Asian Journal of Biochemistry, Genetics and Molecular Biology

6(4): 14-24, 2020; Article no.AJBGMB.63352
ISSN: 2582-3698

An *In silico* Analysis of Some Bioactive Compounds of *Psidium guajava* against Target Proteins of *Vibrio cholerae*

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Authors' contributions

This work was carried out in collaboration among all authors. This research was conducted with considerable contribution of all authors. However, all the authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJBGMB/2020/v6i430158
Editor(s):
(1) Dr. Theocharis Koufakis, Aristotle University, Greece.
Reviewers:
(1) Azhari Hamid Nour, International University of Africa, Sudan.
(2) Idih, Favour Moses, Kogi State University, Nigeria.
Complete Peer review History: http://www.sdiarticle4.com/review-history/63352

Original Research Article

Received 02 October 2020
Accepted 09 December 2020
Published 29 December 2020

ABSTRACT

Introduction: Cholera is a destructive disease that causes extreme and intense water loss in the body. It takes between 12 hours and 5 days for an individual to show symptoms after ingesting contaminated food or water. It causes acute watery diarrhea in children and adults and if left untreated, it can lead to death within hours. Unfortunately, children are the most severely affected. In this study, molecular interactions of 24 bioactive compounds of *Psidium guajava* leaves against *Vibrio cholerae* targets proteins namely: Alanine racemase (PDB ID: 4BEQ), Cholera enterotoxin, A chain (PDB ID: 1S5F) and ToxT (PDB ID: 3GBG) were evaluated.
Methods: Molecular docking study was conducted and the 3D structures of bioactive compounds, Enzymes and the Enzyme-ligand interaction were visualized while Swiss ADME was employed to assess other physiochemical properties of these bioactive compounds.
Results and Discussion: The results from the molecular docking revealed that five bioactive compounds showed promising inhibitory activity, which include Spathulenol (Binding energy; -7.5, -6.5 and -9.1 kcal/mol in 4BEQ, 1S5F and 3GBG), Humulene oxide II (Binding energy; -7.1, -6.0 and

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-8.5 kcal/mol in 4BEQ, 1S5F and 3GBG), Globulol(-)-Globulol were -7.2, -6.5 and -9.0 kcal/mol in 4BEQ, 1S5F and 3GBG), Cadala-1(10),3,8-triene (Binding energy; -7.8, -6.8 and -9.8 kcal/mol in 4BEQ, 1S5F and 3GBG) and Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl (Binding energy; -6.9, -6.7 and -9.4 kcal/mol in 4BEQ, 1S5F and 3GBG) respectively.

Conclusion: In this study, it has been revealed that the carefully chosen bioactive compounds have the potential to be used alone or in combination with other natural products for developing potent antibacterial drugs (against cholera*)*. They can be further subjected to fractionation and isolation to confirm their activity towards in vitro and in vivo studies and can be commercialized as a potent antibacterial agent.

Keywords: Computational toxicology; molecular docking; Vibrio cholera; Psidium guajava; In silico analysis.

1. INTRODUCTION

Cholera is a destructive disease that causes extreme and intense water loss in the body. It takes between 12 hours and 5 days for an individual to show symptoms after ingesting contaminated food or water [1]. Cholera is currently predominant in developing countries in the tropics and subtropics and is endemic in Africa, parts of Asia, the Middle East as well as South and Central America [2]. As a global health problem, it is a marker of socioeconomic deprivation and the absence of social advancement. Epidemiological data revealed that there are 1.3 to 4.0 million cases and 21,000 to 143,000 deaths annually due to cholera [3]. It causes acute watery diarrhea in children and adults and if left untreated, it can lead to death within hours. Unfortunately, children are the most severely affected [4].

Furthermore, *Vibrio cholerae* is the causative agent of cholera which is an acute diarrheal infection caused by the ingestion of food or water contaminated with the bacterium *Vibrio cholerae* that belongs to genus vibrio, family Vibrionaceae [5]. *V. choleare* have several factors that help it to reach and colonize the epithelium of the small intestine and produce a variety of extracellular products that have deleterious effects on eukaryotic cells [6].

The transmission of cholera is primarily through the fecal-oral route of contaminated food or water caused by poor sanitation [2]. Most cholera cases in developed countries are caused by the consumption of contaminated food while in developing countries, it is caused by drinking contaminated water [7]. During the 19th century, cholera spread around the world from the Ganges delta in India [2]. Furthermore, six resulting cholera pandemics killed an enormous number of people all over the world [2]. The earlier (seventh) cholera pandemic began in South Asia in 1961, reached Africa in 1971 and the Americas in 1991 [8]. According to Ali [3], the global estimates for cholera cases and deaths are about 2.9 million and 95,000 per year, respectively. Disproportionately affecting sub-Saharan African countries especially since the onset of the seventh pandemic in 1961 [9]. For instance, 17 African countries reported over 150,000 cholera cases from all the outbreaks in 2017.

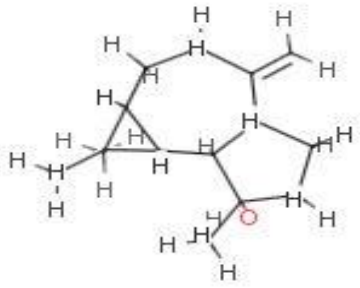
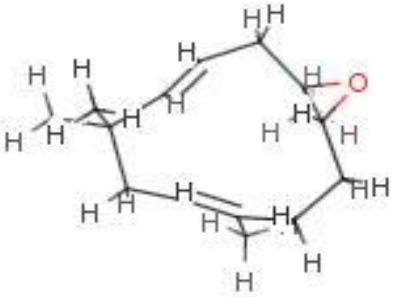
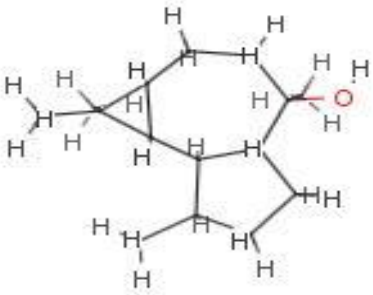
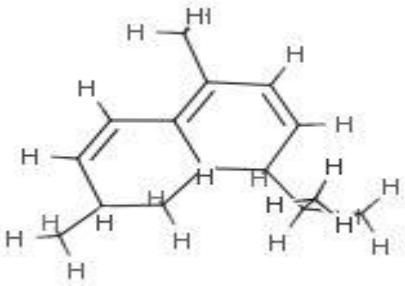
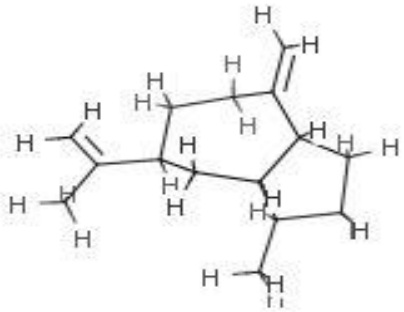
Historically, humans and animal medicine has relied heavily on plant extracts and most cultures of the world have a vast knowledge of herbal medicine for the treatment of animals, human as well as domestic plants. India is also endowed with varieties of plants that are known to have therapeutic qualities and different components of many therapeutic flowers are used for the treatment of various diseases due to their proven medicinal values since the ancient time [10]. More so, most of the medicine derived from naturally occurring plants has less or no side known health effects, which could be one important quality that cannot be overemphasized while most synthetic medicines have known or unknown side effects.

2. MATERIALS AND METHODS

2.1 Protein Preparation

The target protein structure with the PDB ID of 4BEQ, 1S5F and 3GBG for Alanine racemase, Cholera enterotoxin A chain and ToxT respectively, were retrieved from Protein Data Bank (https://www.rcsb.org/). The proteins are prepared by removing their original ligands and water molecules using PyMOL Molecular Graphics System version 1.1 [11]. Then all compounds from the data set were docked in the active site of the studied proteins. The preparation of the PDB file was done using Discovery Studio 2016 [12].

Table 1. Chemical Structures of promising *Psidium guajava* compounds

S/N	Compound Name	Structure	Pubchem ID
1	Spathulenol		92231
2	Humulene oxide II		10704181
3	Globulol(-)-Globulol		12304985
4	Cadala-1(10),3,8-triene		593889
5	Bicyclo[5.3.0]decane,2-methylene-5-(1- methylvinyl)-8-methyl		564533

2.2 Ligand Preparation

A literature database search of phytochemicals for *P. guajava* was carried out. At the end of the literature survey, compounds of the aforementioned plant were screened and used in the present research. 3D or 2D structures of phytochemicals were retrieved from the online database, PubChem (https://pubchem.Ncbi.nlm.nih.gov/) in sdf format. Open Babel molecule format converter was used for the conversion of 2D to 3D conformation and Marvin Sketch software (version 15.10.0) performed the conversion from SDF to pdf (for docking) and mol (for molecular properties prediction) file. Ligand's energy was minimized by relating the mmff94 force field and conjugate gradients optimization algorithm using PyRx- Python prescription 0.8**.**

2.3 Visual Screening, Molecular Docking and ADMET Analysis

Molecular docking analysis was employed to study the binding affinity and the type of interactions between all bioactive compounds and the target proteins.The steps for preparing ligands and proteins (4BEQ, 1S5F and 3GBG) for docking protocol were done in the Autodock 1.5.4 tools from MGL Tools package employing default settings.

A Grid box was positioned to cover the amino acid residues involved in the topology of the primary pocket of the three proteins. The parameters of the three coordinates were recorded, viz; (center X: 11.7114 Y: 25.6607 Z: 6. 2137 and Dimension (Angstrom) X: 25.000 Y: 25.0000 Z: 25.0000); (center X: 29.3138, Y: 40.9673, Z: 5656 and Dimension (Angstrom) X: 51.8995, Y: 53.3197, Z: 56.9062); (center X: 51.6140, Y: 52.4682, Z: 20.5143 and Dimension (Angstrom) X: 25.0000, Y: 25.0000, Z: 25.0000), for proteins 4BEQ, 1S5F and 3GBG respectively. Ligands that bind to the three proteins with high binding affinities in comparison to the standard drugs will be considered for further analysis. The analysis of protein-ligand interaction was done using Discovery studio 2016 and PyMOL. However, the estimation of the ADMET analysis was conducted using Drulito and SWISS ADME online software (http://swissadme.ch/index.php) as applied by previous researchers [13,14].

3. RESULTS AND DISCUSSION

The result in (Table 2) showed the binding affinity of all the twenty-four (24) phytochemicals present in *P. guajava* on 3 target proteins related to *V. cholerae.* Among those docking results, the complete value of binding affinities ranged from -5.4 to -10.0 (kcal/mol; Table 2). In this range, the highest results were recorded in five bioactive compounds, which their binding energies were found to be higher than the standard.

These are Spathulenol, Humulene oxide II, Globulol(-)-Globulol, Cadala-1(10),3,8-triene and Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl which were selected for pharmacophore analysis step. The binding affinities of Spathulenol were -7.5, -6.5 and -9.1 kcal/mol in 4BEQ, 1S5F and 3GBG respectively, Humulene oxide II were -7.1, -6.0 and -8.5 kcal/mol in 4BEQ, 1S5F and 3GBG respectively, Globulol(-)-Globulol were -7.2, -6.5 and -9.0 kcal/mol in 4BEQ, 1S5F and 3GBG respectively, Cadala-1(10),3,8-triene were -7.8, -6.8 and -9.8 kcal/mol in 4BEQ, 1S5F and 3GBG respectively, Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl were -6.9, -6.7 and -9.4 kcal/mol in 4BEQ, 1S5F and 3GBG respectively.

Based on the results obtained from Table 2, Cadala-1(10),3,8-triene showed the highest binding affinity in all three (3) targets proteins. In the same vein, 3GBG protein was the best receptor by showing the highest binding energy to the plant's bioactive compounds.

On the other hand, Humulene oxide II showed the lowest binding to all target proteins. Similarly, 1S5F protein was the least receptor by showing the lowest binding energy to the plant's bioactive compounds. Moreover, the interaction between phytochemicals and active site of 1S5F, 3GBG and 4BEQ proteins, recorded an excellent binding affinity of 100%, 95% and 75% respectively, in contrast with their respective standard drugs.

3.1 Protein-Ligand Interaction

All selected bioactive compounds can form either hydrophobic interaction or hydrogen bond with free residue in the active site of **4BEQ** protein. Spathulenol, Humulene oxide II, Globulol(-)-Globulol, Cadala-1(10),3,8-triene and Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl can build up hydrogen bond with TYR208 (B), TYR394 (A), PRO270 (B) and PRO391 (B) while amino residues, TYR299 (A), PRO270 (B), PRO391 (B), ILE389 (B), TYR78 (B), TYR299 (A), MET347 (A), PRO270 (A), PRO391 (A), ILE389 (A), TYR299 (B),

TYR318 (A), TYR208 (B), as shown in Table 3, the 4BEQ involved in strong hydrophobic bonds with the phytochemicals. Also, the hydrophobic interactions played an important role in docking result. The Cadala-1(10),3,8-triene compound showed strong contact with the receptors because of the presence of two benzene rings. Moreover, based on the Table 3 results, the amino acid residues TYR299 (A) and PRO391 (B) were frequently observed in ligand-receptor interactions, so they could be a critical part of the binding pocket.

1S5F: protein formed hydrogen bonds with bioactive compounds via amino acid residues SER122 (A) while some amino acid residues in the active site of 1S5F protein formed strong hydrophobic interaction with bioactive compounds, the amino acids residues are PHE31 (A), PHE223 (A), ILE222 (A), TYR30 (A), TYR121 (A), TYR226 (A), LYS17 (A), PRO120 (A), VAL218 (A), LYS17 (A), ILE222 (A), PHE223 (A), VAL218 (A), PHE31 (A), PRO120 (A) respectively.

3GBG protein-free residue active site formed a strong hydrophobic bond with selected phytochemicals as follows VAL81 (A), VAL83 (A), TYR12 (A), TYR20 (A), PHE22 (A), PHE33 (A), PHE69 (A), LEU25 (A), LEU61 (A), ILE256 (A), MET259 (A), TYR266 (A), ILE266 LYS31 (A), MET269 (A) respectively.

Table 2. Docking score (Kcal/mol) of the Alanine Racemase, Cholera enterotoxin, A Chain and ToxT (4BEQ, 1S5F & 3GBG) with selected compounds of *P. guajava* detected by molecular docking

	Phytochemical compounds		Binding Affinity (Kcal/mol)		
S/N	**Name**	**Pubchem CID**	**Alanine Racemase (PDB ID: 4BEQ)**	**Cholera enterotoxin, A Chain(PDB ID: 1S5F)**	**ToxT (PDB ID: 3GBG)**
1	Butanoic acid, 2-methyl-, methyl ester	24798703	-7.2	-6.2	-8.6
2	Alpha.-Humulene	5281520	-7.2	-6.5	-8.0
3	Germacrene D	5317570	-7.4	-6.8	-9.4
4	Beta.-Bisabolol	27208	-6.6	-6.0	-7.8
5	Alpha.-bisabolol	10586	-6.6	-5.9	-8.6
6	Beta.-Bisabolene	10104370	-6.8	-5.9	-9.0
7	Alpha.-Copaene	442355	-7.0	-7.2	-8.4
8	Trans-Caryophyllene	26318	-7.5	-6.4	-5.9
9	Delta.-Cadinene	441005	-7.4	-6.1	-10.0
10	(+)-Aromadendrene	11095734	-7.3	-6.3	-9.8
11	Hexadeca-2,6,10,14-tetraen	5365865	-6.7	-5.7	-5.9
12	Globulol(-)-Globulol	12304985	-7.2	-6.5	-9.0
13	Humulene oxide II	10704181	-7.1	-6.0	-8.5
14	Trans-Caryophyllene	5281515	-7.0	-7.0	-8.4
15	(-)-Caryophyllene oxide	1742210	-6.7	-6.9	-8.0
16	Nerolidol B (CIS OR TRANS	5284507	-6.4	-6.0	-8.0
17	cis-alpha-Bisabolene	5352653	-7.2	-6.1	-8.9
18	Cubenol	519857	-7.4	-6.4	-8.7
19	Spathulenol	92231	-7.5	-6.5	-9.1
20	Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl	564533	-6.9	-6.7	-9.4
21	Cadala-1(10),3,8-triene	593889	-7.8	-6.8	-9.8
22	Cis-muurola-3,5-diene	51351708	-6.8	-6.5	-9.7
23	Benzene, (1,3,3-trimethylnonyl)-	569261	-6.2	-6.1	-8.6
24	Eugenol	3314	-5.8	-5.4	-6.7

3.2 ADME/T Prediction of the Selected Compound

Through using SWISSADME online tools, the data was obtained and recorded as shown in Table. 4, various physical descriptors and pharmaceutically important properties were observed for ADME/T prediction. All the carefully chosen phytochemicals displayed essential values for the numerous criteria tested and displayed strong drug-like properties based on Lipinski's rule of five. The data gained were within the range of values for all-natural compounds. The significance of polar surface area (PSA) suggested for good oral bioavailability of natural compounds (Spathulenol, Humulene oxide II, Globulol(-)-Globulol, Cadala-1(10),3,8-triene and Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl). The parameters, such as number of rotatable bonds and number of stable bonds correlated with the product intestinal absorption, showed that all-natural compounds (Spathulenol, Humulene oxide II, Globulol(-)-Globulol, Cadala-1(10),3,8-triene and Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl) are well absorbed. All the bioactive compounds were found to be nontoxic because they are in agreement with five Lipinski's rules as shown in Table 4.

ADME/T prediction was done online using SwissAdme, which revealed that all carefully chosen bioactive compounds were in agreement with five Lipinski's rule. Therefore, it could be concluded that the selected bioactive compounds are good to inhibit all of the target proteins and will be essential to prevent cholera disease.

Table 3. Proteins ligand interaction and lig-plot

ToxT	Standard (Palmitoleic Acid)	Hydrogen bonding	TYR12 (A), TYR226(A), LYS230 (A), LYS31 (A)
		Hydrophobic interactions	VAL81(A), LEU71 (A), MET259 (A), TYR12 (A), TYR20 (A), TYR266 (A), PHE22 (A), PHE33 (A), PHE69 (A)
	Spathulenol	Hydrogen bonding	----------
		Hydrophobic interactions	VAL81 (A), VAL83 (A), TYR12 (A), TYR20 (A), PHE22 (A), PHE33 (A), PHE69 (A), LEU25 (A), LEU61 (A), ILE256 (A), MET259 (A)
	Humulene oxide II	Hydrogen bonding	----------
		Hydrophobic interactions	VAL81 (A), VAL83 (A), PHE22 (A), PHE33 (A), PHE69 (A), LEU25 (A), LEU61 (A), TYR12 (A), TYR20 (A), MET259 (A)
	Globulol(-)-Globulol	Hydrogen bonding	----------
		Hydrophobic interactions	VAL81 (A), VAL83 (A), PHE22 (A), PHE33 (A), PHE69 (A), TYR12 (A), TYR20 (A), TYR266 (A), LEU25 (A), MET259 (A), ILE266 (A)
	Cadala-1(10),3,8-triene	Hydrogen bonding	----------
		Hydrophobic interactions	VAL81 (A), VAL83 (A), TYR12 (A), TYR266 (A), LYS31 (A), MET269 (A), PHE22 (A), PHE33 (A)
	Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl	Hydrogen bonding	----------
		Hydrophobic interactions	VAL81 (A), VAL83 (A), TYR12 (A), TYR20 (A), PHE22 (A), PHE33 (A), PHE69 (A)
	Standard B-D-galactopyronose	Hydrogen bonding	TYR121 (A), TYR226 (A)
		Hydrophobic interactions	--------
	Spathulenol	Hydrogen bonding	----------
		Hydrophobic interactions	PHE31 (A),PHE223 (A), ILE222 (A), TYR30 (A),

			TYR121 (A), TYR226 (A), LYS17 (A), PRO120 (A), VAL218 (A)
Cholera enterotoxin, A chain	Humulene oxide II	Hydrogen bonding	----------
		Hydrophobic interactions	LYS17 (A), ILE222 (A), TYR121 (A), TYR226 (A), PHE223 (A)
	Globulol(-)-Globulol	Hydrogen bonding	SER122 (A)
		Hydrophobic interactions	VAL218 (A), PHE31 (A), ILE222 (A), TYR121 (A), LYS17 (A)
	Cadala-1(10),3,8-triene	Hydrogen bonding	----------
		Hydrophobic interactions	VAL218 (A), PHE31 (A), TYR121 (A), ILE222 (A), LYS17 (A)
	Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl	Hydrogen bonding	----------
		Hydrophobic interactions	VAL218 (A), PHE31 (A), PRO120 (A), TYR226 (A), ILE222 (A)
ALANINE RACEMASE	Standard (Pyridoxal-5-phosphate)	Hydrogen bonding	ASP268 (A), ASP300 (B), PRO391 (A), ARG324 (B)
		Hydrophobic interactions	TYR208 (A), TYR299 (B)
	Spathulenol	Hydrogen bonding	TYR208 (B)
		Hydrophobic interactions	TYR299 (A), PRO270 (B), PRO391 (B), ILE389 (B)
	Humulene oxide II	Hydrogen bonding	TYR208 (B)
		Hydrophobic interactions	PRO391 (B), TYR78 (B), TYR299 (A), MET347 (A)
	Globulol(-)-Globulol	Hydrogen bonding	TYR394 (A)
		Hydrophobic interactions	PRO270 (A), PRO391 (A), ILE389 (A), TYR299 (B)
	Cadala-1(10),3,8-triene	Hydrogen bonding	----------
		Hydrophobic interactions	TYR299 (A), TYR318 (A), TYR208 (B), ILE389 (B)
	Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl	Hydrogen bonding	PRO270 (B), PRO391 (B)
		Hydrophobic interactions	TYR299 (A), TYR318 (A), TYR208 (B), PRO270 (B), PRO391 (B)

Table 4. Prediction of Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) properties of the compounds

Compounds Pubchem ID	MW	LogP	HB acceptor	HB donor	Molecular refractivity
92231	220.18	4.157	1	1	65.87
10704181	220.18	4.314	1	0	68.99
12304985	222.2	5.078	1	1	64.3
593889	202.17	6.076	0	0	68.83
564533	204.19	6.092	0	0	64.16

a. Molecular weight (MW) (acceptable range: <500)
b. Hydrogen bond (HB) donor (acceptable range: ≤5)
c. Hydrogen bond (HB) acceptor (acceptable range: ≤10)
d. High lipophilicity (expressed as LogP, acceptable range: ≤5)
e. Molecular refractivity should be 40-130

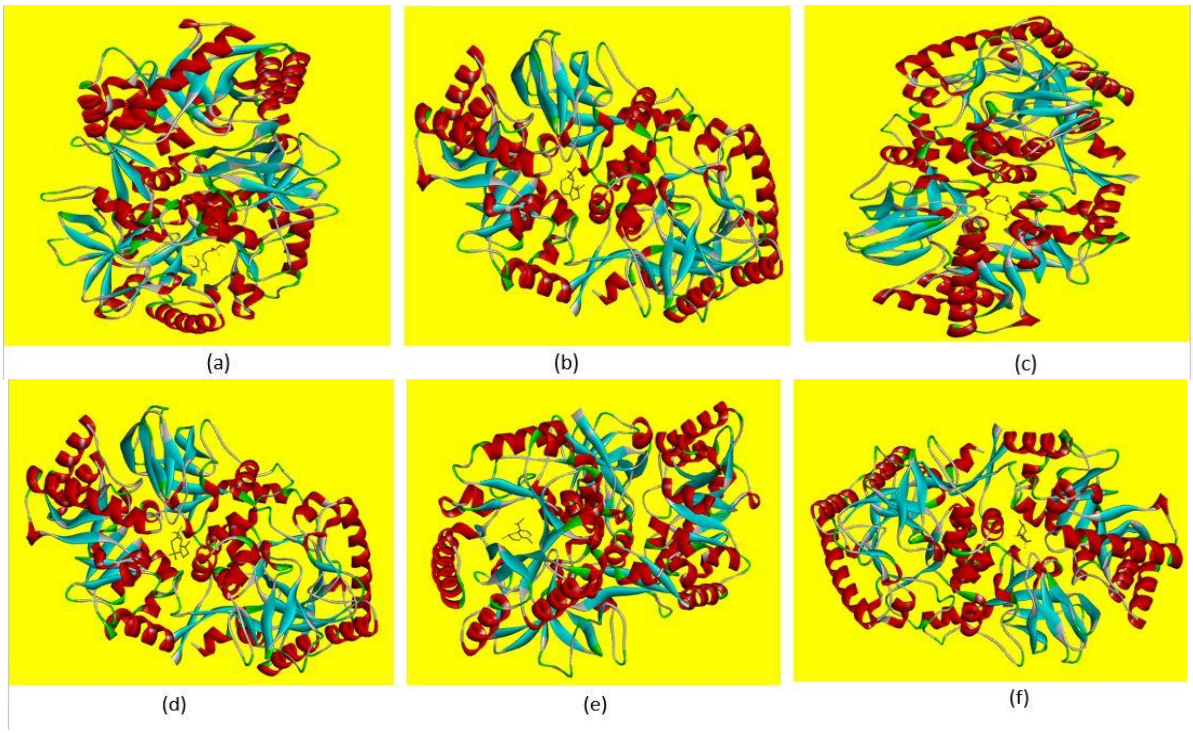


Fig. 1. Ribbon presentation of Alanine Racemase (PDB: 4BEQ) with promising compounds of *P. guajava*. (a) Alanine Racemase-Pyridoxal-5-phosphate (Standard), (b) Alanine Racemase-Spathulenol, (c) Alanine Racemase-Humulene oxide II, (d) Alanine Racemase-Globulol(-)-Globulol, (e) Alanine Racemase-Cadala-1(10),3,8-triene, (f) Alanine Racemase-Bicyclo[5.3.0]decane, 2-methylene-5-(1- methylvinyl)-8-methyl

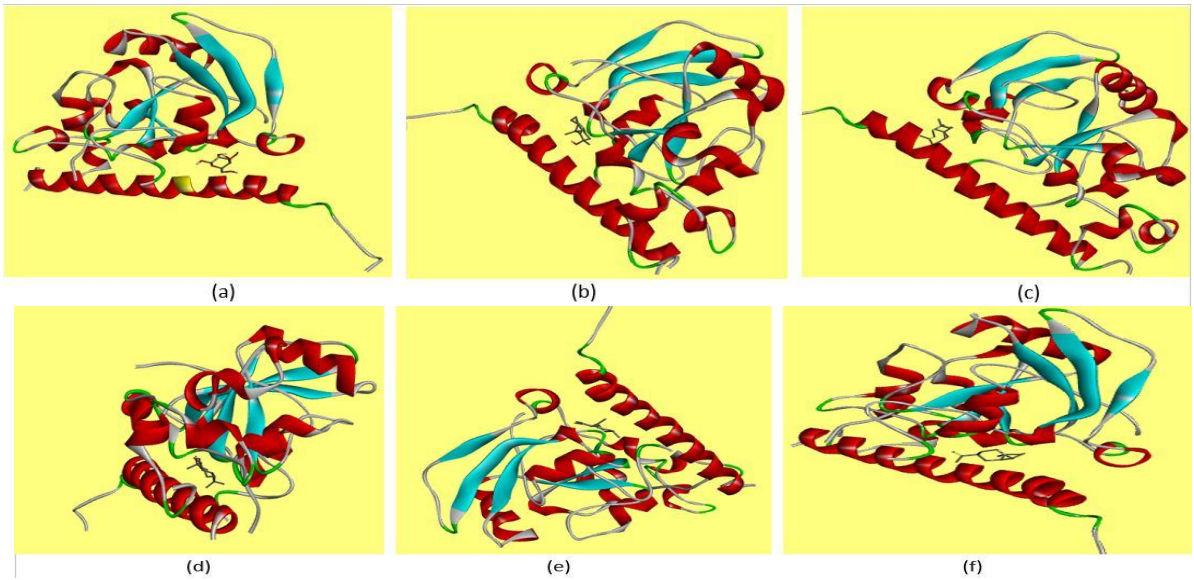


Fig. 2. Ribbon presentation of Cholera enterotoxin, A Chain (PDB: 1S5F) with promising compounds of *P. guajava*. (a) Cholera enterotoxin, A Chain-B-D-galactopyronose (Standard), (b) Cholera enterotoxin, A Chain-Spathulenol, (c) Cholera enterotoxin, A Chain-Humulene oxide II, (d) Cholera enterotoxin, A Chain-Globulol(-)-Globulol, (e) Cholera enterotoxin, A Chain-Cadala-1(10),3,8-triene, (f) Cholera enterotoxin, A Chain-Bicyclo[5.3.0]decane, 2-methylene-5-(1- methylvinyl)-8-methyl

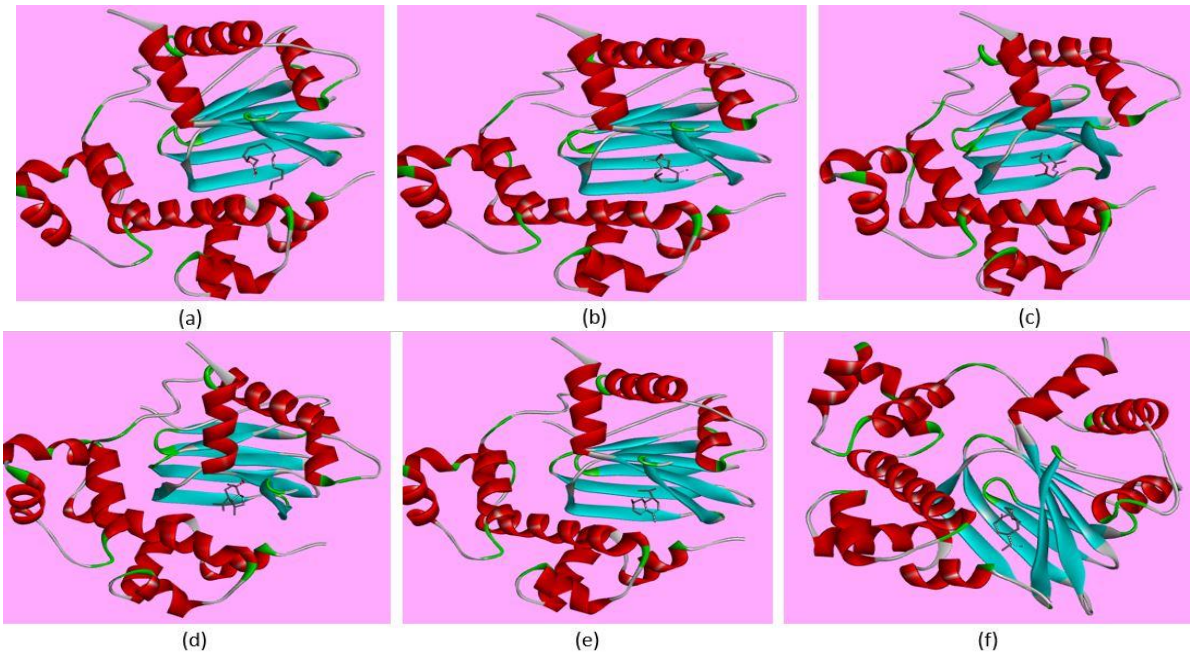


Fig. 3. Ribbon presentation of ToxT (PDB: 3GBG) with promising compounds of *P. guajava*. (a) ToxT-Palmitoleic Acid (Standard), (b) ToxT-Spathulenol, (c) ToxT-Humulene oxide II, (d) ToxT-Globulol(-)-Globulol, (e) ToxT-Cadala-1(10),3,8-triene, (f) ToxT-Bicyclo[5.3.0]decane, 2-methylene-5-(1- methylvinyl)-8-methyl

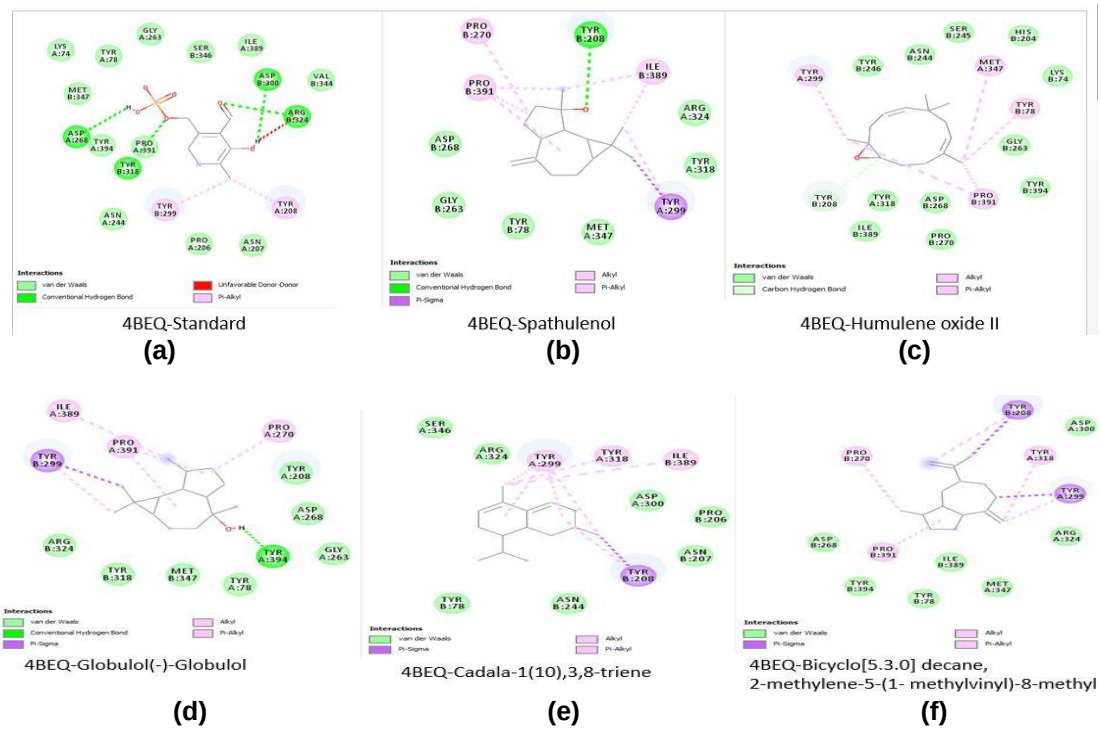


Fig. 4. 2D representation of the interactions between the best pose found for Alanine Racemase (PDB: 4BEQ) with promising compounds of *P. guajava*. (a) Alanine Racemase-Pyridoxal-5-phosphate (Standard), (b) Alanine Racemase-Spathulenol, (c) Alanine Racemase-Humulene oxide II, (d) Alanine Racemase-Globulol(-)-Globulol, (e) Alanine Racemase-Cadala-1(10),3,8-triene, (f) Alanine Racemase-Bicyclo[5.3.0]decane, 2-methylene-5-(1- methylvinyl)-8-methyl

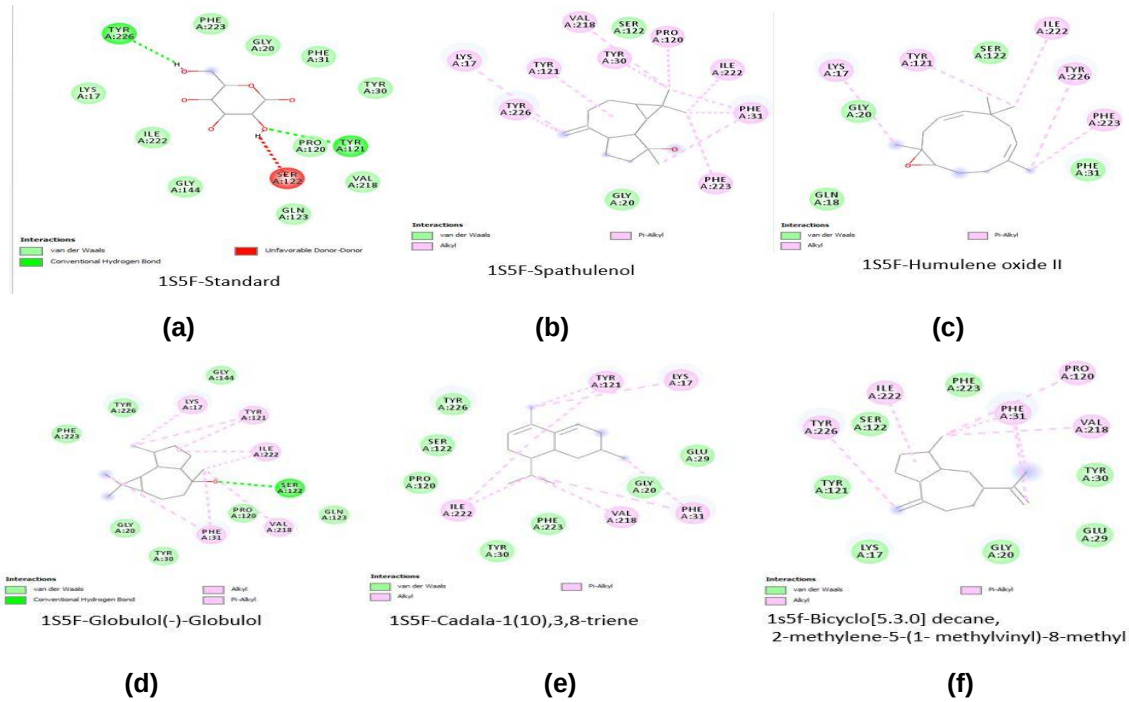


Fig. 5. 2D representation of the interactions between the best pose found for Cholera enterotoxin, A Chain (PDB: 1S5F) with promising compounds of *P. guajava*. (a) Cholera enterotoxin, A Chain-B-D-galactopyronose (Standard), (b) Cholera enterotoxin, A Chain-Spathulenol, (c) Cholera enterotoxin, A Chain-Humulene oxide II, (d) Cholera enterotoxin, A Chain-Globulol(-)-Globulol, (e) Cholera enterotoxin, A Chain-Cadala-1(10),3,8-triene, (f) Cholera enterotoxin, A Chain-Bicyclo[5.3.0]decane, 2-methylene-5-(1- methylvinyl)-8-methyl

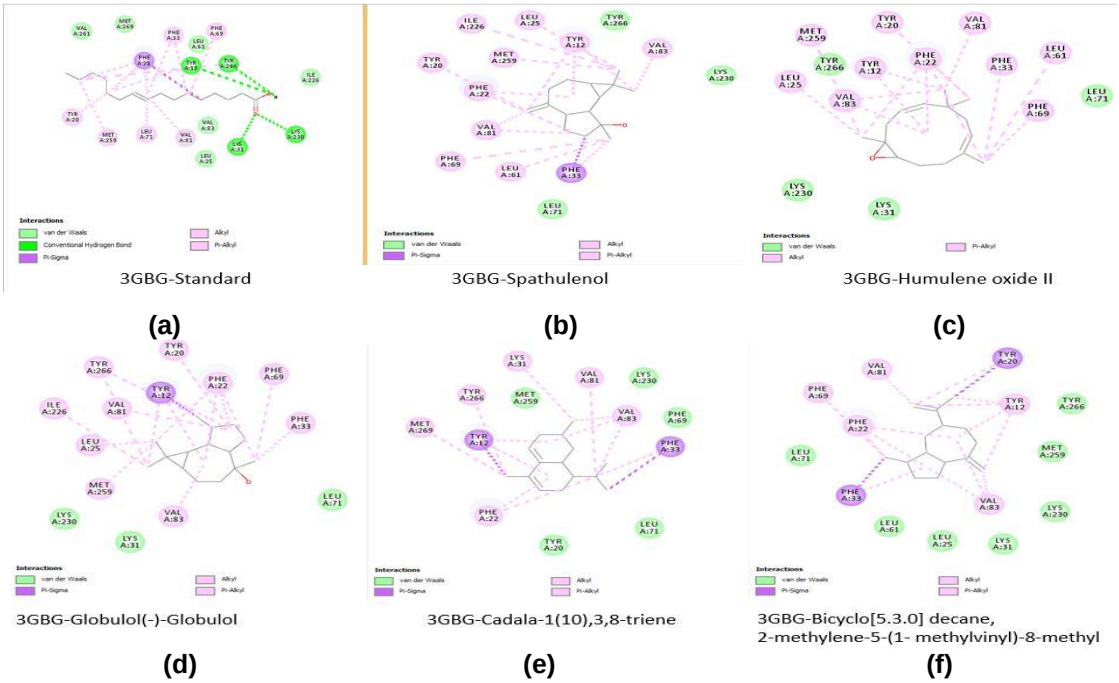


Fig. 6. 2D representation of the interactions between the best pose found for ToxT (PDB: 3GBG) with promising compounds of *P. guajava*. (a) ToxT-Palmitoleic Acid (Standard), (b) ToxT-Spathulenol, (c) ToxT-Humulene oxide II, (d) ToxT-Globulol(-)-Globulol, (e) ToxT-Cadala-1(10),3,8-triene, (f) ToxT-Bicyclo[5.3.0]decane,2-methylene-5-(1- methylvinyl)-8-methyl

4. CONCLUSION

Cholera is a serious disease that pose a great threat to the life of many people, particularly in developing countries, taking this into consideration, there is a need for effective drugs with less/no toxicity and one of the best ways is the use of herbal medicines which mostly have less side effects compared to synthetic drugs. In this study, it has been revealed that the carefully chosen bioactive compounds have good docking score and strong hydrophobic interactions and some H-bonding and follows the Lipinski rules of five. Therefore, these phytochemicals could have the potential to be used alone or in combination with other natural products for developing potent antibacterial drugs (against cholera).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Azman AS, Rudolph KE, Cummings DA, Lessler J. The incubation period of cholera: A systematic review. J Infect. 2013;66(5): 432-8.
   DOI: 10.1016/j.jinf.2012.11.013
2. World Health Organization / Emerging and other Communicable Disease, Surveillance and Control. WHO guidance on formation of national policy on the control of cholera. WHO/CDD/SER/92.16. [Accessed 2018 Jun 14]
   Available:https://www.who.int/topics/cholera/publications/WHO_CDD_SER_92_16/en
3. Ali M, Nelson AR, Lopez AL, Sack DA. Updated global burden of cholera in endemic countries. PLoS neglected tropical diseases. 2015:9(6).
4. Centers for Disease Control and Prevention. Cholera – *Vibrio cholerae* infection; 2014.
   [Accessed 2018 Jun 14]
   Available:https://www.cdc.gov/cholera/index.html
5. Halpern M, Izhaki I. Fish as Hosts of *Vibrio cholerae*. Frontiers in Microbiology. 2017;8:282.
   DOI: 10.3389/fmicb.2017.00282
6. Matthey N, Blokesch M. The DNA-Uptake Process of Naturally Competent *Vibrio cholerae*. Trends Microbiol. 2016;24(2): 98-110.
   DOI: 10.1016/j.tim.2015.10.008
7. Sack DA, Sack RB, Nair GB, Siddique AK. Cholera. Lancet. 2004;363(9404):223-33.
   DOI: 10.1016/S0140-6736(03)15328-7.
8. World Health organization. Cholera - key facts. 2018 [accessed 2018 Jun 14]. Available:http://www.who.int/en/newsroom/fact-sheets/detail/cholera.
9. Clemens JD, Nair GB, Ahmed T, Qadri F, Holmgren J. Cholera. The Lancet. 2017;390(10101):1539–1549.
   DOI: 10.1016/s0140-6736(17)30559-7
10. Verma AK, Maurya SK, Kumar A, Barik M, Yadav V, Umar B, et al. Inhibition of multidrug resistance property of Candida albicans by natural compounds of parthenium hysterophorus L . An In- Silico approach. Journal of Pharmacognosy and Phytochemistry. 2020:9(3);55–64.
11. DeLano WL. The PyMOL Molecular Graphics System, DeLano Scientific LLC, San Carlos, CA. 2002.
12. Pilot P. Dassault Systèmes BIOVIA, discovery studio modelling environment; 2016.
13. Danyaya AI, Verma AK, Kumar A, Shuaibu BS, Hamza UA, Yahya NL, et al. Virtual screening, molecular docking and ADME/T analysis of natural product against cell invasion protein SipB from Salmonella enterica serotype typhi: *In silico* analysis. Acta Scientific Pharmaceutical Science. 2020;4(8);20-30.
14. Lawal M, Verma AK, Umar IA, Gadanya AM, Umar B, Yahaya NL, et al. Analysis of new potent Anti-Diabetic molecules from phytochemicals of pistia strateotes of Homo sapiens for treatment of diabetes mellitus. An silico Approach. IOSR Journal of Pharmacy and Biological Sciences. 2020;15(4):59-73.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/63352