ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 14, Issue 2, 2021

Online - 2455-3891
Print - 0974-2441

Research Article

IN SILICO ANALYSIS OF *BRUGUIERA GYMNORRHIZA* (L.) – LARGE LEAVED MANGROVE FOR EFFICIENT THERAPEUTIC USES

ARUNPRASATH A*, SREERAM S

Department of Botany, PSG College of Arts and Science, Coimbatore, Tamil Nadu, India. Email: arunprasath@psgcas.ac.in

Received: 16 October 2020, Revised and Accepted: 24 November 2020

ABSTRACT

Objective: The study was focused on obtaining the therapeutic advantages of *Bruguiera gymnorrhiza*, a large leafed mangrove through *in silico* studies.

Methods: The collected leaf sample was extracted using ethanol, and the extract was subjected to GCMS analysis to find out the compounds present in them. The obtained compounds underwent absorption, distribution, metabolism, and elimination toxicity test and the chemical structures were obtained from PUBCHEM and the disease which had more susceptibility was taken on the basis of antimicrobial studies and its protein structure was also obtained from Protein Data Bank. Maestro is a freely available, full future molecular visualization tool. It is a powerful tool for interpreting, managing, and sharing the results of computational experiments when coupled with Schrodinger software such as Glide, Prime, or Phase. The compatibility of ligand-protein interaction was visualized through the visualization software that is Pymol.

Results: The retrieved compounds were subjected to analyze the absorption, distribution, metabolism, and excretion properties and the results were tabulated. It was found that the compound 2-Methoxy-4-Vinylphenol; 7786-61-0; 4-Vinylguaiaco from the plant sample *B. gymnorrhiza* shows a glide score (G. score) −7.2 Kcal/mol. The interactions were observed using Pymol.

Conclusion: It was found that the compound 4-Vinylguaiaco from the plant sample *B. gymnorrhiza* can be used as potent drug for the treatment of pharyngitis, which is the inflammation of pharynx. This work can be taken as a base for the works that need to be done in future for the development of an effective drug and also addressing the importance of mangroves in the field of ethnobotany.

Keywords: Mangroves, *In silico*, Pharyngitis, Bruguiera, M-protein.

© 2021 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2021v14i2.40019. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

The pharmaceutical industry has turned on the path of an organic revolution as more projects are being spearheaded by the incorporation of organic compounds in drug making. The way of science being practiced itself is changing nowadays due to such efficient projects. A more sustainable kind of development is going on the pharmaceutical industry rather than synthetically concerned techniques. Nowadays, various kinds of *in silico* techniques are employed for the development of an efficient drug. It has come into notice that unfavorable absorption, distribution, metabolism, and elimination (ADME) properties a major cause of failure of candidate molecules in drug development [1]. The *in silico* tools mainly encompasses of certain software such as Protein Data Bank (PDB), PUBCHEM, ADME/Toxicity (TOX), Prediction of Activity Spectra for Substance, LIGSITE, MASTERO, QikProp, and Pymol. Pharyngitis in short can be termed as sore throat. The 2000 National Ambulatory Medical Care Survey found out that acute pharyngitis accounts for 1.1% of visits in the primary care setting, a peak season of sore throat is usually denoted from late winter and early spring. The spread of such types of virus mainly occurs by hand contact with nasal discharge rather than by oral contact. The symptoms are noticed after a short incubation period of 24–72 h [2]. Group A streptococcus (*Streptococcus pyogenes*) is mainly responsible for the 5–15% of the sore throat infections in adults and 20–30% in children. Streptococcal pharyngitis is mainly observed in children between the age group of 5 and 15. Streptococcal pharyngeal infection is said to cause acute illness, but it also has the ability to trigger post-infectious syndromes of post-streptococcal glomerulonephritis and acute rheumatic fever. Rheumatic fever is still an unknown problem in most of the developed countries, but it remains as a leading cause of acquired heart disease among children in many resource deficit areas such as sub-Saharan Africa, India, and parts of Australia [3]. The onset of the symptoms of pharyngitis infection in patients is swift. It has come into knowledge that other than throat pain certain other conditions such as fever, chills, malaise, headache, and especially in younger children nausea, abdominal pain, and vomiting are diagnosed [4]. The focus of this work mainly pertains to the use of a mangrove species from the west coast of Kerala. Mangroves are facing an inevitable amount of destruction to their habitat as more and more such halophytic forests are being cleared for economic interest. It was discovered that the ethanol extract of some mangrove species has antimicrobial activity. *Bruguiera gymnorrhiza* is a large leaved mangrove belonging to the family of Rhizophoraceae. The mangrove is common in the middle and upper intertidal zones, rather than the lower intertidal zones or along the seaward edge of mangrove stands. This particular mangrove is said to be a more shade loving plant. The bark of this plant is said to be rich in tannin content and can be utilized for the biotreating of tanning leather. The medicinal uses of the fruits encompass for the treatment of shingles and eye diseases. The bark is mainly used as an astringent for the treatment of diarrhea and malaria [5,6]. The ethanol extract of *B. gymnorrhiza* showed when analyzed using GC–MS showed the presence of some vital compounds which has the capability of being used as a potent drug. When these compounds were run using the *in silico* methods, a good result was obtained and came into conclusion that the organic compounds obtained from this leaf extract of *B. gymnorrhiza* do have a therapeutic effect on the disease pharyngitis.

METHODS

The leaf sample of *B. gymnorrhiza* was collected from the Vypin islands of Cochin and the exact location will be Malipuram (10.0215° N, 76.2246° E). The preparation of leaf extract was done in the standard way, that is, the leaves were subjected to shade drying and then 25 g of the powdered leaf sample of *B. gymnorrhiza* was successively extracted using 250 mL of

ethanol using the Soxhlet extractor for 8–10 h [7]. The extract was then filtered through Whatman No. 1 filter paper to remove all the undissolved matter, including cellular materials and other constituents that are insoluble in the extraction solvent. The sample was then taken for GC–MS analysis so as to get the clear idea of compounds present in the leaf sample. The microorganism which was more susceptible to the compounds in the sample was selected based on the antimicrobial sensitivity test. The *in silico* activity was then carried out, using various tools. PDB, this is one of the online tools to obtain the protein structure of the compound. The M-protein structure was obtained from the PDB. The chemical structure of compounds identified through GC–MS was obtained from PubChem. The ADME TOX was run to find out the ADME/TOX properties of chemical compounds along the discovery process rather than at the final stages. Maestro is a freely available, full future molecular visualization tool that also serves as the interface to all Schrodinger's computational chemistry software. It is a powerful tool for interpreting, managing, and sharing the results of computational experiments when coupled with Schrodinger software such as Glide, Prime, or Phase. The compatibility of ligand-protein interaction was visualized through the visualization software that is Pymol.

RESULTS

The retrieved compounds were subjected to analyze the absorption, distribution, metabolism, and excretion properties and the results were tabulated. It is very important to have the first-hand knowledge of this information as it is necessary for the completion of drug discovery (Fig. 1). The lipophilicity was calculated to determine the range of solubility and permeability in octanol/water partition coefficient, to understand the mechanism of transportation brain/blood barrier to be determined. The Lipinski's rule of five is also called as Pfizer's rule of five or the rule of thumb to evaluate drug likeness to indicate the following properties such as molecular weight, octanol/water partition coefficient, and hydrogen bond donor and acceptor. The rule has some limits in multiple of five, hence, the name has been given as rule of five. Apart from these parameters, other functions such as surface area in square Armstrong (polar surface area), brain/blood barrier, and percentage of human oral absorption were also predicted. It was found that the compound 2-Methoxy-4-Vinylphenol; 7786-61-0; 4-Vinylguaiaco from the plant sample *B. gymnorrhiza* shows a glide score (G. score) −7.2 Kcal/mol. The interactions were observed using Pymol. The compounds that behaved as a potent drug were 2-methoxy-4-vinylphenol; 7786-61-0; 4-vinylguaiaco, 2-furancarboxaldehyde, 5-(hydroxymethyl), oxime; 37110-03-5, dihydromaltol; unii-l0fid5vwf6; l0fid5vwf6, tetrahydrofuran-2-carbaldehyde; 7681-84-7; tetrahydro-2-furancarboxaldehyde, 9-oxa-bicyclo[3.3.1]nona-3,6-dien-2-one;ac1lc9gg; schembl10515551, methyl propyl disulfide; 2179-60-4; disulfide, methyl propyl, diacetone alcohol; 4-hydroxy-4- methyl-2-pentanone; 123-42-2, diethyl carbonate; 105-58-8; ethyl carbonate, 4-(methylisopropylamino)-3-penten-2-one, n,n-dimethylformamide; dimethylformamide; 68-12-2, 3,4,5,6-tetramethyloctane; octane, 3,4,5,6-tetramethyl-; 62185-21-1, ditolylethane; ethane, ditolyl-; dl-2,3-diphenylbutane, palmitic acid; hexadecanoic acid; 57-10-3, 7-tridecanone; tridecan-7-one; 462-18-0, 9-octadecene; (e)-octadec-9-ene; 9-octadecene, (e), hexadecane; n-hexadecane; and cetane (Tables 1 and 2, Fig. 2).

DISCUSSION

The *in silico* studies on the leaf extract of *B. gymnorrhiza* revealed that 2-methoxy-4-vinyl phenol in short called as p-Vinyl guaiacol showed a glide score (G. score) −7.2 Kcal/mol. It was a very good value and showed the characteristic feature of the plant compound to be treated as a drug. *In silico* studies prove to be an excellent parameter on choosing an effective compound as drug against a particular disease. It has reduced the time and effort put in to make an efficient drug. In 2016, the cytotoxicity of cell line was predicted for the prediction of the cytotoxic effect of phytosterols against non-transformed and cancer cell lines based on their corresponding structural formula [8]. These results highlighted the potential of these sterols against adenocarcinoma, followed by carcinoma and mesothelioma. A Pa value, 0.816 against stomach adenocarcinoma cells (MKN 74) was obtained for cycloartanol, was followed by 0.746 for 24-methylene cycloartanol, 0.707 for campesterol, 0.684 for stigmasterol, and 0.638 for γ-sitosterol. The mangrove-derived bioactive molecules such as avicenol, betulinic acid,

Table 1: Absorption, distribution, metabolism, and elimination property of plant compounds

Molecule	Mol_MW (Molecular weight)	DonorHB (Donor-hydrogen Bonds)	AccptHB (acceptor Hydrogen bonds)	QPlogPo/w	QPlogBB (Predicted brain/blood Partition coefficient)	Human oral absorption	Percent human oral absorption	Rule of five	Rule of three
Range	130–725	0–6	2.0–20.0	−2.0–6.5	−3.0–1.2	1-Low, 2-Medium, 3-high	>80% is high <25% is poor	Maximum 4	Maximum 3
p-Vinyl guaiacol	150.2	1	1.5	1.9	−0.1	3	100.0	0	0
Palmitic acid	256.4	1	2.0	5.3	−1.5	3	87.6	1	0
N,N-Dimethylformamide	73.1	0	3.0	−1.0	0.0	2	73.9	0	0
Diethyl carbonate	118.1	0	2.0	1.3	−0.3	3	90.7	0	0
Tridecan-7-one	198.3	0	2.0	4.1	−0.4	3	100.0	0	0
n-Hexadecane	226.4	0	0.0	4.0	1.2	1	100.0	1	1
Methyl propyl disulfide	122.2	0	1.0	2.6	0.2	3	100.0	0	0
Ditolylethane	210.3	0	0.0	5.8	0.5	1	100.0	1	1
Tetrahydrofuran-2-carbaldehyde	100.1	0	3.7	−0.3	0.0	3	84.8	0	0
Diacetone alcohol	116.2	0	1.8	1.3	-0.2	3	93.6	0	0
Octane, 3,4,5,6-tetramethyl	170.3	0	0.0	6.4	1.1	1	100.0	1	1
SCHEMBL13226520	136.2	0	3.7	0.2	0.2	3	91.0	0	0
(3Z)-3-Hexadecene	224.4	0	0.0	5.1	1.5	1	100.0	1	1
9-Octadecene	252.5	0	0.0	4.6	1.6	1	100.0	1	1
Phytol	296.5	1	1.7	6.3	−0.9	1	100.0	1	1
Dihydromaltol	128.1	1	3.5	0.2	−0.2	3	83.0	0	0
2-Furancarboxaldehyde, 5-(hydroxymethyl)-, oxime	141.1	2	5.4	−0.5	−0.9	2	71.7	0	0
Chlorobutanol, (S)	177.5	1	0.8	2.2	0.6	3	100.0	0	0
CTK1F9237	206.3	1	3.7	2.1	−0.4	3	96.3	0	0
4-(Methylisopropylamino)-3-penten-2-one	155.2	1	3.0	2.0	0.2	3	100.0	0	0

Table 2: Interaction of plant compounds with M-protein

Name of ligand	Residues interacted	Bond length (Å)	Number of bonds formed
p-Vinyl guaiacol	HIS-28(N-H)	2.1	1
N,*N*-dimethylformamide	ARG-27(H-O)	2.1	1
Diethyl carbonate	HIS-28(N-O)	2.3	1
Tridecan-7-one	HIS-28(N-O)	3.0	2
	ARG-27(N-O)	3.1	
Tetrahydrofuran-2-carbaldehyde	HIS-28 (N-O)	3.1	2
	ARG-27(N-O)	3.0	
Diacetone alcohol	HIS-28(N-O)	3.1	1
Dihydromaltol	ASP-29(O-O)	2.9	3
	LYS-32(N-O)	3.1	
	LYS-32(N-O)	2.9	
2-Furancarboxaldehyde, 5-(hydroxymethyl)-, oxime	ASP-31(O-O)	3.0	3
	ARG-27(N-O)	3.1	
	ARG-22(O-O)	2.8	

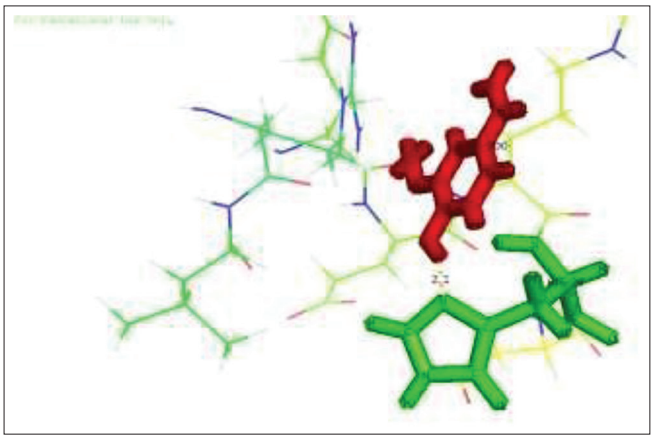

Fig. 1: Interactions of M-Protein with p-Vinyl guaiacol

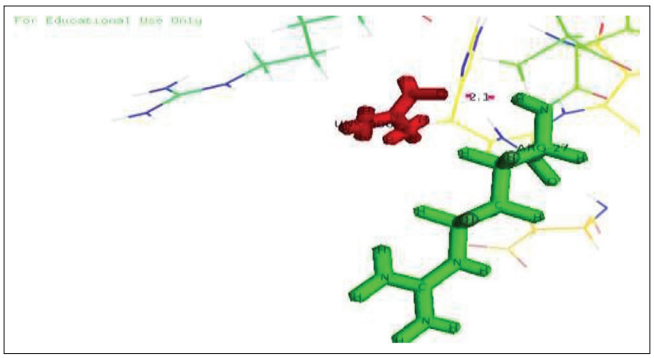

Fig. 2: Interaction of M-protein with N,N-dimethylformamide

lupeol, quercetin, triterpenoid and its binding energy, and hydrogen bond interaction distance between hydrogen donor and acceptor atoms of Aβ ligand. Among these, betulinic acid had significant binding energy –5.54 kcal/mol and interacted with a receptor protein in LYS16 amino acid residue. Among molecular interactions of five mangroves on acetylcholine esterase receptor, the triterpenoid had significant binding energy –46.79 kcal/mol and the compounds interacted with a receptor protein in TYR 72 amino acid residue [9].

CONCLUSION

The current study on the mangrove plant *B. gymnorrhiza* revealed the potential of the plant to be used an effective therapeutic agent against various bacterial diseases and also its importance in maintaining the balance in the ecosystem. Further studies can be carried out on this mangrove species to undermine its effectiveness as a very high potential drug.

ACKNOWLEDGMENT

The authors are grateful to acknowledge the PG and Research Department of Botany, PSG College of Arts and Science, Coimbatore, for providing the necessary facilities during the study.

AUTHORS' CONTRIBUTIONS

Sreeram S and Arunprasath A designed the research, performed the virtual screening, and revised the manuscript. Sreeram S carried out the bioinformatics analysis and drafted the manuscript. Arunprasath A made the final structures and carried out the necessary corrections. Both the authors have read the final manuscript.

CONFLICTS OF INTEREST

The authors claim no conflicts of interest in the study.

AUTHORS' FUNDING

The project was self-funded.

REFERENCES

1. Butina D, Segall MD, Frankcombe K. Predicting ADME properties *in silico*: Methods and models. Drug Discov Today 2002;7:S83-8.
2. Vincent MT, Celestin N, Hussain AN. Pharyngitis. Am Fam Physician 2004;69:1465-70.
3. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of Group A streptococcal diseases. Lancet Infect Dis 2005;11:685-94.
4. Wannamaker LW. Perplexity and precision in the diagnosis of streptococcal pharyngitis. Am J Dis Child 1972;124:352-8.
5. Rudjiman. *Bruguiera gymnorrhiza* (L). Savingy. In: Lemmens RH, Wulijarni-Soetjipto N, editors. Prosea, Plant Resource of Southeast Asia 3. Dye and Tannin producing Plants. Indonesia: Bogs Indonesia Press; 1992. p. 53-5.
6. Othman S. *Bruguiera gymnorrhiza* Lamk. In: Sosef MS, Hong LT, Prawirohatmodjo S, editors. Prosea, Plant Resource of South-East Asia 5(3) Timber Treesl; Lesser Known Timbers. Indonesia: Bogor Indonesia Press; 1998. p. 122-5.
7. Gafner S, Wolfender JL, Hostettmann K, Stoeckli-Evans H, Mavi S. Phenols, acetylenes, and sesquiterpene lactones from *Inulanthera nuda*. Helv Chim Acta 1998;81:2062-71.
8. Thomas A, Peter KJ, Chandramohanakumar N. A profiling of anti-tumour potential of sterols in the mangrove fern *Acrostichum aureum*. Int J Pharmacogn Phytochem Res 2016;8:1828-32.
9. Manigandan V, Ramanathan T. *In silico* docking of mangrove derived ligands against Alzheimer's receptor proteins. Curr Res Neurosci 2014;4:18-24.