude extracts, plant phytochemicals such as terpenoids, alkaloids, and flavonoids have been reported to show good *C. albicans* biofilm inhibitory activity (Raut and Karuppayil, 2016). The phytochemical baicalein inhibited about 70% of *C. albicans* biofilm on prosthetic surfaces (Cao *et al*., 2008). The phytochemicals such as curcumin, sesquiterpenes, and purpurin have shown good *Candida* biofim inhibition in various studies (Shahzad *et al*., 2014; Tsang *et al*., 2012; Xie *et al*., 2015)

Lipinski's rule of five is used to assess the drug likeliness and durability of a phytochemical or chemical compound (Benet *et al*., 2016). This rule gives the description about the molecular properties that are essential for the pharmacokinetic property of a drug (Lipinski *et al*., 2012). Therefore, Lipinski's rule of five is essential for a phytochemical to be used as an oral drug. Phytochemicals that satisfy the Lipinski's rule are subjected to docking studies.

MATERIALS AND METHODS

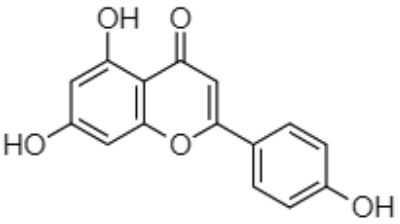
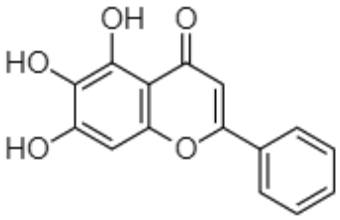
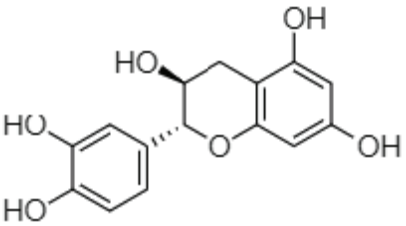
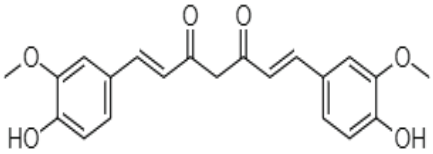
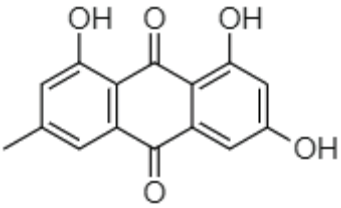
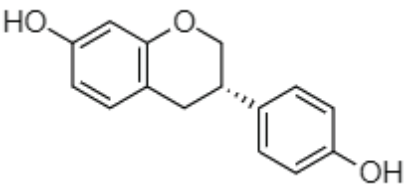
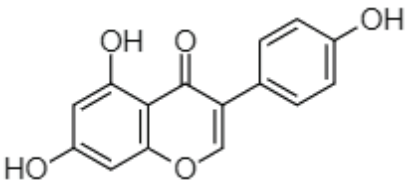
Bioactive compounds from plant secondary metabolites

The following are the plant phytochemicals obtained from the various PubMed Literatures: (1) apigenin, (2) baicalein, (3) cianidanol, (4) curcumin, (5) emodin, (6) equol, (7) genistein, (8) gingerol, (9) kaempferol, (10) myricetin, (11) pachypodol, (12) quercetin, (13) resveratrol, (14) silymarin, and (15) taxifolin. These phytochemicals have shown anti-*Candidal* activity cited in PubMed Literatures, and thus were selected to study the mode of interations of these compounds with the active site of *C. albicans* SAP5 enzyme. The information about the above-mentioned phytochemicals such as structure, molecular formula, and chemical formula were retrieved from the PubChem database is tabulated in Table 1. Lipinski's rule of five parameters such as molecular weight, log P, number of hydrogen bond donors, number of hydrogen bond acceptors, and molar refractivity were taken from the PubChem database for the above-mentioned phytochemicals. Table 2 represents the information about Lipinski's rule of various phytochemicals.

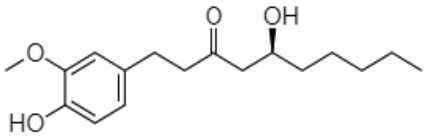
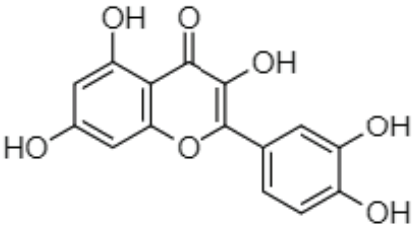
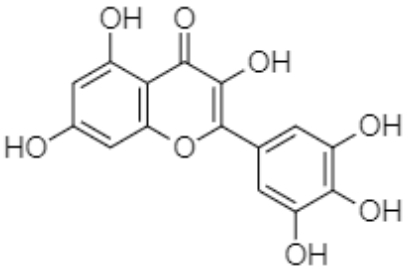
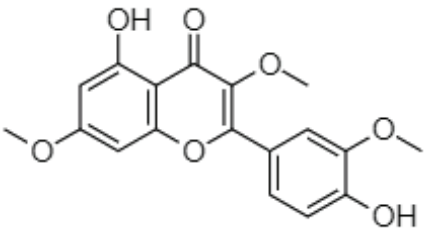
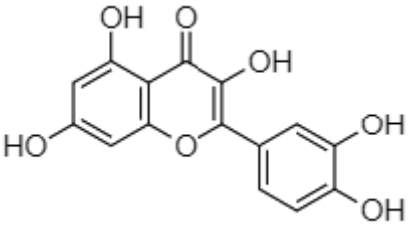
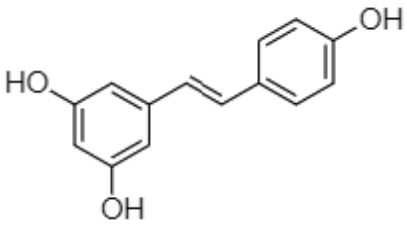
SAP5 protein structure

The three-dimensional protein structure of SAP5 was retrieved from the protein data bank (PDB) protein database. The obtained 3D structure is depicted in Figure 1. The PDB is a world renowned online open access database that provides the user about the structure, functions, and properties of various macromolecules like nucleic acids (Berman *et al*., 2002). The PDB ID of the SAP5 protein is 2QZX. The water molecules were removed from the protein macromolecule for effective ligand binding. SAP5 is one of the 10 acidic hydrolases that possesses a molecular weight of 37 KDa and is active at a pH of 3.0–7.0 (Aoki *et al*., 2011; Borg-von Zepelin *et al*., 1998;). The protein consists of two chains namely A and B. (Fig. 1). Each of this chain consists of 342 amino acid residues. It is considered as one of the key virulence factors that affect the host (Schaller *et al*., 2000). This enzyme provides the fungus with nutrients and is capable of destroying the host's defense attack. The enzyme is prime responsible for skin infections such as cutaneous candidiosis in human models (Korting *et al*., 1998). This enzyme performs the key role of penetrating into the tissue during infection in immunocompromised individuals. This enzyme acts attack against the hemoglobin through proteolysis and produces several diverse varieties of antimicrobial hemocidins to fight against diverse variety of microorganisms of the same physiological niche (Schaller *et al*., 2001). The ligand pepstatin A is the most potent inhibitor of the aspartyl proteinases (Cadicamo *et al*., 2013; Koelsch *et al*., 2000). This ligand shows a very high binding efficiency with the SAP5. A set of strong hydrogen bonds in the SAP5 involves aspartic residues Asp32 and

Table 1. Details of plant phytochemicals.

S. No	Compound	IUPAC name	Structure	Chemical formula
1	Apigenin	5,7-dihydroxy-2-(4-hydroxyphenyl)chromen-4-one		$C_{15}H_{10}O_5$
2	Baicalein	5,6,7-trihydroxy-2-phenylchrom-4-one		$C_{15}H_{10}O_5$
3	Cianidanol	(2R, 3S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol		$C_{15}H_{14}O_6$
4	Curcumin	(1E, 6E)-1,7bis(4-hydroxy 3-methoxyphenyl) hepta-1,6-diene-3,5-dione		$C_{21}H_{20}O_6$
5	Emodin	1,3,8-trihydroxy-6-methylanthracene -9,10-dione		$C_{15}H_{10}O_5$
6	Equol	3-(4-hydroxyphenyl)-3,4-dihydro-2H-chromen-7-ol		$C_{15}H_{14}O_3$
7	Genistein	5,7-dihydroxy-3-(4-hydroxyphenyl)chromen-4-one		$C_{15}H_{10}O_5$

(Continued)

8	Gingerol	(5S)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decan-3-one		$C_{17}H_{26}O_4$
9	Kaempferol	3,5,7-trihydroxy-2-(4-hydroxyphenyl) chromen-4-one		$C_{15}H_{10}O_6$
10	Myricetin	3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl) chromen-4-one		$C_{15}H_{10}O_8$
11	Pachypodol	5-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-3,7-dimethoxychromen-4-one		C18H16O7
12	Quercetin	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one		$C_{15}H_{10}O_7$
13	Resveratrol	5-[(E)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol		$C_{14}H_{12}O_3$

(Continued)

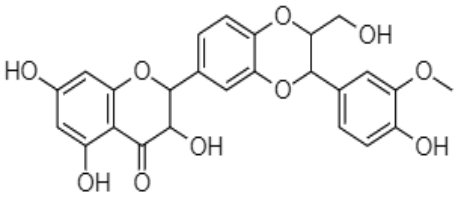
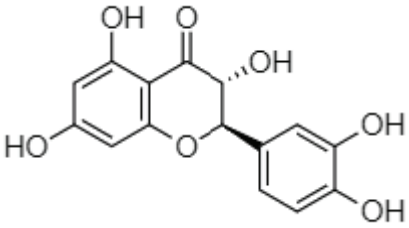
14	Silymarin	3,5,7-trihydroxy-2-[3-(4-hydroxy-3-methoxyphenyl)-2-(hydroxymethyl)-2,3-dihydro-1,4-benzodioxin-6-yl]-2,3-dihydrochromen-4-one		$C_{25}H_{22}O_{10}$
15	Taxifolin	(2R,3R)-2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-2,3-dihydrochromen-4-one		$C_{15}H_{12}O_7$

Table 2. Lipinski properties of diverse plant phytochemicals.

S. no	Phytochemical active compounds	Molecular weight (<500 Da)	Log P (<5)	H-bond donor (<5)	H-bond acceptor (<10)	Molar refractivity (<130)
1	Apigenin	270.24	2.42	3	5	70.81
2	Baicalein	270.24	2.42	3	5	70.81
3	Cianidanol	290.27	1.54	5	6	72.62
4	Curcumin	368.38	3.37	2	6	102.01
5	Emodin	270.24	1.88	3	5	69.48
6	Equol	242.27	2.81	2	3	68.15
7	Genistein	270.24	2.11	3	5	71.00
8	Gingerol	294.39	3.23	2	4	82.75
9	Kaempferol	286.24	2.30	4	6	72.38
10	Myricetin	318.23	1.71	6	8	75.71
11	Pachypodol	344.32	2.70	2	7	88.20
12	Quercetin	302.34	2.01	5	7	74.05
13	Resvaratrol	228.24	2.97	3	3	66.80
14	Silymarin	482.44	2.36	5	10	119.45
15	Taxifolin	304.25	1.18	5	7	73.24

Asp218 along with the residues Gly34, Gly85, Asp86, Gly220, and Thr222. These catalytic aspartic residues are highly conserved. The inhibitor binding at residues 83 and 221 are mainly taking part in the hydrogen bonding, thereby forming a network of interactions. The active site region of SAP5 enzyme in complex with inhibitors isovaleric acid and statine retrieved from PDBsum (Fig. 2).

Docking studies using AutoDock 4.2.6

Docking studies were performed using the phytochemical active compounds mentioned in Table 1 against the enzyme SAP5 using an automated bioinformatics docking tool-AutoDock 4.2.6. AutoDock 4.2.6 is one of most used software by the scientific community to study protein-ligand interactions. The AutoDock 4.2.6 software is based on the principle of Lamarckian genetic algorithm (Meenambiga *et al*., 2015). The docking interactions between the ligand and the target receptor leading to structure-based drug designing and developmental process are performed using this software. The AutoDock 4.2.6 constitutes two methodologies namely Rapid grid-based energy evaluation and effective search of torsional freedom to accomplish the drug development process (Meenambiga *et al*., 2015).

Discovery Studio Visualizer 3.1

Discovery Studio Visualizer 3.1, developed and distributed by Accelrys, is a free software used for visualizing the macromolecule-ligand interactions. This software is used to study the simulation of small molecules and large macromolecules. The main scope of this software includes structure-based design, simulations, ligand design, macromolecule engineering, macromolecule design and validation (tools for antibody design

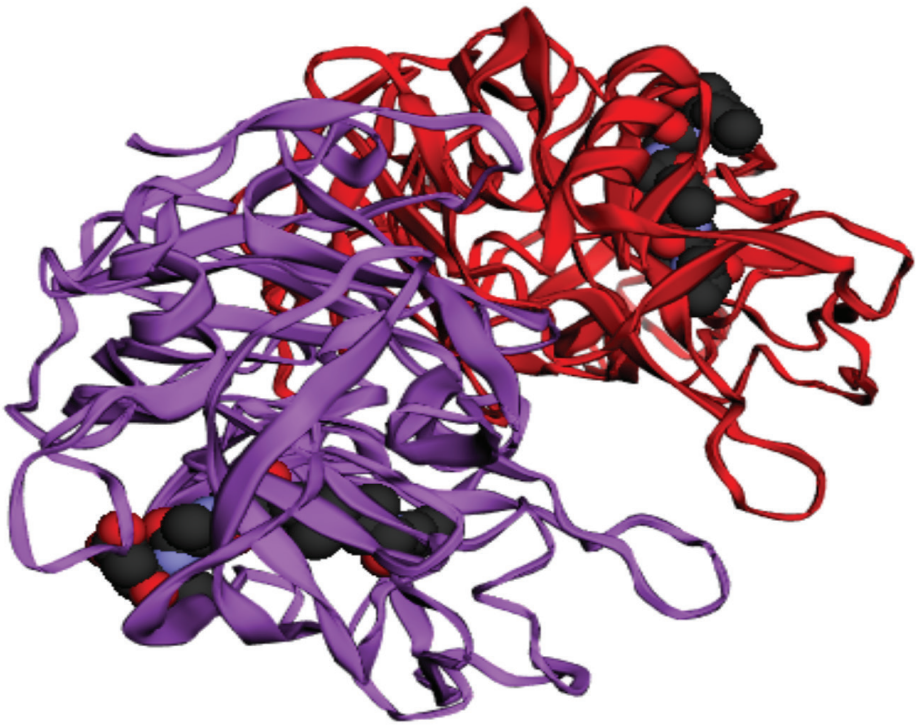


Figure 1. Secreted aspartic proteinase 5 (SAP5). PDB Id: 2QZX with chains A and B in complex with a selective inhibitor.

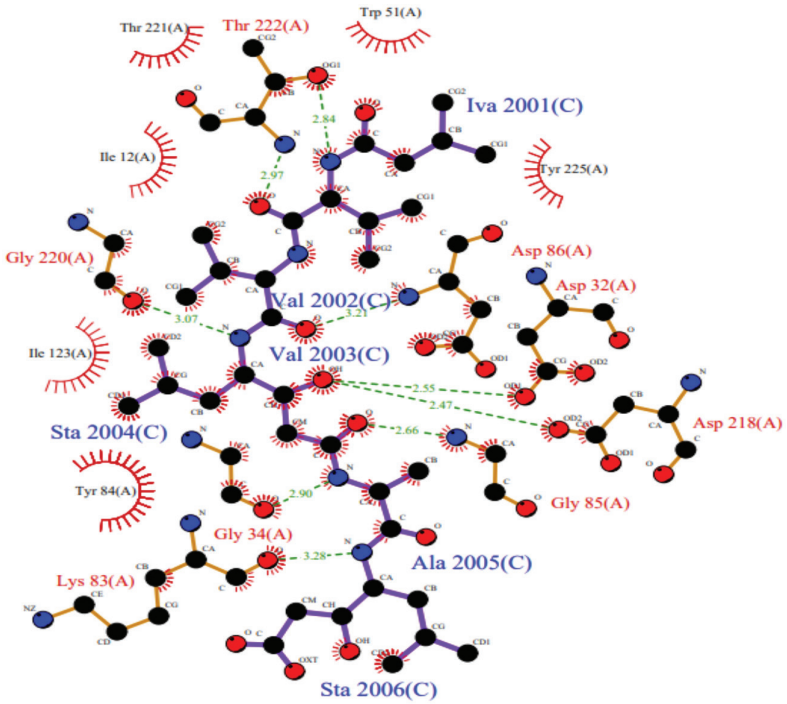


Figure 2. SAP5 in complex with selective inhibitors Isovaleric acid (IVA) and Statine (Sta) showing the active site region.

& optimization, protein-protein docking), and pharmacophore modeling (Almagro *et al*., 2011; Corradi *et al*., 2011; Luu *et al*., 2011; Sutter *et al*., 2011). It generates 2D and 3D structures to visualize and analyze the ligand-protein interaction patterns between them.

RESULT AND DISCUSSION

Globally, about more than 7.5 million people are affected by invasive Candidiasis with approximately 40% mortality rate. The undesirable side effects, the ineffectiveness and rapid development of resistance by the fungi have exacerbated the need

for new antifungals (Carmona and Limper, 2017). Plant phenolic compounds possess antifungal properties against *C. albicans* but the knowledge on their mechanism of action is still under scarce (Teodoro *et al*., 2015a; 2015b). The SAPs are used to degrade foreign tissue and evade the host defense mechanism (Lan *et al*., 2004). Strains of *C. albicans* with deleted SAP1, SAP2, and SAP3 are less virulent and caused little damage to the *in vitro* model (Schaller *et al*., 1999). 7-hydroxycalamenene and hydroxylated sesquiterpene isolated from *Croton cajucara were shown to inhibit SAP (*Azevedo *et al*., 2016). The ethanol extract of *Lycopodium cernuum* contained triterpene compounds and showed inhibitory effects against *C. albicans* secreted aspartic proteases (Zhang *et al*., 2002).

In silico analysis of plant compounds was analyzed using Lipinski's rule of five followed by molecular docking studies. All the compounds taken for this study satisfied Lipinski's rule of five and tabulated in Table 2. The binding energy obtained for each ligand, hydrogen bond contacts, and other interactions were tabulated in Table 3. The anthraquinone compound emodin has the highest binding energy with the active site region of SAP5 and the docked confirmation is given in Figure 3. Emodin forms hydrogen bonds with Asp 32, Thr 221, and Thr 222 at the active site region of SAP5 enzyme (Fig. 4). The inhibitory property of emodin on biofilm formation and hyphae development of *C. albicans* was studied by Janeczko *et al*. (2017). The binding efficiency of equol with the active site of SAP5 enzyme was found to be good with a strong *pi* it should be italics bond interaction and this compound was proved to have fungicidal activity against *C. albicans* (Lee and Chee, 2010) (Fig. 5). Thus, based on the molecular interactions analyzed, a lead to develop a drug that specifically inhibits the SAP enzyme pathway of *C. albicans* was studied.

The flavonoid compounds pachypodol, baicalein, and apigenin have found to be more potent as SAP5 inhibitors through comparative analysis in this docking experiment (Figs. 6 and 7).

Table 3. Molecular docking analysis of plant phytochemicals against *Candida albicans* SAP5 enzyme**.**

No.	Compound name	Binding energy (kCal/mol)	Vanderwaal's interacting residues	No. of H bonds	H bond interaction residues	No. of direct contacts (all polar, non-polar interactions)
1.	APIGENIN	−5.62	SER 35, ASP 32, ASP 218, ASP 86, TYR 84, GLY 220, ILE 12, THR 222. THR 221, GLY 85	3	GLY 34, ILE 223, TYR 225	13
2.	BAICALEIN	−5.92	ILE 223, TYR 225, THR 221, GLY 85, ILE 305, TYR 84, SER 35, ILE 123, GLY 220, ASP 218, ASP 86, THR 222	2	ASP 32, GLY 34	14
3.	CATECHINS	−5.35	GLY 34, SER 35, ILE 123, TYR 84, ILE 30, ARG 120, ASP 86, THR 13, THR 221, LEU 216, ILE 305, GLY 85	5	ILE 12, THR 222, ASP 218, ASP 32, GLY 220	17
4.	CURCUMIN	−5.84	GLY 34, SER 35, ILE 123, TYR 84, ILE 223, GLY 220, THR 222, THR 221, TYR 225, ILE 305, ASP 86, ARG 120, ILE 12, ASP 308, GLY 85, ILE 30, ASP 218	2	THR 222, TYR 225	19
5.	EMODIN	−6.35	GLY 85, ASP 218, ILE 305, ILE 12, ARG 120, THR 13, ILE 30, ASP 86, ILE 123, GLY 220, TYR 84, SER 35, GLY 34	3	THR 222, THR 221, ASP 32	16
6.	EQUOL	−6.29	SER 35, ILE 30, THR 222, ASP 86, GLY 220, THR 221, GLY 85, TYR 84, ILE 123	3	ILE 223, TYR 225, ASP 32	12
7.	GENISTEIN	−3.44	THR 222, ILE 12, GLY 85, TYR 84, SER 35, GLY 34, ASP 218, THR 221, ASP 86	2	ILE 223, GLY 220	13
8.	GINGEROL	−4.17	ASP 218, THR 221, ILE 123, ILE 30, ASP 86, THR 222, TYR 84, ARG 120, SER 35, GLY 34, GLY 85	3	GLY 220, ILE 12, THR 13	14
9.	KAEMPFEROL	−5.40	ILE 223, TYR 225, ILE 305, ASP 218, ASP 32, TYR 84, SER 35, GLY 85, GLY 220, ASP 86, THR 13, ILE 30, ARG 120, ILE 12	3	THR 222, THR 221, GLY 34	17
10.	MYRICETIN	−5.86	TYR 225, ILE 305, SER 35, TYR 84, ASP 218, GLY 85, GLY 220, ASP 86, ILE 30, THR 13, ARG 120, ILE 12	4	THR 222, THR 221, GLY 34, ASP 32	16
11.	PACHYPODOL	−6.12	TYR 225, THR 222, THR 221, GLY 220, ASP 86, ASP 218, LEU 216, SER 35, ASP 32, GLY 85, ILE 123, TYR 84, ILE 12, ILE 223	1	THR 222, THR 221	15
12.	QUERCITIN	−5.57	ILE 305, TYR 225, ILE 223, ILE 12, ARG 120, THR 13, ILE 30, GLY 220, ASP 86, THR 221, TYR 84, ASP 218, GLY 34, GLY 85	2	GLY 85, THR 222	16
13.	RESVERATOL	−5.61	THR 221, GLY 220, ASP 32, TYR 84, SER 35, GLY 85, ASP 218, ASP 86, THR 222, ILE 12	3	ILE 223, TYR 225, GLY 34	13
14.	SILIMARIN	2.04	ILE 30, ALA 119, TRP 39, ILE 123, TYR 84, GLY 85, SER 35, LEU 216, ASP 218, ILE 305, TYR 225, THR 221, ASP 32, GLY 220, THR 222, ILE 12, THR 13	3	LYS 121, GLY 34, ARG 120	20
15.	TAXIFOLIN	−5.57	ILE 223, THR 221, ILE 123, ILE 30, SER 35, GLY 34, TYR 84, LEU 216, GLY 86, ASP 86, GLY 220, TRP 51, ILE 12	2	ASP 32, THR 222	15

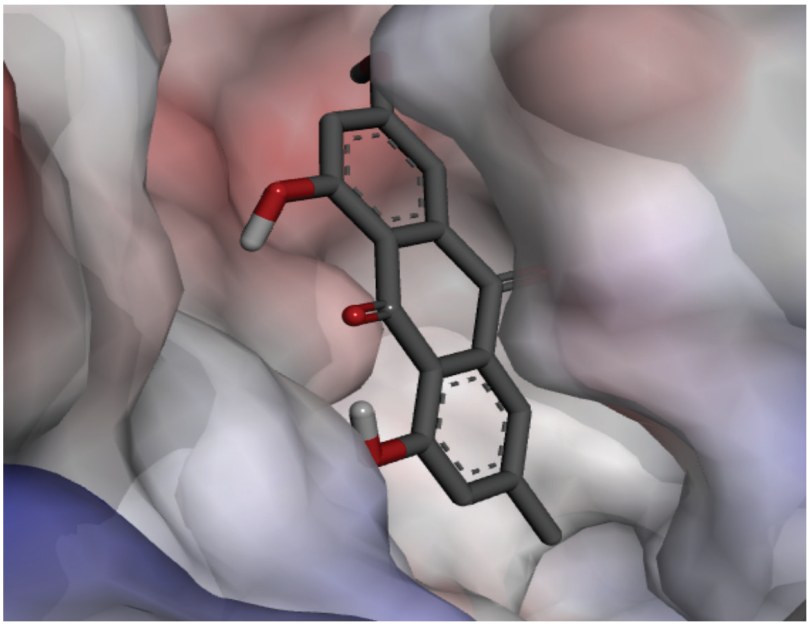


Figure 3. Docked confirmation of the compound emodin with SAP5.

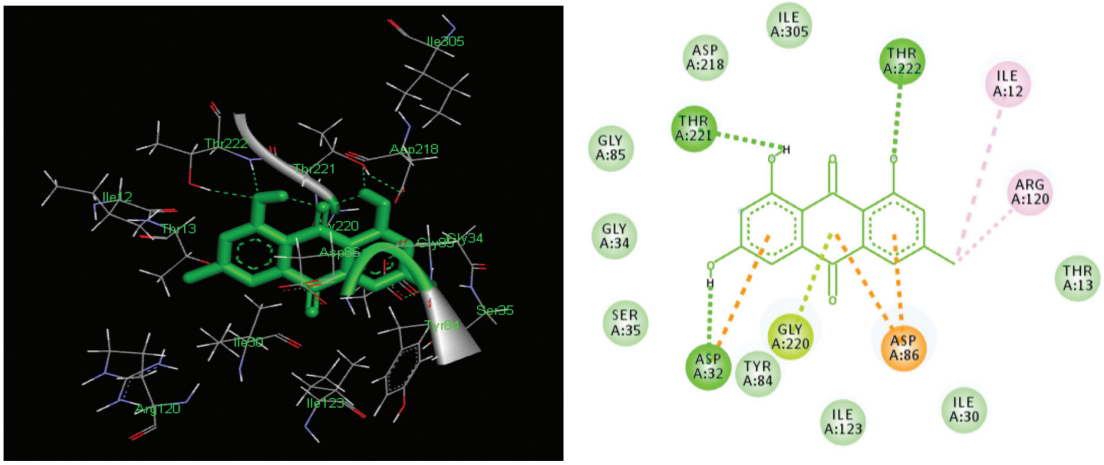


Figure 4. 3D and 2D residual interaction maps of the compound emodin with the active site region of SAP5 enzyme (PDB Id: 2QZX).

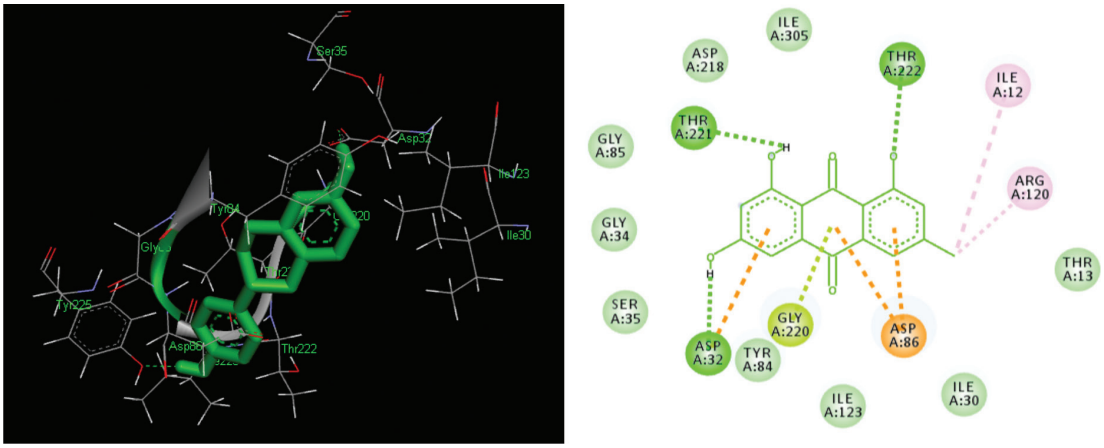


Figure 5. 3D and 2D residual interaction maps of the compound equol with the active site region of SAP5 enzyme (PDB Id: 2QZX).

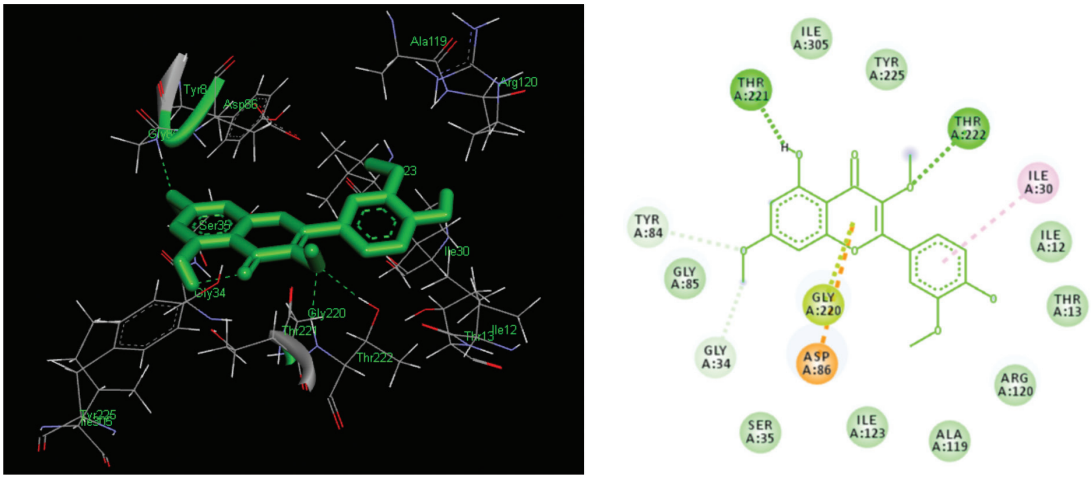


Figure 6. 3D and 2D residual interaction maps of the compound pachypodol with the active site region of SAP5 enzyme (PDB Id: 2QZX).

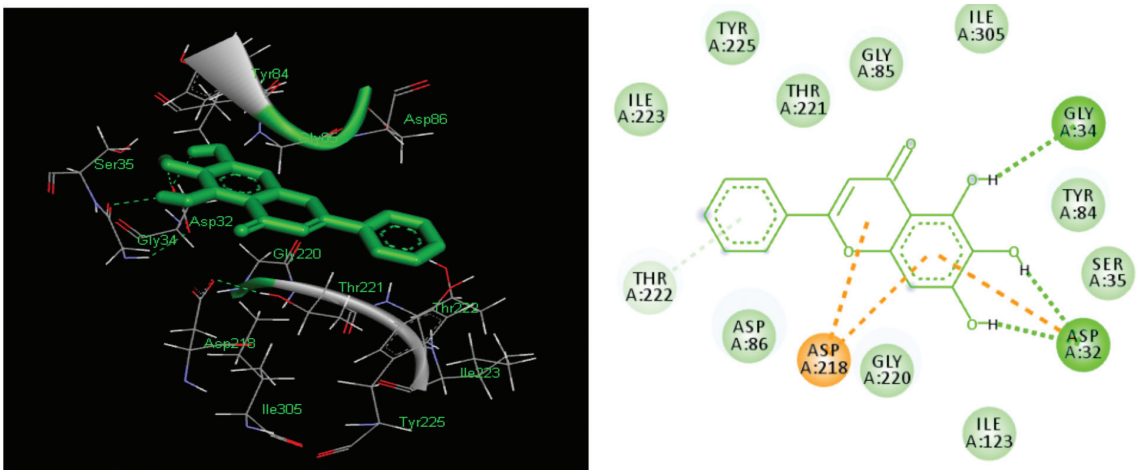


Figure 7. 3D and 2D residual interaction maps of the compound baicalein with the active site region of SAP5 enzyme (PDB Id: 2QZX).

These compounds bind in the active site pocket of SAP5 which is similar to that of the binding of selective inhibitors as shown in Figure 2 (Citoglu *et al*., 2003; Martins *et al*., 2008). Docking studies of curcumin with SAP enzyme of *C. albicans* provides us with a knowledge of exact molecular interactions for designing novel curcumin analogues for *Candida* treatment. Apigenin, a natural flavone has a very good anti-carcinogenic properties and also have proven to inhibit *C. albicans* cell shrinkage, ultimately reducing the biofilm mass (Lee *et al*., 2018). *In vitro* analysis of flavonoids such as apigenin and kaempferol showed the reduced adherence of *C. albicans* toward the human epithelial cells (Yordanov *et al*., 2008). Flavonoids present in the extract of endophytic fungi have also been studied for their inhibitory activity against N-myristoyltransferase enzyme of *C. albicans* through molecular docking analysis (Meenambiga and Rajagopal, 2018). Polyphenols such as taxifolin inhibit the transcriptional factors responsible for transcription of DNA to mRNA. The transcriptional factors that provoke the virulence through hyphal growth are found to be as Tec1 and Rfg1. The Tec1 and Rfg1 pathways are inhibited by taxifolin (Mishra *et al*., 2017). Taxifolin also inhibits the SAP proteins. Flavonoids heterosides such as quercetin and kaempferol extracts from *Equisetum giganteum* constitute to the inhibition of oral *Candida* biofilm (Raut *et al*., 2016). Thus, these phytochemicals have the potential to inhibit the active site of the SAP5 protein leading to the inhibition of biofilm formation.

CONCLUSION

The development of natural compounds with biological activity is needed for the treatment of resistant infections. *Candida albicans* is one such organism with increased virulence and resistance. In the present study, docking results revealed the binding of plant phytochemicals with the secreted aspartic proteinase (SAP) enzyme of *C. albicans*. Among those compounds, "emodin" and "equol" have good binding energies greater than −6.4 kCal/mol at the active site region of SAP enzyme and all the phytochemicals satisfy Lipinski's rule which forms the basis for the compound to be used as an oral drug. On the whole, it is concluded that the plant phytochemicals especially flavonoids could be potent drugs for treating *Candida* infections through SAP enzyme inhibition and this could be further used for research as a pharmacophore for the development of SAP enzyme inhibitors.

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CONFLICTS OF INTEREST

The authors declare that they do not have any conflicts of interest.

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