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2D QSAR, Admet prediction and multiple receptor molecular docking strategy in bioactive compounds of *Gracilaria corticata* against *Plasmodium falciparum* (contractile Protein)

Abhishek Biswal R, A. Aishwarya, Akshata Sharma, Vivek Pazhamalai *

Department of Bio-Engineering, School of Engineering, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, India

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ABSTRACT

Background: Delivering a safer drug is a challenge for medicinal chemistry. In this study, bioactive compounds of *Gracilaria corticata* were screened by predicting their drug-like properties such as solubility, permeability, efficacy, metabolic stability, and toxicity. The potential drug optimization against virulent enzymes was calculated by docking algorithm using AutoDock 4.2.3. Molecular docking analysis reveals that the compounds are insoluble and impermeable, with better potential inhibition against virulent enzymes.

Materials and methods: The bioactive compounds of *Gracilaria corticata* were screened for drug likeliness using the Lipinski rule of five and ADMET prediction. The structurally based docking analysis was done between organic compounds of plants against virulent proteins that are mainly responsible for causing disease. The interaction of rigid structure docked compounds was visualized using Discovery Studio. The QSAR studies of the compounds that have high binding energy against virulent enzymes were studied.

Results: The structurally based drug screening of bioactive compounds resulted in better drug properties with controlled lipophilicity level, without causing toxicity that harms the natural habitat of humans. The compound Mono (2-Ethylhexyl) phthalate has the highest binding energy of −8.73 kcal/mol followed by 2-ethylhexyl isohexyl ester −7.73 kcal/mol against virulent enzymes. The QSAR studies of Mono (2-Ethylhexyl) phthalate were done to show the relationship between the set of atoms with correlative factors. Hence, molecular docking and *in silico* ADMET studies play a major role in improving prediction of drug compounds, and these compounds are able to act as potential inhibitors against contractile proteins of *Plasmodium falciparum.*

1. Introduction

The search for new drugs against virulent enzymes is a challenge for medicinal chemistry. Contractile proteins that were mainly responsible for plasmodium actins are arranged into a regular standard for better investigation of the segment. Sarcomeres are divided into units that are derived by I bands and the area unit bisected by Z discs and A bands with a dark M within the center [1,2]. I bands accommodate skinny simple protein filaments, troponin, and tropomyosin. The thick filaments area unit is created from globulin. The A band consists of overlapping skinny and thick filaments and alternative proteins [3–5]. The actins of plasmodium have short filaments with noncanonical links between ATP molecules, but some microfilaments that constrain structural factors are unknown. The active site of this protein contains potassium ions during hydrolysis by leaving the phosphate group, which correlates with three-letter coding amino acids such as arginine, lysine, aspartic acid, and histidine [6,7]. The loops of the tertiary protein are connected with the actin protomer that links inner and outer domains. The role of an enzyme (Actin) in *Plasmodium falciparum* is to bind with protein molecules that provides ATP actin with large filamentous structures. The unusual actins in parasitic organisms are incorporated with ADP actins and catalyze ADP –ATP exchange to promote actin polymerization. This makes the microorganism adapt to normal conditions by excreting toxic materials. The world's plant and animal species include marine organisms in which biologically active compounds are present [8–10]. Among these marine species, seaweed is an important natural resource, used for animal feed and also as a human food source [11]. Seaweeds contains various essential molecules including polysaccharides, vitamins, minerals, and amino acids, that play an important role in a human diet. Seaweeds are used as a traditional diet in countries such as Japan and

* Corresponding author.
E-mail address: viveksncet2011@gmail.com (V. Pazhamalai).

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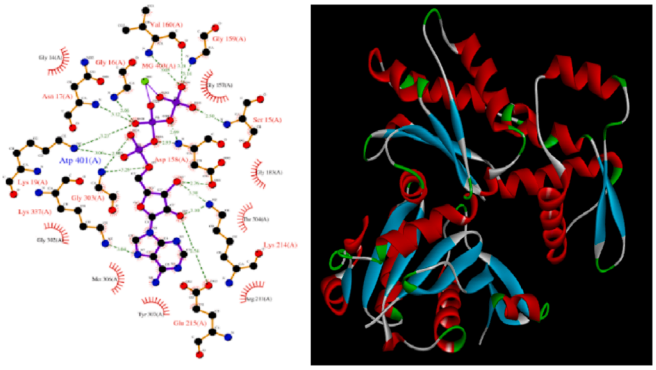

Fig. 1. Ligplot and 3D structure of A chain contractile protein.

Korea; recently the usage of seaweeds in western countries are also increased. Among these seaweeds, a particular type of marine red algae species called *Gracilaria corticata*, which is of family Rhodophyceae has exhibited various properties including antioxidant, antibacterial, anti-inflammatory, antiviral, and anticoagulant [12,13]. These algae also contain amino acids such as aspartic acid, alanine, glutamic acid, and glutamine. These amino acids give a typical flavor to the algae, which can respond to stress. These types of algae can concentrate the minerals present in seawater and have 10–20 times higher mineral content than terrestrial plants [14]. These algae contain a valuable source of minerals that have important nutrient functions. *Gracilaria corticata* is most commonly found in tropical and subtropical seas. *Gracilaria corticata* is available in Palk Bay on the southeast coast of India in all seasons. This is one of the commercially edible seaweeds in India [15].

1.1. Phytochemical analysis

Studies show that compounds such as carbohydrates, glycosides, tannins, saponins, phenols, proteins, and flavonoids were present in the ethanol extract of *Gracilaria corticata* while performing phytochemical screening qualitatively [16]. The most common compounds present were carbohydrates, phenols, and proteins. The phenolic compounds mainly possess antioxidant activities to free radicals, and induce detoxification of enzymes that mainly inhibit harmful microorganisms. Some phytochemicals like flavonoids have specific activities for Detoxification of carcinogens and acting as estrogen antagonists. These marine plants are widely found and have been used in biological and pharmacological activities. These plants have high concentrations of carbohydrates, phenols, and proteins. About 60–80% of phenols and 40–80% of tannins are present in this species [17]. The seaweeds are considered as a nutraceutical product which has many health and medical benefits. The medical benefits include the prevention and treatment of disease. A study has revealed that the crude extracts of acetone and ethanol show good inhibition activity against diarrhea-causing organisms like *E. coli* and *S. typhi* in the stool samples of children and diarrhea patients [18]. These seaweeds are rich in secondary metabolites which are biologically active, and have antibacterial and antioxidant properties. Thus, *Gracilaria corticata* can be used in the food and the pharmacological industry as they contain natural antioxidants.

2. Materials and methods

2.1. Determination of bioactive compounds from Gracilaria corticata

The seaweeds were collected from the coastal area Thondi in Palk Bay, south coast of India. The methanolic extract of the plant was analysed by using Gas Chromatography-Mass Spectroscopy in which various bioactive compounds like Sulfurous acid, Decane, 2-Ethylhexyl isohexyl ester, Undecane, Tridecanol, Hexatriacontane, Tricosane, Octacosane, Benzene, Mono (2-Ethylhexyl) phthalate, 10-Methylnonadecane, 1-Iodo-2-methylundecane, Pentatriacontane, Tritriacontane, and Nonacosane were analysed [19].

2.2. Protein and ligand library preparation

Plasmodium falciparum contractile protein (Actin) crystal structure was retrieved from a protein data bank (http://www.rcsb.org/) with PDB ID: 6I4L. The heteroatomic atoms and hydrophobic molecules were removed from the selected protein by using MOE *protein preparation module* to check the complex structure of protein [20]. The confirmation of protein was viewed by using the PyMOL viewer for the bound confirmation to identify the active site as shown in Fig. 1.

The ligand library was retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov/) which was maintained by the National Center of Biotechnology Information. The ligands were further screened for Lipinski rule of five by following certain criteria such as rotatable bonds $\leq$10, logP $\leq$5, hydrogen bond donor $\leq$5, hydrogen bond acceptor $\leq$10 and molar refractivity $\leq$130. After filtration, ligand size was reduced by using metaPocket and LigPrep module.

2.3. Virtual screening docking protocol

Structure based ligand – protein docking was done against enzyme (Actin) of *Plasmodium falciparum* by using AutoDock 4.2.3 software. This software includes a method of selecting receptor side chains for conformational bindings with active sites. A two step docking protocol was performed in which the grid parameters were set by adding hydrogen atoms and charges. Docking to a set of various receptor structures expected a vary of flexibility within the receptor. This is also obtained from multiple structural determinations or simulation. The AutoDock field of force includes primarily based contributions, as well as a direct hydrogen-bonding term with specific polar hydrogens. Additionally, the parameterization of AutoDock is accessible to the user, to permit standardisation for specific systems if desired. The prediction of valence shells by a rapid grid-based energy evaluation search of torsional freedom was done to accomplish the drug development process [21].

2.4. ADME/T properties

The Absorption Distribution Metabolism Excretion and Toxicity levels of the ligand molecules were screened using SwissADME software. These properties define the actual state of ligand by analyzing water solubility, gastrointestinal absorption, and penetration of ligand in the blood-brain barrier and central nervous system. The toxicity level of the drug molecules were also screened with dosage level for human and rat. These properties mainly run based on the principle of a vector based algorithm that can easily analyze datasets of known inhibitor/non-inhibitor as well as substrate/non-substrate [22,23].

2.5. 2D QSAR

The quantitative structure-activity relationship (QSAR) has a major application of combinatorial chemistry that investigates experimental information and builds numerical models of the information for prediction and interpretation. 2D QSAR analysis was performed for confirmation of docked compounds. A QSAR correlation plot was generated by plotting the values of pLC50 on the coordinate axis and also the foretold values (SPRED) on the coordinate axis for all the top compounds. Moreover, to spot active compounds within the information set QuaSAR-Contingency, application was enforced and followed by principal component analysis (PCA) by plotting a 3D graphical scatter plot with three vector values [24]. The abbreviation of the values predicted in 2D QSAR was shown in Table 1.

Table 1
Abbreviation of the values to be predicted.

Abbreviation	Name
CM	Cluster Model
PI	Prediction Interval
R^2	Determination co-efficient
Q^2	Cross-validated determinant co-efficient
HC	Hierarchical Clustering
NN	Nearest Neighbour
SV	Sum of atomic Van der Waals volumes
Mp	Mean atomic polarizability
Ms	Mean electropological state
nAT	Number of atoms
SCBO	Sum of Conventional Bond Orders
Hy	Hydrophilic factor
Ui	Unsaturation index

3. Results and discussion

This section represents the result obtained from structure-based drug designing with rigid docking of protein and ligand. Various methods of calculation were done against the bioactive compounds of *Gracilaria corticata* for analysing the drug likeliness. These are followed by docking analysis to investigate the interactions in ligand families against the virulent protein.

3.1. Screening of drug properties

As mentioned above, the drug properties were screened by Lipinski rule of five and ADME/T properties. The Lipinski rule of five was checked in which various parameters like hydrogen donor, hydrogen acceptor, molecular weight, lipophilicity, and molar refractivity were screened [25]. The compounds that satisfy the Lipinski rule of five are sulfurous acid, decane, 2-ethylhexyl isohexyl ester, undecane, tridecanol, benzene, Mono (2-ethylhexyl) phthalate, and 1-Iodo-2-methylundecane, as shown in Table 2. The Lipinski satisfied compounds were then screened for ADME/T properties.

In recent years a stream of drug candidates have been introduced in the development of an extended series of unsuccessful outcomes. The importance of predicting compound safety in humans has been larger for the health minded chemistry scientist, who considers these drugs with rigorous regulative needs. In this context, procedural approaches are used to assess the ADMET properties of compounds at the first stages of drug discovery and development. This study tends to evaluate drug-like properties of compounds through *in silico* predictions by victimization ADMET predictor software version. ADMET Predictor is a sophisticated technique that permits researchers to speedily predict an oversized variety of ADMET properties from molecular structure. Its prognostic models are based on the principle of vector algorithm square measure, with parameters like absorption, distribution, metabolism, excretion, and toxicity.

3.1.1. Absorption

After oral administration of drug, a convenient method of medication process will be very complicated. Lipophilicity is very important in *in silico* model, and is directly related to absorption properties like water solubility, gastrointestinal absorption, calcium carbonate permeability, and skin permeability. Molecular descriptors of *Gracilaria corticata* were calculated using ADME/T Predictor. The compound sulfurous acid is greater in intestinal fluid than other compounds. The gastric fluid absorption of the molecular descriptors ranges from 87 to 97% while in taking the drug compounds. However, the solubility of undecane simulated in fasted state of viscous fluid and fed state internal organ fluid didn't increase. Although, the solubility of sulfurous acid in fed state of internal organ was expected to have reduced permeability and

Table 2
Screening of Lipinski rule of five in bioactive compounds of *Gracilaria corticata*.

Compound Name	Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGp	Molar Refractivity
Sulfurous acid	82	2	3	0.54	13.53
Decane	142	0	0	4.14	48.28
2-ethylhexyl isohexyl ester	278	0	3	5	77.55
Undecane	156	0	0	4.53	52.09
Tridecanol	200	1	1	4.28	63.54
Hexatriacontane	506	0	0	14.21	168.32
Tricosane	325	0	0	9.21	108.30
Octacosane	394	0	0	11.16	131.38
Benzene	78	0	0	1.68	26.44
Mono (2-ethylhexyl) phthalate	278	1	4	3.75	76.98
10-Methylnonadecane	282	0	0	7.90	94.38
1-Iodo-2-methylundecane	297	0	0	5	70.66
Pentatriacontane	492	0	0	13.89	163.70
Tritriacontane	464	0	0	13.11	154.47
Nonacosane	408	0	0	11.55	136.00

Table 3
Absorption properties of drug compounds.

Compound Name	Water solubility (log mol/L)	Caco2 permeability (Log Pabb in 10^{-6} cm/Sec)	GI absorption (%)	Skin permeability (Log Kp)	P-glycoprotein substrate	P-glycoprotein I inhibitor
Sulfurous acid	0.859	1.083	87.69	−2.777	No	No
Decane	−5.586	1.38	93.10	−0.975	No	No
2-ethylhexyl isohexyl ester	−4.504	1.814	92.10	−2.19	No	Yes
Undecane	−6.156	1.379	92.76	−1.115	No	No
Tridecanol	−5.557	1.467	90.83	−1.829	No	No
Benzene	−1.817	1.544	95.90	−1.433	No	No
Mono (2-ethylhexyl) phthalate	−2.775	0.955	97.04	−2.731	No	No
1-Iodo-2-methylundecane	−6.913	1.393	92.30	−2.074	No	No

Table 4
Distribution screening of drug compounds.

Compound Name	VDss (human) (Log L/kg)	Fraction unbound (human) (Fu)	BBB permeability (Log BB)	CNS permeability (Log PS)
Sulfurous acid	−0.923	0.808	−0.469	−3.083
Decane	0.485	0.3	0.826	−1.744
2-ethylhexyl isohexyl ester	0.134	0.248	0.458	−2.218
Undecane	0.537	0.247	0.844	−1.69
Tridecanol	0.424	0.221	0.742	−1.901
Benzene	0.186	0.44	0.409	−1.557
Mono (2-ethylhexyl) phthalate	−1.265	0.257	−0.085	−2.247
1-Iodo-2-methylundecane	0.57	0.167	0.866	−1.684

Table 5
Metabolism screening of drug compounds.

Compound Name	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor
Sulfurous acid	No	No	No	No	No	No	No
Decane	No	No	No	No	No	No	No
2-ethylhexyl isohexyl ester	No	Yes	No	No	No	No	No
Undecane	No	No	No	No	No	No	No
Tridecanol	No	No	No	No	No	No	No
Benzene	No	No	Yes	No	No	No	No
Mono (2-ethylhexyl) phthalate	No	No	No	No	Yes	No	No
1-Iodo-2-methylundecane	No	No	No	No	No	No	No

logP as shown in Table 3. The absorption risk calculable by ADME/T Predictor, showed as S+Deflt_Risk, additionally confers improved fraction absorbed for all compounds than undecane and decane for oral administration, as according within the literature.

3.1.2. Distribution

Tissue distribution prediction of a drug is another necessary parameter in drug development. Molecular descriptors like logP, relative molecular mass, pKa, and logBBB play a major role in modelling the distribution parameter. Volume of distribution (VD) is another necessary parameter that relates the number of a drug within the body to its measured concentration, and is mainly relevant in deep tissue compartments.The distribution of all compounds below studied with regard to volume of distribution (VD), Blood Brain Barrier, Fraction unbound and Central Nervous System permeability was screened. This low volume of distribution for all compounds ensured diminished deep tissue penetration. Compounds like sulfurous acid and Mono (2-ethylhexyl) phthalate have satisfactory rate of distribution properties, as shown in Table 4. All of the compounds are stable and do not penetrate into the brain as well as the central nervous system. Some compounds have negative values, which mean they didn't have the ability to affect the immune system.

3.1.3. Metabolism

The biotransformation of enzymatic metabolism plays a major role in conversion of drug compounds. In the body, the enzymatic concentration will be constant at a particular active site with different drug concentrations. There are abundant enzymes that play a major role in catalysing the reaction with low relative drug concentration by following the principle of a first order process. The major enzyme cytochrome P450 catalyzes the oxidation reactions. The metabolism character was screened by phase 1 and phase 2, which was found to be metabolised via CYP3A4 and CYP2D6. The genetic variant isoforms of cytochrome – P450 includes CYP2C9 and CYP2C19 enzymes. The substrate and inhibitor of all compounds obey the rules except benzene and Mono (2-ethylhexyl) phthalate as shown in Table 5.

3.1.4. Excretion and toxicity

The excretion level of the kidney has been screened, in which all of the compounds have satisfied except 2-ethylhexyl isohexyl ester. The toxicity risk for all compounds was predicted as shown in Table 6. The dosage level for human as well as rat was screened by using the ADMET Modeler™ module in ADMET Predictor, in which the computational toxicology was built. All compounds can be used for oral intake, because none of the compounds have liver toxicity. All of the compounds have hepatoprotective activities with no phospholipid. Some compounds

Table 6
Excretion and Toxicity screening of drug compounds.

Compound Name	Renal OCT2 substrate	AMES toxicity	Max. tolerated dose (human) (Log mg/kg/day)	hERG I inhibitor	Oral Rat Acute Toxicity (LD50) (mol/kg)	Oral Rat Chronic Toxicity (LOAEL) (Log mg/kg)	Liver Toxicity	Skin Sensitisation
Sulfurous acid	No	No	1.394	No	1.963	2.594	No	No
Decane	No	No	0.463	No	1.637	2.613	No	No
2-ethylhexyl isohexyl ester	Yes	No	0.612	No	1.962	2.179	No	Yes
Undecane	No	No	0.389	No	1.597	2.689	No	Yes
Tridecanol	No	No	0.23	No	1.562	1.244	No	Yes
Benzene	No	No	1.051	No	1.872	2.131	No	No
Mono (2-ethylhexyl) phthalate	No	No	0.801	No	2.05	2.367	No	No
1-Iodo-2-methylundecane	No	No	0.285	No	1.983	1.228	No	Yes

Table 7
Interactions of various bioactive compounds of *Gracilaria corticata* against contractile proteins.

Compound	Binding energy	Van der Waals Interaction	No. Of hydrogen bonds	Hydrogen interactions	Total no of residues
Sulfurous acid	−5.79	GLN 138, GLY 75, ASN 13, ALA 109, GLY 14, ILE 72, SER 15, GLY 159, GLY 157, ASP 158, VAL	0	0	GLN 138, GLY 75, ASN 13, ALA 109, GLY 14, ILE 72, SER 15, GLY 159, GLY 157, ASP 158, VAL
Decane	−4.15	GLN 138, GLY 75, ASN 13, ALA 109, GLY 14, ILE 72, SER 15, GLY 159, GLY 157, ASP 158, VAL 160, ASP 155, PRO 110, HIS 162, ALA 139	0	0	GLN 138, GLY 75, ASN 13, ALA 109, GLY 14, ILE 72, SER 15, GLY 159, GLY 157, ASP 158, VAL 160, ASP 155, PRO 110, HIS 162, ALA 139
2-ethylhexyl isohexyl ester	−7.73	GLY 159, ASP 155, ASN 17, LYS 19, GLY 14, ASP 12, VAL 340, TRP 341, TYR 338, SER 339, LYS 337, GLY 302, GLY 303, PRO 110, SER 156, SER 161, GLN 138, ALA 109, GLY 75, HIS 162, GLY 157, VAL 160	3	SER 15, ASP 158, GLY 16	SER 15, ASP 158, GLY 16, GLY 159, ASP 155, ASN 17, LYS 19, GLY 14, ASP 12, VAL 340, TRP 341, TYR 338, SER 339, LYS 337, GLY 302, GLY 303, PRO 110, SER 156, SER 161, GLN 138, ALA 109, GLY 75, HIS 162, GLY 157, VAL 160
Undecane	−4.33	HIS 162, VAL 164, GLN 138, ASP 158, ALA 109, GLY 159, SER 15, GLY 14, ASN 13, GLY 75, GLY 157, VAL 160, SER 161, VAL 160, ASP 155, ALA 139, PRO 1100	0	0	HIS 162, VAL 164, GLN 138, ASP 158, ALA 109, GLY 159, SER 15, GLY 14, ASN 13, GLY 75, GLY 157, VAL 160, SER 161, VAL 160, ASP 155, ALA 139, PRO 110
Tridecanol	−5.87	LYS 19, ASP 12, ASP 155, SER 161, G;Y 157, VAL 160, HIS 162, SER 15, GLY 159, ASP 158, GLY 302, SER 142, TYR 338, TRP 341, LYS 337, SER 301	3	ARG 336, SER 339, VAL 340	ARG 336, SER 339, VAL 340, LYS 19, ASP 12, ASP 155, SER 161, G;Y 157, VAL 160, HIS 162, SER 15, GLY 159, ASP 158, GLY 302, SER 142, TYR 338, TRP 341, LYS 337, SER 301
Benzene	−3.20	VAL 340, ASP 12, LYS 19, TRP 341, TYR 338, LYS 337, SER 339, SER 301, ARG 336, GLY 302, ASP 155	0	0	VAL 340, ASP 12, LYS 19, TRP 341, TYR 338, LYS 337, SER 339, SER 301, ARG 336, GLY 302, ASP 155
Mono (2-ethylhexyl) phthalate	−8.73	GLY 303, LYS 337, GLY 302, ASP 12, GLY 157, ASN 13, GLY 75, GLN 138, ASP 155, HIS 162, G;LY 159, VAL 160, PRO 110, GLY 14, LYS 19	4	ASN 17, SER 15, GLY 16, ASP 158	ASN 17, SER 15, GLY 16, ASP 158, GLY 303, LYS 337, GLY 302, ASP 12, GLY 157, ASN 13, GLY 75, GLN 138, ASP 155, HIS 162, G;LY 159, VAL 160, PRO 110, GLY 14, LYS 19
1-Iodo-2-methylundecane	−5.57	LYS 19, TYR 338, TRP 341, SER 339, VAL 340, LYS 337, GLY 302, ASP 155, GLY 16, VAL 160, ASP 158, ASN 17, GLY 157, GLY 159, SER 15, GLY 14, GLN 138, ASP 12	0	0	LYS 19, TYR 338, TRP 341, SER 339, VAL 340, LYS 337, GLY 302, ASP 155, GLY 16, VAL 160, ASP 158, ASN 17, GLY 157, GLY 159, SER 15, GLY 14, GLN 138, ASP 12

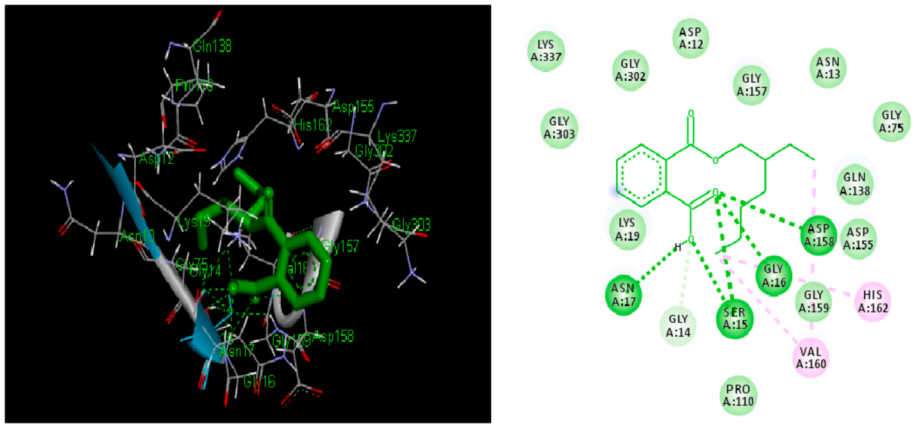

Fig. 2. 3D and 2D interactions of Mono (2-ethylhexyl) phthalate with amino acid coding.

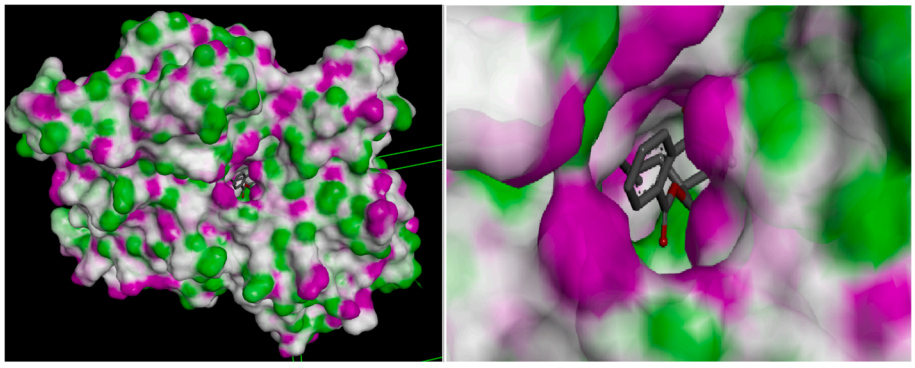

Fig. 3. Confirmation surface image of Mono (2-ethylhexyl) phthalate.

Table 8
QSAR Screening of Mono (2-ethylhexyl) phthalate.

Predictions	QSAR values of Mono (2-ethylhexyl) phthalate
CM	1316
PI	5.07 ± 1.41
R^2	0.758
Q^2	0.734
HC	5.07
NN	4.38
Sv	24.6227
Mp	0.6236
Ms	2.550
nAT	42.0
SCBO	25.0
Hy	−3.025
Ui	3.1699

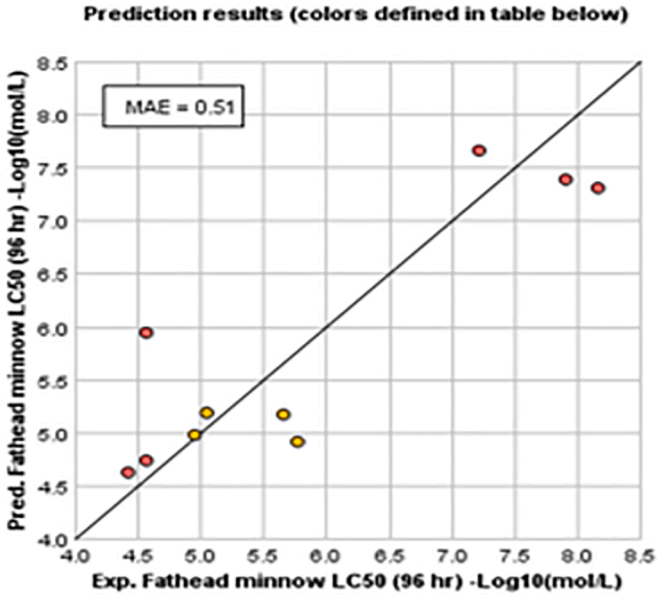

Fig. 4. Graphical representation of QSAR Mono (2-ethylhexyl) phthalate by predicting and experimenting for Fathead minnow.

have skin sensitisation properties that may be irritable physically in nature.

3.2. Molecular docking

Molecular docking plays a major role in identifying novel drug-like compounds that exhibit high binding affinity with selective targets and reasonable ADMET properties. The binding mode of the compounds was predicted using AutoDock 4.2.3 software [26,27]. As the first step, the crystal structure of protein compounds were retrieved from the PDB (Protein Data Bank) with ID: 6I4L that contains monastrol and allosteric binding sites. The binding sites of the atoms were visualized by Discovery Studio, in which hydrogen interactions, Van der Waals interaction, and polar and non-polar bonds were shown [28–30]. The interactions of the inhibited compounds with essential binding sites are exhibited in Table 7 and Figs. 2 and 3. The compounds result in a potent inhibitor against *Plasmodium falciparum*, with better binding affinity.

By investigating the binding mode of Mono (2-ethylhexyl) phthalate, it is clearly shown that the interactions were considered an important factor, in which we docked into an allosteric binding site, as shown in Fig. 1. The additional binding interactions like polar and non-polar bonds were also considered as strong potential candidates for inhibiting virulent enzymes.

3.3. QSAR prediction

The Quantitative Structure Activity Relationship plays a major role in predicting several parameters against Mono (2-ethylhexyl) phthalate, which has highest binding energy. The correlative values of set atoms present in drug molecules have cluster with nearest neighbour of atoms that has Van der Waals interactions with active sites. The compound has good state of atomic polarizability and electropological state. The hydrophilic factor of the compound Mono (2-ethylhexyl) phthalate may play a major role in increasing the binding affinity of drug compounds against virulent enzymes by showing potential inhibition, as noted in Table 8 and Fig. 4.

4. Conclusion

The designing of healthful drugs is a challenging problem that may be sorted out using advanced computational technologies. Structure-based ligand docking is an emerging tool being used for identification of drug molecules. The contractile protein that is mainly responsible for causing disease like *Plasmodium falciparum* has been retrieved from PDB. The crude crystal structure of the protein was scrutinized by removing heteroatomic molecules and hydrophobic molecules. The drug compounds of *Gracilaria corticata* were evaluated for their drug-like properties through *in silico* docking analysis along ADMET properties. Our research reveals that the bioactive compounds present in *Gracilaria corticata* have drug properties without any disturbance in the normal habitat of human internal conditions, that was confirmed by the Lipinski rule of five and ADMET properties. Among all of the studied compounds, the compound Mono (2-ethylhexyl) phthalate exhibited the highest binding energy of – 8.73 kcal/mol against contractile proteins, followed by compound 2-ethylhexyl isohexyl ester with binding energy −7.73 kcal/mol. Good correlations between protein ligand and ADMET prediction was observed. The QSAR predictions also show a better relationship with atom polarizability, electropological state, and hierarchical clustering. We concluded that a combination of ADMET and molecular docking helped to improve the potential inhibitor of drug compounds. For further studies, *in vitro* and *in vivo* studies will be carried out for developing drug ability of *Gracilaria corticata* against contractile proteins.

Ethics

Animal studies were not done in this research article.

Declaration of competing interest

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

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