

Molecular docking prediction on antibacterial potential of *Corbichonia decumbens* against TSST-1OF *Staphylococcus aureus* through *In Silico* techniques.

Sankaravel Velmani¹, Sreeram Sudhir², Vino Udappusamy³ and Arunprasath Arumugam^{1*},

¹Assistant Professors, Department of Botany,

²Research Scholar, Department of Botany,

PSG College of Arts & Science, Coimbatore – 641 014, Tamil Nadu, India.

³Research Assistant, Department of Biotechnology,

PSGR Krishnammal College for Women, Coimbatore – 641 014, Tamil Nadu, India.

*Corresponding author's : Arunprasath Arumugam

Abstract

Medicinal plants have long served as a reservoir for secondary metabolites, offering cures for various human ailments since ancient times. One significant target for these treatments is Toxic Shock Syndrome Toxin-1 (TSST-1) from *Staphylococcus aureus*, a key agent in toxic shock syndrome that causes inflammation. This study focused on isolating chemical compounds from *Corbichonia decumbens* and identifying potential drug molecules through docking analysis and molecular dynamics against TSST-1. The protein structure of TSST-1 was retrieved from the PDB database, and several compounds from *Corbichonia decumbens* were analyzed. Adhering to Lipinski's rule of five, the biological activity of these compounds was assessed using the PASS online tool, evaluating their probability of being active (Pa) and inactive (Pi). Among the compounds, 2,4-Dichloro-5H-pyrrolo[3,2-d]pyrimidine exhibited the highest binding energy of -5.41 Kcal/mol in molecular docking studies, forming hydrogen bonds with active sites of the protein. Furthermore, 1-Methyl-3,5-dinitro-1,2,4-triazole showed significant inhibiting activity, comparable to control compounds. These findings suggest that the identified bioactive compounds have potential as efficient drug molecules. Future research should focus on determining the stability of these protein-compound interactions through further docking studies and exploring additional bioactive compounds to discover potent therapeutic agents. Molecular docking continues to identify promising compounds, indicating a hopeful future for new solutions in critical areas of human health.

Keywords: *Staphylococcus aureus*, *Corbichonia decumbens*, Lipinski Rule, Pass online, Inflammation and Molecular docking.

Introduction

Plants have contributed a lot of medicinal compounds being used today to treat diseases such as cancer, hormonal imbalances, jaundice, diabetes, inflammation, etc. Plants are commonly available in abundance, especially in the tropics [1]. Plant leaves have been used as an herbal medicine for their healing properties since ancient times. Some bioactive compounds within these plants are responsible for their medicinal value. The most prominent of these bioactive compounds are alkaloids, tannin, flavonoid, and phenolic compounds [2]. There is the considerable potential of raw plant material for a higher exposure to bioactive phytochemicals such as glucosinolates and their hydrolysis products like flavonoids, and Vitamin C [3]. The plant family, lophiocarpaceae is comprised of two genera with approximately 25 species. These plants are commonly known as stone plants or carpet weeds. *Corbichonia decumbens* is a creeping, well-branched, diffuse-ascending, and prostrate to the procumbent, semi-succulent, and annual herb of Tamil Nadu [4].

Bacterial superantigens (SAGs) comprise a large family of disease-associated proteins that are produced primarily by *Staphylococcus aureus* and *Streptococcus pyogenes*. Toxic shock syndrome toxin1 (TSST-1), an exotoxin secreted by *S. aureus*, was identified as a major causative agent of TSS some 25 years ago [5]. A major causative agent of TSS is toxic shock syndrome toxin1 (TSST-1), which is unique relative to other bacterial SAGs owing to its structural divergence and its stringent TCR specificity. Here, we report the crystal structure of TSST-1 in complex with an affinity matured variant of its wild type TCR ligand, human T cell receptor β chain variable domain [6]. Toxic shock syndrome (TSS) is a rare but severe disease characterized by fever, hypotension, a skin rash with subsequent desquamation, and multiple organ dysfunctions [7]. It can occur in healthy menstruating women using intravaginal protection, such as tampons or menstrual cups, and colonized by *Staphylococcus aureus* producing toxic shock syndrome toxin 1 (TSST-1) [8].

To analyze structures of proteins of a particular class, these need to be extracted from Protein Data Bank (PDB) files. In the case of antibodies, there are several special considerations: (i) identifying antibodies in the PDB is not trivial, (ii) they may be crystallized with or without antigen, (iii) for analysis purposes, one is normally only interested in the Fv region of the antibody, (iv) structural analysis of epitopes, in particular, requires individual antibody-antigen complexes from a PDB file which may contain multiple copies of the same, or different, antibodies and (v) standard numbering schemes should be

applied (1). Organic compounds with low molecular weights (usually less than 1,000 Da) are commonly categorized as small molecules. Small molecules are major targets for drug and biomarker discoveries. Over the last decade of drug discovery, a reduced level of productivity (defined as new drugs developed per research and development dollars spent) has been consistently lamented, most notably by the US Food and Drug Administration (2004) [9]. The various sources of compound attrition throughout the discovery and development process have been extensively outlined and discussed and significant efforts within the industry to reduce the widely ranging causes of attrition continued. The Rule of 5 methodologies appears to be as useful today in defining drugability as when it was proposed but recognizing that the database that we used includes only drugs that successfully reached the market. In DrugBank, the result of the analysis based on Lipinski's rule of five is studied using the prediction software ChemAxon and the value found in the predicted properties table will be presented as "Yes" or "No" depending on if the molecule follows or no at least 3 conditions of the rule of five [10].

Molecular docking is one of such frequently used methods in structure-based drug designing because of its ability to predict with a high level of accuracy, the conformation of small-molecule ligands within the appropriate target binding site. Thus, it can be employed to study the interaction between phytochemicals. Molecular docking works in a two-step process which starts with compiling different ligand conformations in the identified active site of the receptor and then ranking them according to their binding conformation energies for each binding conformation [11]. Various commercially available software like Auto Dock, Argus Lab, FLEX, and GOLD are extensively used for estimating docking binding energies of various ligand-receptor conformations [12]. The identification of the most appropriate binding conformations is carried out by exploring the large conformational space depicting various binding sites and then accurately predicting the interaction energy associated with the respective binding conformations [13 & 14]. This process is carried out recursively until converging to a solution of minimum energy.

Materials and Methods

The 3D protein structure for Toxic shock syndrome toxin-1 (TSST-1) of *staphylococcus aureus* is recovered from the Protein Data Bank database (PDB ID: 2IJ0). Dynamic web page region was anticipated utilizing LigSite online apparatus. The concoction mixes from the referenced plants are recovered from the PubChem database. The PASS ONLINE predicts 4130 types of biological activities, for which the difference between

probabilities will be active (P_a) and probabilities will be inactive (P_i) was calculated. The P_a - P_i values for activities randomly selected from the total list of predicted biological activities will be used as independent regression variables are perused.

Lipinski's rule of 5 helps in distinguishing between drug-like and non-drug-like molecules. It predicts a high probability of success or failure due to drug-likeness for molecules complying with 2 or more of the following rules [15]. Molecular mass less than 500 Dalton

- High lipophilicity (expressed as LogP less than 5)
- Less than 5 hydrogen bond donors
- Less than 10 hydrogen bond acceptors
- Molar refractivity must between 40-130

MGL tools with AutoGrid4 and AutoDock4 [16] will be used to set up and to perform blind docking calculations between the Ligands and Protein. A crystallized 3-dimensional structure was obtained from the Protein Data Bank (PDB). Receptor (protein) and ligand (complex) files were prepared using Auto Dock Tools. The protein was enclosed in a box with grid points in x, y, and z directions and a grid spacing of 0.375 Å. The center of the grid is set to -6.516, 30.278, and -1.951 Å. Lamarckian genetic algorithms, as implemented in Auto Dock, were employed to perform docking calculations. All other guidelines are default settings. For every individual docking case, the lowest energy docked confirmation, according to the Auto Dock scoring function and the number of hydrogen bonds was selected as the binding mode. The output from Auto Dock was rendered with PyMol [17].

PyMOL is one of a few open-source visualization tools which are used in structural biology. A part of the software's name refers to the fact that it extends, and is extensible by the Python programming language. All the bindings are visualized by using the Structure Visualising tool Pymol viewer, the interaction between the chemical compounds and target protein.

Results

The 3D structure of a protein Toxic shock syndrome toxin-1 (TSST-1) was recovered from the Protein Data Bank (PDB) and the information was mentioned (Table 1). It was visualized by utilizing the visualizing tool pymol. The three-dimensional structure of the protein was distinguished utilizing the Ligsite online device. The 3D structures of the phytochemical compounds of the plants chosen in the current investigation were retrieved

from the PubChem Chemical database. The compounds which are segregated and revealed from the earlier mentioned plant were organized (Table 2) along with their molecular weight, molecular formula, and PubChem ID, where PubChem is the database for getting small molecules. The biological activity of those compounds was broken down utilizing the pass online device which predicts the pharmacological and biochemical properties. The estimation of Probability to be dynamic Pass activity and inactivity. The properties anticipated for each plant compound were recorded (Table 3).

The compounds were first oppressed for dissecting Absorption, Distribution, Metabolism, and Excretion properties. Earlier ADME profiling of little atoms is noteworthy committed to the field of medication revelation by having sway on cost, work request, and length [18]. Computational estimation of the docked phytochemical's medication likeliness was found based on limits set by "Lipinski's Rule of Five" through Drug examine apparatus at Molinspiration server. The subjective appraisals of ingestion, statement, digestion, discharge, and poisonousness profile of these hits were anticipated basically by utilizing ADMET SAR worker [19]. In the current investigation, Lipinski's standard of five in any case called Pfizer's standard of five or general guideline to assess tranquilize similarity shows the accompanying properties like atomic weight, octanol/water parcel coefficient, hydrogen bond giver, and acceptor. After the filtration involving Lipinski rule 5 out of 10 bioactive compounds from *C. decumbens*. Since the standard has a cutoff point in products of five, the name has been given as a rule of five. Aside from the above properties, extra boundaries, such as surface territory in square Armstrong (polar surface region, PSA); cerebrum/blood hindrance, and level of human oral assimilation have additionally anticipated The result of the analysis based on Lipinski's rule of five is studied and the predicted properties were presented depending if the molecule follows or no at least 3 conditions of the rule of five (Table 4).

Molecular Docking Study

The results of docking studies on 6 compounds including 1 control compound for the comparison of the effectiveness of the retrieved compounds were recorded (Table 5). The compound 1-Methyl-3,5-dinitro-1,2,4-triazole / 542691 had Bindin energy of -5.41 Kcal/mol and formed 4 hydrogen bonds with the residue THR 78 O-H showing the bond length of 1.9 Å & 2.0 Å and residue LYS 20 O-H showing the bond length of 2.3 Å & 2.0 Å. The compound Quinoline/7047 had Binding energy of -4.93 Kcal/mol and formed hydrogen bonds with the residue LYS 20 H-O showing the bond length of 2.0 Å. The compound

[(2R,3S,4R)-5-(2,6-Dioxo-3H-purin-9-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate /122282 had Binding energy of -4.57 Kcal/mol and formed hydrogen bonds with the residue LYS 20 O-H showing the bond length of 1.9 Å & 2.0 Å. The compound 2,4-Dichloro-5H-pyrrolo[3,2-d] pyrimidine /5375053 had Binding energy of -4.52 Kcal/mol and formed hydrogen bonds with the residue THR 19 H-O, THR 21 H-O, and THR 38 H-O showing the bond length of 2.7 Å, 1.9 Å, and 2.0 Å & 2.6 Å. The compound 1,1-Diethoxy-2-methylpropane/519415 with a binding energy of -3.7 Kcal/mol and formed hydrogen bonds with the residue LYS 20 O-H showing the bond length of 2.1 Å and 2.0 Å. Finally, the control compound was analyzed and compared with retrieved compounds. The compound Naproxen (Control) 156391 with a binding energy of -7.5 Kcal/mol and formed hydrogen bonds with the residue LYS 20 O-H and GLU 22 H-O showing the bond length of 2.3 Å & 1.9 Å and 2.0 Å. The interactions of plant compounds with the target would compare to the presently available drug molecule, to study its potency. As well as the simulation studies would provide an insight into the stability of the protein-compound complex. The plant compounds indicating collaboration with the protein are arranged with the Binding energy. The plant compounds and the information of their hydrogen bond, collaborating deposits, and individual bond lengths were organized independently (Table 5). Utilizing the Pymol tool, the cooperation between the synthetic mixes and the target protein is visualized and the communication of all compounds including control has appeared in figure 1.

Discussion

The findings revealed that five out of the seven compounds fulfill the oral drugability of Lipinski's rule of five (RO5) while two slightly meet the criteria of RO5. Conversely, five of the compounds are predicted to be mutagen while the remaining two are predicted to be safe for the body. Additionally, stigmasterol glucoside has a higher binding affinity (7590) with GLUT4 when compared to doxorubicin (6600) in the control [20]. The ADMET analysis and docking results revealed nine phytochemicals, i.e., Silymarin, Flavobion, Derrisin, Isosilybin, Mundulinol, Silydianin, Isopomiferin, Narlumericine, and Oxysanguinarine to have potential inhibitory properties against DENV and can be considered for additional in vitro and in vivo studies to assess their inhibitory effects against DENV replication. They exhibited binding affinity ≥ -8 kcal/mol against DENV4-NS4B. Furthermore, DFT-based analysis revealed high reactivity for these nine phytochemicals in the binding pocket of DENV4-NS4B, based on ELUMO, EHOMO, and band energy gap [21].

The results show that Autodock outperforms largely ArgusLab in the binding energy correlation with biological activity. Phytochemicals having anticancer property retrieved from Dr. Dukes phytochemical and ethnobotanical database were then docked using Autodock. The phytochemical ajmaline was identified to have a high affinity to the target protein which can be modified to get potent novel JAK2 inhibitors [22]. Due to the presence of hesperidin, the bound structure of ACE2 and spike protein fragments becomes unstable. As a result, this natural product can impart antiviral activity in SARS CoV2 infection. The antiviral activity of these five natural compounds is further experimentally validated with a QSAR study[23].

Molecular docking and drug-likeness studies were made using ADMET properties while Lipinski's rule of five was performed for the phytochemicals to evaluate their anti-prostate cancer activity. The results showed that Isobavachin exhibited the best binding affinity of -13.73 kcal/mol with AR followed by Glabranin, Anthocyanin, and Eriosemation. Our studies, therefore, reveal that these four phytochemicals could be promising candidates for further evaluation for PCa prevention or management [24].

Selected phytochemicals with potential anticancer activities were examined for their binding affinities to the selected VEGFR and EGFR receptors. The receptor protein 3D structures were obtained from Protein Data Bank, and the molecular docking was performed using UCSF Chimera software with its AutoDock Vina tool. Out of 18 compounds screened, flavin, and Genistein have shown the highest binding energies. The findings of this study should be further evaluated for their potential use in CRC treatment, management, and prevention [25].

Conclusion

The development of computational methods for protein flexibility is still in its infancy and thereby remains one of the major future directions in protein-ligand docking. Rising new contagious species and the occurrence of raised medication obstruction for fungal infections keeps on rising and the height of contagious contaminations is disturbing. Medicinal plants are an important part of our natural health. They serve as important therapeutic agents as well as valuable raw materials for manufacturing numerous traditional and modern medicines. *Corbichonia decumbens* leaves have been traditionally used worldwide for their versatile therapeutic properties. A study of molecular docking simulation was undertaken to identify and access the binding capacity of ligands. The chemical compounds are used to cure disease and those compounds are found in aerial parts of the plant. The purpose of this study is to

analyze the inhibitory potential toxic shock syndrome toxin-1 through *in silico* molecular docking studies on active compounds of plant extract. The protein and ligand docking studies are done by using the 3D structure of the protein. Most of the molecular docking studies successfully predict the binding modes of small-molecule ligands within receptor binding sites. The phytochemical compounds of 1-Methyl-3,5-dinitro-1,2,4-triazole/542691 was isolated from *C. decumbens* exhibit a good binding efficiency with the target showing high binding energy of -5.41 Kcal/mol is used to treat the Inflammation. The biological activity of plant compounds is predicted using pass prediction and the results are proved the chemical compounds have an anti-inflammatory property. The compounds are compared with the control showed the nearby range of binding energy. This indicates that the compound 1-Methyl-3,5-dinitro-1,2,4-triazole has the highest inhibiting activity and also other plant compounds. Those bioactive compounds should be explored more to identify efficient and potential drug molecules. As shown in the highlighted case studies, molecular docking has been able to identify promising compounds that might represent future solutions in critical areas of human health.

Acknowledgments

The authors are grateful to acknowledge the Department of Botany, PSG College of Arts & Science College, Coimbatore for providing requirements during the study.

Reference

1. Padmanabhan P, Jangle SN. Evaluation of the in-vitro anti-inflammatory activity of herbal preparation, a combination of four medicinal plants. International journal of basic and applied medical sciences. 2012;2(1):109-16.
2. Thirumurugan K, Shihabudeen MS, Hansi PD. Antimicrobial activity and phytochemical analysis of selected Indian folk medicinal plants. steroids. 2010;1(7):430-34.
3. Simoes M, Bennett RN, Rosa EA. Understanding antimicrobial activities of phytochemicals against multidrug-resistant bacteria and biofilms. Natural product reports. 2009; 26 (6):746-57.
4. Roskov Y, Kunze T, Paglinawan L, Orrell T, Nicolson D, Culham A, Bailly N, Kirk P, Bourgoin T, Baillargeon G, Hernandez F. Species 2000 & ITIS Catalogue of Life, 2013 Annual Checklist.

5. Bergdoll M, Reiser R, Crass B, Robbins R, Davis J. A new staphylococcal enterotoxin, enterotoxin F, is associated with toxic-shock-syndrome *Staphylococcus aureus* isolates. *The Lancet*. 1981 9;317(8228):1017-21.
6. Moza B, Varma AK, Buonpane RA, Zhu P, Herfst CA, Nicholson MJ, Wilbuer AK, Seth NP, Wucherpennig KW, McCormick JK, Kranz DM. Structural basis of T-cell specificity and activation by the bacterial superantigen TSST-1. *The EMBO journal*. 2007 21;26(4):1187-97.
7. Nonfoux L, Chiaruzzi M, Badiou C, Baude J, Tristan A, Thioulouse J, Muller D, Prigent-Combaret C, Lina G. Impact of currently marketed tampons and menstrual cups on *Staphylococcus aureus* growth and toxic shock syndrome toxin 1 production in vitro. *Applied and environmental microbiology*. 2018 15;84(12).
8. Mitchell MA, Bisch S, Arntfield S, Hosseini-Moghaddam SM. A confirmed case of toxic shock syndrome associated with the use of a menstrual cup. *Canadian Journal of Infectious Diseases and Medical Microbiology*. 2015 1;26(4):218-20.
9. Benet, L.Z., Hosey, C.M., Ursu, O. and Oprea, T.I., 2016. BDDCS, the rule of 5 and drugability. *Advanced drug delivery reviews*, 101, pp.89-98.
10. Singh AN, Baruah MM, Sharma N. Structure Based docking studies towards exploring potential anti-androgen activity of selected phytochemicals against Prostate Cancer. *Scientific reports*. 2017 16;7(1):1-8.
11. Seyedi SS, Shukri M, Hassandarvish P, Oo A, Shankar EM, Abubakar S, Zandi K. Corrigendum: computational approach towards exploring potential anti-Chikungunya activity of selected flavonoids. *Scientific reports*. 2016;6.
12. Lounnas V, Ritschel T, Kelder J, McGuire R, Bywater RP, Foloppe N. Current progress in structure-based rational drug design marks a new mindset in drug discovery. *Computational and structural biotechnology journal*. 2013 1;5(6):e201302011.
13. Ferreira LG, Ricardo N. Dos Santos, Glaucius Oliva, and Adriano D. Andricopulo. *Molecules*. 2015;20:13384-421.
14. Yuriev E, Ramsland PA. Latest developments in molecular docking: 2010–2011 in review. *Journal of Molecular Recognition*. 2013 May;26(5):215-39.
15. López-Vallejo F, Caulfield T, Martínez-Mayorga K, A Giulianotti M, Nefzi A, A Houghten R, L Medina-Franco J. Integrating virtual screening and combinatorial chemistry for accelerated drug discovery. *Combinatorial Chemistry & High Throughput Screening*. 2011 Jul 1;14(6):475-87.

16. Liu Y, Dao Z, Yang C, Liu Y, Long C. Medicinal plants used by Tibetans in Shangri-la, Yunnan, China. *Journal of Ethnobiology and Ethnomedicine*. 2009;5(1):1-0.
17. DeLano WL. The PyMOL molecular graphics system. <http://www.pymol.org>. 2002.
18. Sharma NL, Mahajan V, Sharma RC, Sharma A. Subcutaneous phaeohyphomycosis in India—A case report and review. *International journal of dermatology*. 2002;41(1):16-20.
19. ul Qamar MT, Maryam A, Muneer I, Xing F, Ashfaq UA, Khan FA, Anwar F, Geesi MH, Khalid RR, Rauf SA, Siddiqi AR. Computational screening of medicinal plant phytochemicals to discover potent pan-serotype inhibitors against dengue virus. *Scientific reports*. 2019 5;9(1):1-6.
20. OyinloyeBE, Adekiya TA, Aruleba RT, Ojo OA, Ajiboye BO. Structure-based docking studies of GLUT4 towards exploring selected phytochemicals from *Solanum xanthocarpum* as a therapeutic target for the treatment of cancer. *Current drug discovery technologies*. 2019 1;16(4):406-16.
21. Qaddir I, Rasool N, Hussain W, Mahmood S. Computer-aided analysis of phytochemicals as potential dengue virus inhibitors based on molecular docking, ADMET and DFT studies. *Journal of vector borne diseases*. 2017 1;54(3):255.
22. Achutha AS, Pushpa VL, Manoj KB. Comparative molecular docking studies of phytochemicals as Jak2 inhibitors using Autodock and ArgusLab. *Materials Today: Proceedings*. 2020 26.
23. Basu A, Sarkar A, Maulik U. Molecular docking study of potential phytochemicals and their effects on the complex of SARS-CoV2 spike protein and human ACE2. *Scientific reports*. 2020 19;10(1):1-5.
24. Singh AN, Baruah MM, Sharma N. Structure Based docking studies towards exploring potential anti-androgen activity of selected phytochemicals against Prostate Cancer. *Scientific reports*. 2017 16;7(1):1-8.
25. Qawoogha SS, Shahiwala A. Identification of potential anticancer phytochemicals against colorectal cancer by structure-based docking studies. *Journal of Receptors and Signal Transduction*. 2020 2;40(1):67-76.

Table 1. Structure of Protein

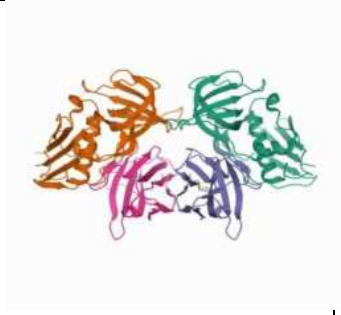
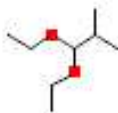
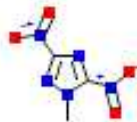
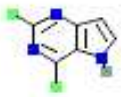
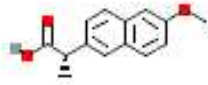
ORGANISM NAME	PROTEIN NAME & ID	STRUCTURE	RESIDUES COUNT
<i>Staphylococcus aureus</i>	Toxic shock syndrome toxin-1 (TSST-1) &2IJ0		74

Table 2. List of compounds isolated from medicinal plants

S.No	Compound Name	Pubchem ID	Molecular formula	Molecular Weight
1.	Quinoline	7047	C ₉ H ₇ N	129.16 g/mol
2.	[(2R,3S,4R)-5-(2,6-Dioxo-3H-purin-9-yl)-3,4-dihydroxyoxolan-2-yl] methyl dihydrogen phosphate	122280	C ₁₀ H ₁₃ N ₄ O ₉ P	364.21 g/mol
3.	1,1-Diethoxy-2-methylpropane	519415	C ₈ H ₁₈ O ₂	146.23 g/mol
4.	1-Methyl-3,5-dinitro-1,2,4-triazole	542691	C ₃ H ₃ N ₅ O ₄	173.09 g/mol
5.	2,4-Dichloro-5H-pyrrolo[3,2-d] pyrimidine	5375053	C ₆ H ₃ Cl ₂ N ₃	188.01 g/mol
6.	Naproxen (Control)	156391	C ₁₄ H ₁₄ O ₃	230.26 g/mol

Table 3. Prediction of pharmacological activity for plant compounds

Compound Name & Id	Compound structure	Compound Activity
Quinoline 7047		0,280 0,029 Aldosterone antagonist 0,256 0,005 Protein kinase B alpha inhibitor 0,304 0,053 Tyrosine 3 hydroxylase inhibitor 0,254 0,003 Heat shock protein agonist ★ 0,275 0,025 Phosphoenolpyruvate-protein phosphotransferas inhibitor 0,283 0,033 Antineoplastic (brain cancer) 0,284 0,035 CYP2B2 substrate
[(2R,3S,4R)-5-(2,6-Dioxo-3H-purin-9-yl)-3,4-dihydroxyoxolan-2-yl] methyl dihydrogen phosphate 122280		0,041 0,038 Galectin 3 antagonist 0,007 0,004 mRNA (nucleoside-2'-O-)-methyltransferase inhibitor 0,004 0,001 CO-methylating acetyl-CoA synthase inhibitor 0,004 0,001 Aspartate N-acetyltransferase inhibitor 0,083 0,082 Heat shock protein antagonist ★ 0,114 0,114 Sphinganine-1-phosphate aldolase inhibitor 0,154 0,154 Ribonucleoside triphosphate reductase inhibitor
1,1-Diethoxy-2-methylpropane 519415		0,260 0,155 MAP3K5 inhibitor 0,139 0,034 Putrescine oxidase inhibitor 0,126 0,022 N-acetylglucosamine kinase inhibitor 0,133 0,029 Heat shock protein 70 agonist ★ 0,179 0,076 CYP1B substrate 0,198 0,095 Carnitinamidase inhibitor 0,177 0,073 UGT1A5 substrate 0,152 0,049 Antithyroid 0,126 0,024 Cytokine modulator
1-Methyl-3,5-dinitro-1,2,4-triazole 542691		0,238 0,084 Farnesoid X receptor antagonist 0,169 0,015 Tardive dyskinesia treatment 0,197 0,044 Alkene monooxygenase inhibitor 0,203 0,050 CYP2B1 substrate 0,219 0,066 Prunasin beta-glucosidase inhibitor 0,173 0,020 Heat shock protein agonist ★ 0,190 0,038 Allantoinase inhibitor 0,237 0,085 5 Hydroxytryptamine 2B agonist
2,4-Dichloro-5H-pyrrolo[3,2-d] pyrimidine 5375053		0,092 0,046 Carboxylate reductase inhibitor 0,067 0,021 Nucleoside deoxyribosyltransferase inhibitor 0,101 0,055 Glycine transaminase inhibitor 0,097 0,052 CTP synthase inhibitor 0,135 0,090 Heat shock protein agonist ★ 0,136 0,091 Methyltransferase substrate 0,135 0,090 Vomilenine glucosyltransferase inhibitor 0,104 0,059 Glucan 1,3-beta-glucosidase inhibitor
Naproxen (Control) 156391		0,283 0,014 GABA B receptor agonist 0,309 0,042 DNA ligase (ATP) inhibitor 0,287 0,021 Bile-salt sulfotransferase inhibitor 0,272 0,005 HIV-1 integrase (Overall Integration) inhibitor 0,279 0,013 2-Oxoisovalerate dehydrogenase (acylating) int 0,367 0,102 Heat shock protein 27 antagonist ★ 0,335 0,070 Radioprotector 0,295 0,030 Snopalysin inhibitor 0,278 0,014 Thrombolytic

★ The Symbol indicates the main activity of the compound for the disease.

Table 4. ADME toxicity for plant molecules

Molecule ID	Molecular weight	High lipophilicity LOGP	Donor Hydrogen Bonds	Acceptor Hydrogen Bonds	Molar Refractivity
Normal range	Molecular mass less than 500 Dalton	High lipophilicity LogP less than 5	Less than 5 hydrogen bond donors	Less than 10 hydrogen bond acceptors	Molar refractivity should be between 40-130
7047	129.00	2.23	0	1	41.74
122280	198.00	-0.36	0	6	49.41
519415	146.00	2.04	0	2	41.87
542691	173.00	-0.3	0	6	44.31
5375053	188.00	2.26	1	2	43.90
156391 (control)	230.00	3.03	1	3	66.55

Table 5. Interaction of *C. decumbens* compounds with 2IJ0

S. No	Name of the ligand / PubChem ID	Residues Interaction	Bond length(Å)	No of Bonds	Binding score (Kcal/mol)
1.	1-Methyl-3,5-dinitro-1,2,4-triazole/542691	THR 78 O-H	2.2	4	-5.41
			2.1		
		LYS 20 O-H	2.3		
			2.0		
2.	Quinoline/7047	LYS 20 H-O	2.0	1	-4.93
3.	[(2R,3S,4R)-5-(2,6-Dioxo-3H-purin-9-yl)-3,4-dihydroxyoxolan-2-yl] methyl dihydrogen phosphate /122282	LYS 20 O-H	1.9	2	-4.57
			2.0		
4.	2,4-Dichloro-5H-pyrrolo [3,2-d] pyrimidine /5375053	THR 19 H-O	2.7	4	-4.52
		THR 21 H-O	1.9		
		THR 38 H-O	2.0		
			2.6		
5.	1,1-Diethoxy-2-methylpropane/519415	LYS 20 O-H	2.1	2	-3.7
			2.0		
6.	Naproxen (Control) 156391	GLU 22 H-O	2.0	3	-7.5
		LYS 20 O-H	2.3		
			1.9		

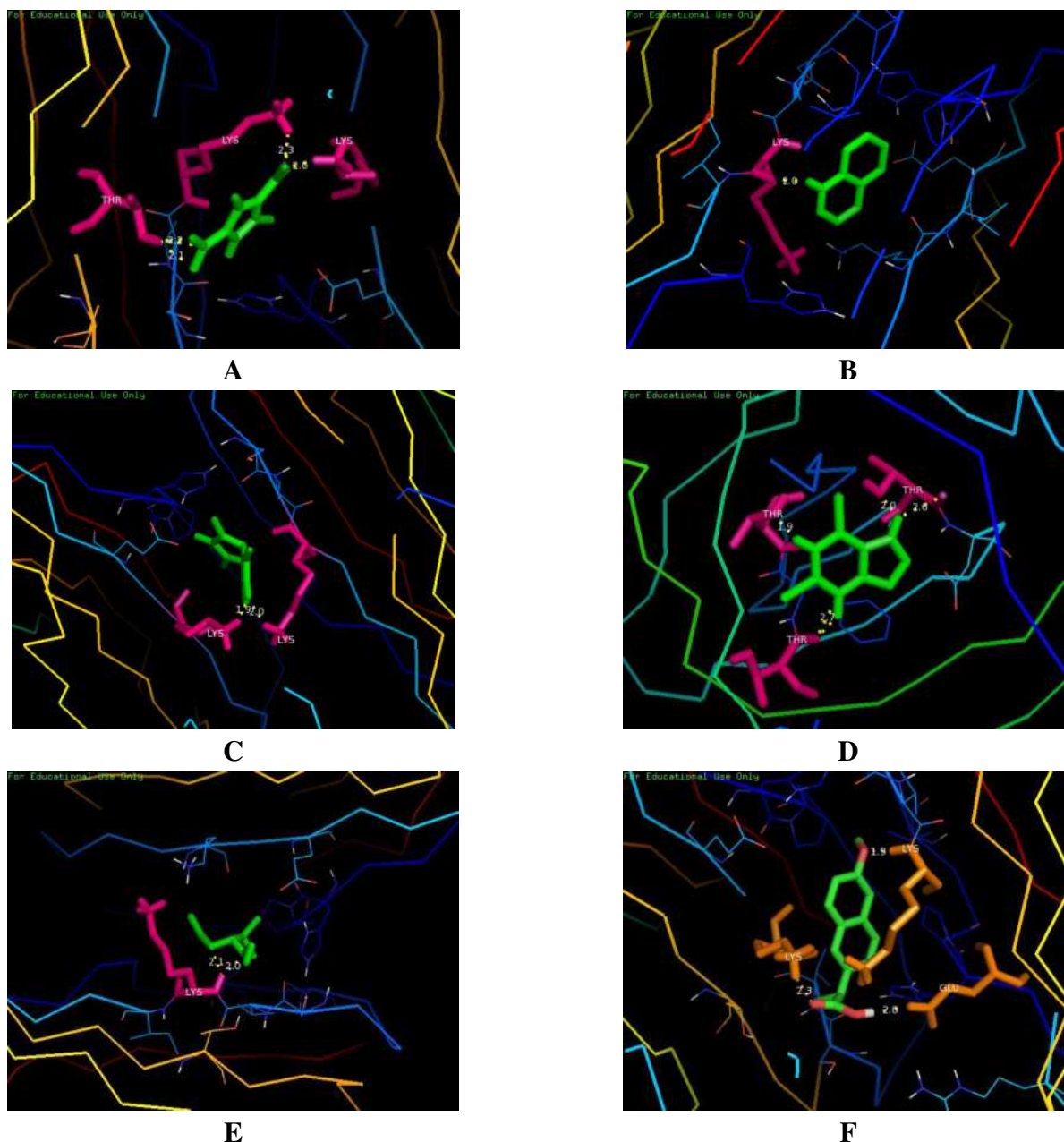


Figure 1. Interaction of compounds with the target protein.

Intermolecular interactions between compounds derived from *Corbichonnia decumbens* and the binding site of the Toxic shock syndrome toxin-1 (TSST-1) protein (PBP3). A. 1-Methyl-3,5-dinitro-1,2,4-triazole, B. Quinoline, C [(2R,3S,4R)-5-(2,6-Dioxo-3H-purin-9-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate, D. 2,4-Dichloro-5H-pyrrolo[3,2-d]pyrimidine E. 1,1-Diethoxy-2-methylpropane and F Naproxen (control). The ligand was exposed in Green color and interacting residues in pink color, whereas in the control compound interacting residues in orange color. The dotted lines indicating the hydrogen bond formation.