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RESEARCH ARTICLE

Fragaria Indica ethanolic extracts: bioactive compounds identification, ADMET analysis and putative inhibitors of bla-TEM beta-lactamase from foodborne bacterial pathogens

Abdullah, K.[1], Rahman, H.[1*], Tabassum, T.[1], Sadiq, A.[2], Alzahrani, F.M.[3], Alzahrani, K.J.[3], Alsharif, K.A.[3]

[1]Department of Microbiology, Abdul Wali Khan University Mardan, Pakistan
[2]Department of Pharmacy, University of Malakand, Chakdara, Pakistan
[3]Department of Clinical Laboratories Sciences, College of Applied Medical Sciences, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia
*Corresponding author: hazirrahman@awkum.edu.pk

ARTICLE HISTORY

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ABSTRACT

Fragaria indica stem, leaf, and root extract was used to assess the antimicrobial activity against bla-TEM beta-lactamase producing *Shigella flexneri*, *Salmonella typhi*, and *Escherichia coli.* Ethanolic extracts of *F. indica* leaves exhibited a maximum zone of inhibition of 20 ± 1.2 mm ($p \leq 0.001$), 18 ± 1.4 mm ($p \leq 0.001$), and 16 ± 1.5 mm ($p \leq 0.001$) against *E. coli*, *S. flexneri*, and *S. typhi*, respectively. To identify different compounds, the bioactive ethanolic leaf extracts were further processed for HPLC, GC-MS, ADMET, and docking analysis. In the ethanolic leaf extract, 19 phenolic compounds were identified in HPLC analysis. Three phenolic compounds, including Isorhamnetin-3-rutinoside, 5, 7-Dihydroxy-4' -methoxyflavone, and Luteolin, were for the first time reported in *F. indica.* In GC-MS analysis, sixteen compounds were identified. From the literature search, among the identified compounds, Alpha-Himachalene, 1,3-Diphenyl-1-((trimethylsilyl)oxy)-1(Z)-heptene, 1H-Benzocycloheptene, Bicyclo[5.2.0] nonane, cis-1,1,3,4-Tetramethylcyclopentane, Bicyclo[2.2.2]octane-cis-2,3-diyl Carbonate, Beta-Himachalene and 2-methylene-4,8,8-trimethyl-4-vinyl were reported for the first time in *F. indica*. Two compounds, including Alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate, having good water solubility, drug likeness, and medicinal characteristics, were selected for docking analysis. Docking of Alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate showed interaction with Pro-26, Phe-22, and Ala-23 residues of bacterial bla-TEM beta-lactamase. Similarly, Bicyclo[2.2.2] octane-cis-2,3-diyl carbonate interacts with amino acid residues of Ala-235 and Ser-233 of bla-TEM beta-lactamase. Further studies will help to characterize the anti-infective compounds against bla-TEM producing foodborne bacterial pathogens.

Keywords: *Fragaria indica*; bla-TEM bacteria; bioactive compounds; ADMET; molecular docking.

INTRODUCTION

Plants are a potential source of bioactive compounds. These compounds include a range of phytochemicals that have the ability to function in oxidative stress, anti-cancer, and antimicrobial (Chang *et al*., 2016; Samuel *et al*., 2023; Soingam & Srithaworn, 2023). *Fragaria indica* or *Duchesnea indica*, belongs to the family Rosaceae, widely distributed in the Southeast Asian region. The *Fragaria* fruit is a rich source of vitamin C, iron, protein, calcium, potassium, and magnesium, while its leaves as an aqueous extract are in use for several diseases (Mundnic *et al*., 2009; Hussain *et al*., 2011). *Fragaria indica* is used for mucous lining irritation, laryngitis, and acute tonsillitis (Saju & Sivaraman, 2021). Gastrointestinal diseases accounted for a global prevalence of over 200 million (Wang *et al*., 2023). Almost half of the digestive diseases are attributable to foodborne transmission, and about 30% of food-transmitted diseases are caused by bacteria (Mead *et al*., 1999). *Shigella flexneri, Escherichia coli,* and *Salmonella typhi* are foodborne pathogens causing diarrheal and enteric diseases (Kirk *et al*., 2015; Horn & Bhunia, 2018).

A high resistance rate is reported among these gastrointestinal pathogens against available antibiotics (Asrat, 2008). Further, antibiotic resistance, particularly from extended-spectrum β-lactamase producing (ESBL), poses a significant global health challenge that leads to the failure of empirical antibiotic therapy (Husna *et al*., 2023). The bla-TEM beta-lactamase has been recognized as among the most prevalent ESBL, conferring antibiotic resistance in pathogenic bacteria worldwide. Traditional bla-TEM beta-lactamase hydrolyzes the beta-lactam ring, and its overexpression results in cephalosporin resistance (Dirar *et al*., 2020). bla-TEM is previously reported in *E. coli* and *Salmonella* (Tran *et al*., 2021).

Nowadays, analytical methods coupled with computational tools have been successfully employed to screen medicinal molecules. The evaluation of a compound's absorption, distribution, metabolism, excretion, and toxicity (ADMET) along with Lipinski's

rule are important tools to explore the drug-likeness, synthetic chemistry, and biological characteristics of lead molecules (Lipinski *et al*., 2001; Daina *et al*., 2017). Further docking has been performed to assess the interaction between the lead and protein residues (Bouamrane *et al*., 2022). A growing body of literature is available on *F. indica* extract activity (Mundnic *et al*., 2009; Hussain *et al*., 2011; Amit *et al*., 2023); however, there is a lack of data on the *F. indica* extract against bla-TEM producing foodborne bacterial pathogens.

In the present study, *F. indica* extracts have been evaluated against *S. flexneri*, *E. coli* and *S. typhi*. Further ADMET and molecular docking analysis of the identified compounds was performed. The study will help to explore novel medicinal molecules against bla-TEM producing foodborne pathogens.

MATERIALS AND METHODS

Collection and extraction of plant

Fragaria indica was obtained from Dir (lower), Khyber Pakhtunkhwa, Pakistan. The plant taxonomist at the Department of Botany, Malakand University, Chakdara, Pakistan, has identified the plant and submitted it with a voucher number (HUOM.BG.551). Plant extracts were prepared as described earlier (Tabassum *et al*., 2022). *Fragaria indica* leaves, stems, and roots were separately dried and ground. Each of the plant materials (100g) was soaked in 1000 ml of ethanol and distilled water for 8 days. Each beaker was agitated continuously 2 times a day for 5 minutes for complete extraction. After filtration, the crude extract (stem, leaves, and roots) was dried using a rotary evaporator at 44°C. For further research, the plant extract was kept in sterile glass bottles.

Collection of MDR gastrointestinal bacterial strains

The MDR bla-TEM producing bacteria (*S. typhi, S. flexneri, E. coli*) were obtained from the Department of Microbiology, Kohat University, Kohat, Pakistan.

Antimicrobial activity of *F. indica* extracts

Fragaria indica extracts were prepared as previously reported (Tabassum *et al*., 2022). A fresh bacterial culture equivalent to the turbidity standard (0.5 McFarland) was inoculated on a Mueller-Hinton agar plate separately. Plant extracts were added in each well and incubated for 24 hours at 37°C. Gentamicin was taken as an antibiotic control. A scale in millimeters was used to measure the zone of inhibition.

HPLC analysis for phenolic compounds

Ethanolic extracts of *F. indica* leaves were processed for HPLC. Briefly, plant extract (40 ml) was diluted in 100% methanol (10 ml). The sample was kept in shaking incubation for one hour. Samples were filtered by using a 0.45 µm PFTE filter (Agilent Technologies, Germany) into vials where 50 µL was the injection volume. In parallel, known phenolic compound standards were run as described previously (Zeb, 2015). Three experimental replicates were processed for HPLC analysis.

GC-MS analysis of leaves ethanolic extract

Ethanolic extracts were processed for GC-MS. The GS-MS dependent on the fragmentation spectra and nature of parent ions. For all the analysis, the parameters were the same as described earlier (Ayaz *et al*., 2017). The structure of identified compounds was compared with the library.

GC-MS was performed (USB-393752, Agilent Technologies, Palo Alto, CA, USA) with a acapillary column (30 m × 0.25 mm × 0.25 µm film thickness) prepared with a mass selective detector (Agilent HP-5973). Further, the electron impact mode with ionization energy was set at 70 eV. Three experimental replicates were processed for GC-MS analysis.

ADMET analysis

The structure parameters and SMILES of bioactive compounds were determined by using the online database program PubChem (https://pubchem.ncbi.nlm.nih.gov/, accessed on 15 March 2025). The SWISS-ADME (http://www.swissadme.ch/, retrieved on 19 March 2025) and ProTox 3.0 (https://tox.charite.de/protox3/, accessed on 20 March 2025) online tools were used for ADMET analysis and toxicity parameters.

Preparation of bal-TEM for docking analysis

The bla-TEM protein sequence was obtained from the UniProt. The bla-TEM protein structure (AF-P62594-F1-model_v4) was retrieved from the Protein Data Bank (https://www.rcsb.org/). The Autodoc (https://www.swissdock.ch/, accessed on 10 March 2025) (Jerome *et al*., 2021) and MOE software (2016.08) were used for docking.

Data analysis

ANOVA was used, and $p \leq 0.05$ was considered significant. The experiments were replicated three times.

RESULTS

Fragaria indica crude extracts antibacterial activity against MDR GI bacteria

The plant materials of *F. indica* were obtained from the hilly area of Dir, Khyber Pakhtunkhwa, Pakistan (Figure 1).

Figure 1. *Fragaria indica* plant collected from Lower Dir, Pakistan.

Table 1. *Fragaria indica* crude extracts activity against bla-TEM producing foodborne pathogens

Plant Parts Used	Plant extract	Bacteria	Zone of Inhibition (mm)
Roots	Aqueous	*S. typhi*	13 ± 1.5***
		S. flexneri	10 ± 1.0***
		E. coli	8 ± 1.2***
	Ethanol	*S. typhi*	11 ± 1.5***
		S. flexneri	12 ± 1.4***
		E. coli	10 ± 0.8**
Stem	Aqueous	*S. typhi*	12 ± 1.5***
		S. flexneri	10 ± 1.4***
		E. coli	7 ± 1.3*
	Ethanol	*S. typhi*	14 ± 1.5***
		S. flexneri	16 ± 1.6***
		E. coli	15 ± 1.2***
Leaves	Aqueous	*S. typhi*	14 ± 1.5***
		S. flexneri	13 ± 1.1***
		E. coli	15 ± 1.4***
	Ethanol	*S. typhi*	16 ± 1.5***
		S. flexneri	18 ± 1.4***
		E. coli	20 ± 1.2***
Gentamicin	*S. flexneri*		21 ± 0.80
	S. typhi		23 ± 1.10
	E. coli		27 ± 0.20

Note: *= $p \leq 0.05$; **= $p \leq 0.01$; ***= $p \leq 0.001$.

Table 2. Phenolics profile of *F. indica* leaves using HPLC

Peak	Identity	Mean	RT (min)	STD
1.	p-Hydroxybenzoic acid	445.7	1	7.3
2.	Kaempferol-7-glucoside	22.1	8.5	0.3
3.	Ellagic acid	52.7	10.9	0.5
4.	Ellagic acid deoxyhexoside	4.1	18.9	0.02
5.	5-Vanilloylquinic acid	4.2	3.4	0.08
6.	Kaempferol-3-glucoside	21.4	12.5	0.5
7.	Apigenin-7-glucuronide	10.9	7	0.1
8.	Kaempferol-7-glucuronide	5.8	15.6	0.09
9.	Quercetin-3-rutinoside	40.6	11.6	0.6
10.	Ellagic acid-pentoside	7.7	16.3	0.1
11.	Kaempferol-7-(6”-malonyl)-glucoside	5.5	17.3	0.06
12.	5, 7-Dihydroxy-42 -methoxyflavone	3.2	19.4	0.0
13.	Isorhamnetin-3-rutinoside	6.5	14.6	0.07
14.	Quercetin 3-(methoxycaffeoyldiglucoside)-7-Glucoside	9.6	31.7	0.1
15.	Quercetin-7-(6”-*O*-malonyl)-glucoside	7.2	28	0.06
16.	Petunidin-3-glucoside	6.1	33.5	0.1
17.	Quercetin	5.5	23.6	0.1
18.	Luteolin	2.4	24.8	0.06
19.	Quercetin-3-*O*-63 -acetylglucoside	2.9	22.5	0.1

The *F. indica* extracts of the roots, leaves, and stem of *F. indica* were checked for antimicrobial activity against *S. typhi, S. flexneri* and *E. coli*. Among the extracts, the ethanolic leaf extracts exhibited a zone of inhibition against *S. typhi* (16 ± 1.5 mm), *S. flexneri* (18 ± 1.4 mm), and *E. coli* (20 ± 1.2 mm) (Table 1).

Elucidation of compounds in leaves ethanolic extracts of *F. indica*

The bioactive ethanol extracts were processed for the identification of phenolic compounds on HPLC. 19 phenolic compounds were identified (Figure 2, Table 2).

On GC-MS, among the 16 identified compounds, 7 compounds were for the first time reported in *F. indica* (Table 3). The physicochemical, pharmacokinetic, druggable, and medicinal characteristics of the new compounds are listed (Table 4). Based on water solubility and druglikeness characteristics, only two compounds, including Alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate, were selected for docking analysis.

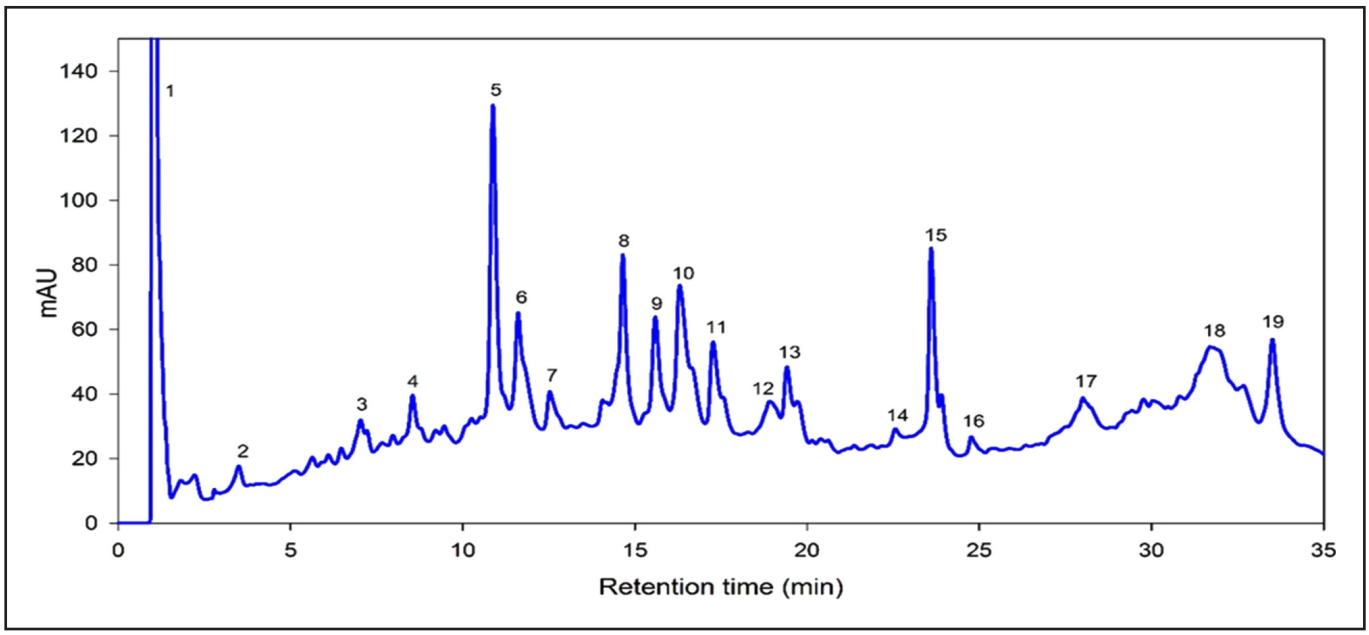
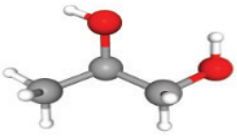
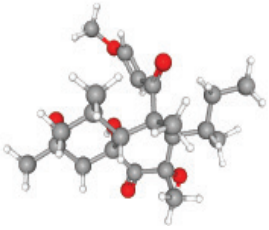
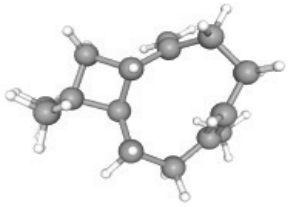
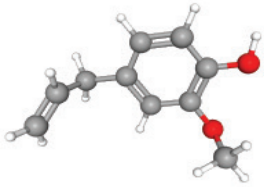
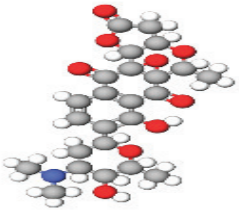
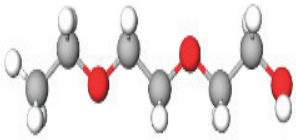
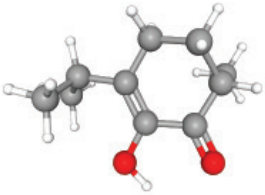


Figure 2. HPLC chromatogram of ethanolic extract of *F. indica* leaves.

Table 3. *Fragaria indica* ethanolic extract for GC-MS

S. No.	Name	Molecular Weight	Molecular Formula	Hits (db)	RT	3D Structure
1.	1,2-Propanediol	76	$C_3H_8O_2$	10	3.65	
2.	7,9-(p-Methoxyphenylidenedioxy)-5 -methoxy-2,4,6,8-tetraamethylnonan -1,3-diol	396	$C_{22}H_{36}O_6$	6	70.377	
3.	alpha-Himachalene	204	$C_{15}H_{24}$	10	12.067	
4.	Phenol, 2-methoxy-4-(2-propenyl)	164	$C_{10}H_{12}O_2$	10	10.769	
5.	2,3-di-O-isopropylidene-4-benyloxy-5 -[(1'-benzoyloxymethyl-1'-nitromethyl-1	473	$C_{24}H_{27}NO_9$	10	6.073	
6.	2-(2-Ethoxyethoxy) ethanol	134	$C_6H_{14}O_3$	10	5.511	
7.	2-Cyclohexen-1-one, 6-methyl-3-(1-methylethyl)	152	$C_{10}H_{16}O$	10	14.069	

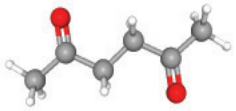
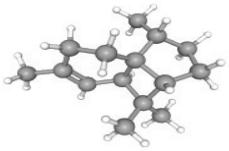
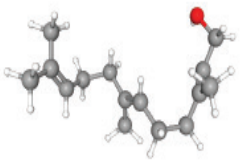
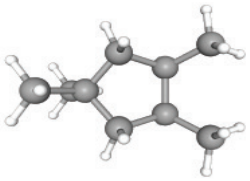
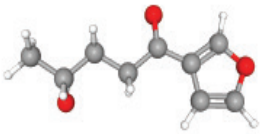
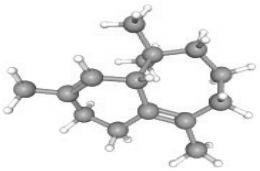
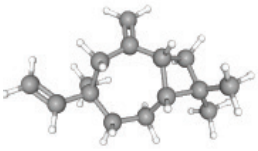
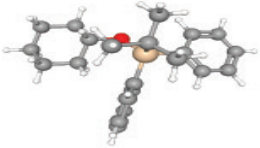
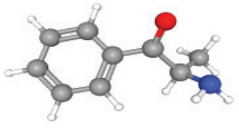
8.	2-Formyl-2-methyl-tetrahydrofuran	114	$C_6H_{10}O_2$	10	4.55	
9.	Italicene	204	$C_{15}H_{24}$	10	14.547	
10.	7-hydroxy-6,7-dihydro-5, 6E-dehydronerolidol	220	$C_{15}H_{26}O$	4	16.49	
11.	cis-1,1,3,4-Tetramethylcyclopentane	126	C_9H_{18}	10	6.642	
12.	Bicyclo[2.2.2]octane-cis-2,3-diyl Carbonate	168	$C_9H_{12}O_3$	10	12.422	
13.	beta-Himachalene	204	$C_{15}H_{24}$	10	12.692	
14.	Bicyclo[5.2.0]nonane, 2-methylene-4, 8,8-trimethyl-4-vinyl	204	$C_{15}H_{24}$	10	82.777	
15.	1,3-Diphenyl-1-((trimethylsilyl)oxy)-1(Z)-heptene	338	$C_{22}H_{30}OSi$	10	72.836	
16.	4-(2-Propen-1-yloxy) benzeneamine	149	$C_9H_{11}NO$	10	20.41	

Table 4. ADMET analysis of seven compounds identified in *F. indica*

Description	Characteristics of druggable compounds						
	alpha-Himachalene	1,3-Diphenyl-1-((trimethylsilyl)oxy)-1(Z)-heptene	1H-Benzocycloheptene, Bicyclo[5.2.0]nonane	cis-1,1,3,4-Tetramethylcyclopentane	Bicyclo[2.2.2] octane-cis-2,3-diyl Carbonate	beta-Himachalene	2-methylene-4,8,8-trimethyl-4-vinyl
1. *Physico-chemical Profile*							
Atoms heavy (n)	15	24	9	9	12	15	15
Heavy atoms aromatic (n)	0	12	0	0	6	0	0
Fraction (Csp3)	0.73	0.36	1.00	1.00	0.33	0.73	0.73
Bonds rotatable (n)	0	8	0	0	3	0	1
Acceptors H-bond (n)	0	1	0	0	3	0	0
Donors hydrogen (n)	0	0	0	0	0	0	0
Molar refractivity	68.78	108.43	41.15	43	45.92	68.78	68.52
Å^2 TPSA	0.00	9.23	0.00	0.00	27.69	0.00	0.00
2. *Lipophilicity*							
P-MLOG	4.63	5.15	4.13	4.13	1.18	4.63	4.63
P-WLOG	4.73	6.85	2.98	3.08	1.71	4.87	4.58
P3-XLOG	4.46	7.63	4.08	3.86	1.73	3.94	5.07
P-iLOG	3.24	4.50	2.50	2.64	2.37	3.26	3.33
IT-SILICOS-	4.19	4.86	2.91	2.66	1.82	4.30	4.51
Log $P_{o/w}$ Consensus	4.25	5.80	3.32	3.27	1.76	4.20	4.42
3. *Water solubility*							
E-SOL (mg/ml; mol/l)	-3.92 2.48e-02; 1.21e-04	-6.59 8.74e-05; 2.58e-07	-3.18 8.20e-02; 6.60e-04	-3.05 1.11e-01; 8.82e-04	-2.14 1.21e+00; 7.17e-03	-3.59 5.26e-02; 2.58e-04	-4.24 1.19e-02; 5.82e-05
Class	Soluble	Less soluble	Soluble	Soluble	Soluble	Soluble	Moderately soluble
Ali (Log *S)* (mg/ml; mol/l)	-4.18 1.35e-02; 6.62e-05	-7.66 7.36e-06; 2.17e-08	-3.79 2.04e-02; 1.64e-04	-3.56 3.50e-02; 2.78e-04	-1.93 1.99e+00; 1.18e-02	-3.64 4.68e-02; 2.29e-04	-4.81 3.15e-03; 1.54e-05
Class	Moderately soluble	Less soluble	Soluble	Soluble	Very soluble	Soluble	Moderately soluble
IT (SILICOS) (mg/ml; mol/l)	-3.77 3.49e-02; 1.71e-04	-7.63 7.97e-06; 2.36e-08	-1.87 1.67e+00; 1.35e-02	-2.30 6.28e-01; 4.98e-03	-2.77 2.84e-01; 1.69e-03	-3.97 2.19e-02; 1.07e-04	-3.89 2.61e-02; 1.28e-04
Class	Soluble	Less soluble	Soluble	Soluble	Soluble	Soluble	Soluble

4. *Pharmacokinetics*							
GI (Absorption)	Low	Low	Low	Low	High	Low	Low
BBB (Permeability)	No	No	Yes	Yes	Yes	No	No
P-g proteins substrate	No	Yes	No	No	No	No	No
CYP2C-19	Yes	Yes	No	No	No	No	Yes
CYP1A-2	No	No	No	No	No	No	No
CYP3A-4	No	No	No	No	No	No	No
CYP2D-6	No	Yes	No	No	No	No	No
CYP2C-9	Yes	Yes	Yes	Yes	No	Yes	Yes
Skin (cm/s)	-4.38	-2.95	-4.16	-4.33	-6.10	-4.75	-3.95
5. *Druglikeness*							
Violation (Lipinski)	1	1	1	0	0	1	1
Violation (Veber)	0	0	0	0	0	0	0
Violation (Egan)	0	1	0	0	0	0	0
Violation (Ghose)	0	1	1	1	0	0	0
Violation (Muegge)	1	2	2	2	1	1	1
Score (Bioavailability)	0.55	0.55	0.55	0.55	0.55	0.55	0.55
6. *Medicinal Chemistry*							
Alert (PAINS)	0	0	0	0	0	0	0
Alert (Brenk)	1	2	0	0	0	1	1
Violation (Lead likeness)	2	2	2	2	1	2	2
Accessibility (Synthetic)	4.15	4.22	2.93	2.49	1.63	4.08	3.79
7. *Toxicity*							
LD50 predicted (mg/kg)	4400	540	1850	4100	700	4390	5050
Toxicity class	5	4	3	5	4	5	6
Hepatotoxic	No	No	No	No	No	No	No
Nephrotoxic	No	No	No	No	No	No	No
Cardiotoxic	No	No	No	No	No	No	No
Neurotoxic	Yes	Yes	Yes	Yes	No	Yes	No
Blood rain barrier toxic	No	No	Yes	Yes	Yes	Yes	Yes
Respiratory toxicity	No	No	Yes	No	No	No	No
Carcinogenic	No	No	Yes	No	Yes	No	No
Cytotoxic	No	No	No	No	No	No	No
Mutagenic	No	No	No	No	Yes	No	No
Immunotoxic	Yes	No	No	No	No	No	No
Ecotoxicity	Yes	Yes	Yes	No	Yes	No	Yes
Nutritional toxicity	No	No	No	No	No	No	No
Clinical toxicity	No	No	No	No	No	Yes	No

Table 5. Ligand interaction analysis of the alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate

S. No.	Compound	Ligand	Receptor	Association	Distance	E (kcal/mol)
1.	alpha-Himachalene	CD2 12	O PHE 22	(A) H-donor	3.14	-0.7
2.	Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate	O1	OG SER 233	(A) H-donor	3.04	-0.9
		O2	N ALA 235	(A) H-acceptor	3.17	-0.7

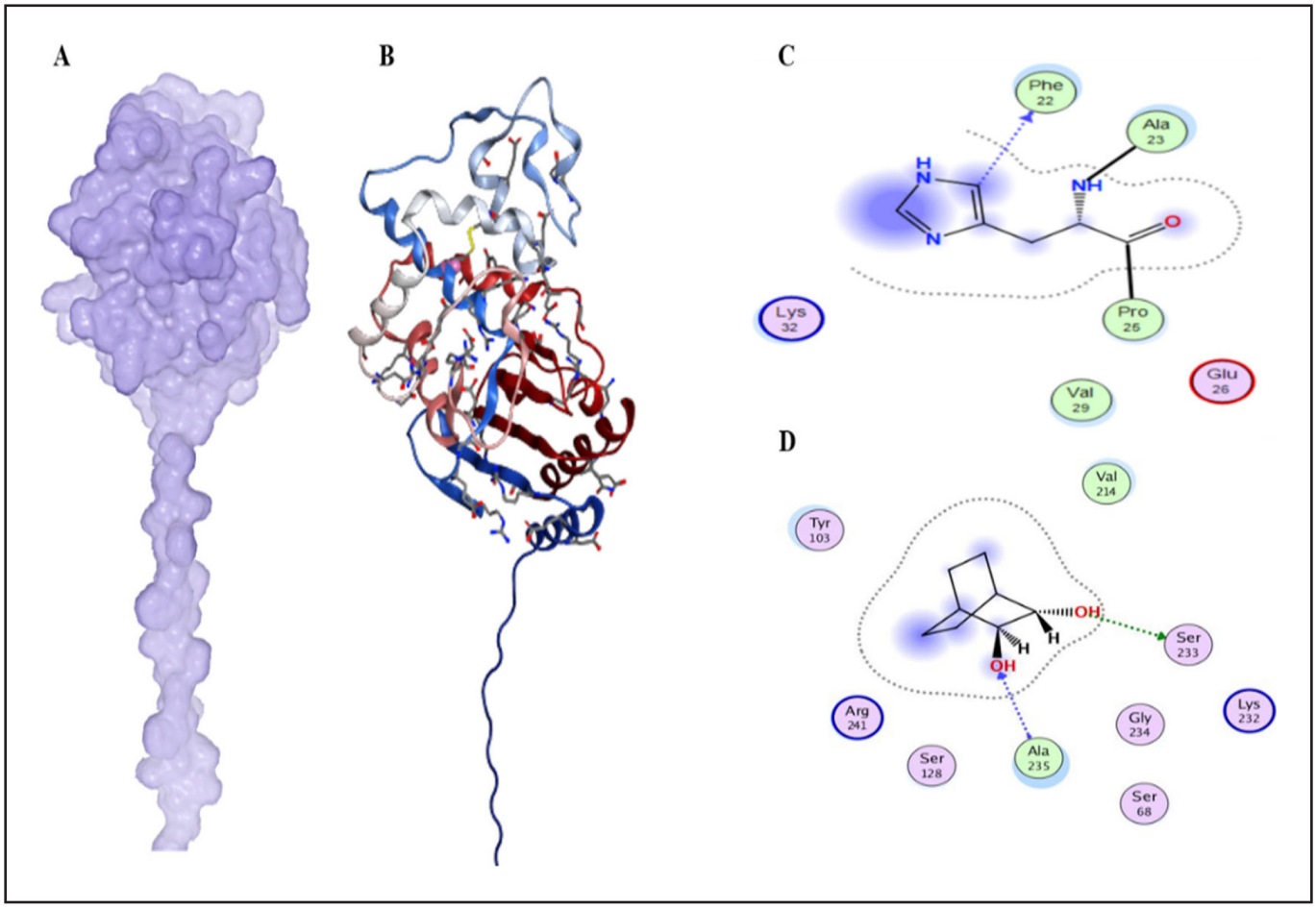


Figure 3. Molecular docking analysis of alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate within the active site of bla-TEM enzyme: (A) bla-TEM surface; (B) structure of bla-TEM (C) interaction map of alpha-Himachalene and with amino acid residues of bla-TEM; (D) Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate intercatrion with amino acid residues of bla-TEM.

Putative bla-TEM inhibitors

On water solubility, druglikeness and potent medicinal chemistry, two compounds, including Alpha-Himachalene and Bicyclo[2.2.2] octane-cis-2,3-diyl carbonate were selected for molecular docking analysis with bla-TEM beta-lactamase of *S. typhi, E. coli* and *S. flexneri*. Alpha-Himachalene interacts with Pro-26, Phe-22, and Ala-23 residues of bacterial bla-TEM beta-lactamase. Similarly, Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate interacts with amino acid residues of Ala-235 and Ser-233 of bla-TEM beta-lactamase. The interaction type, distance, energy (kcal/mol) and visual interaction map are listed in Table 5 and Figure 3.

DISCUSSION

Plants are an alternative source of bioactive compounds with possible medicinal applications. For human health, natural medicines derived from plants are more satisfactory than current synthetic drugs (Dembitsky *et al*., 2020). The current study investigated the antimicrobial activity of *F. indica* stem, roots, and leaves against MDR gastrointestinal bacterial pathogens, including *S. flexneri, S. typhi*, and *E. coli*. Among all the extracts, the leaves ethanolic extract exhibited the maximum zone of inhibition against *S. typhi, S. flexneri*, and *E. coli.* Other studies on plant leaves showed similar findings against *S. typhi* and *E. coli* (Muhammad *et al.,* 2012; Rovcanin *et al*., 2015). These findings signify the *F. indica* leaf extracts against MDR GI pathogens.

Plant phytochemicals could be an alternative medicinal source. Phenolics derived from plants have attributed antibacterial activity against drug-resistant pathogens (Miklasińska *et al*., 2018). A range of 19 phenolic compounds in *F. indica* have been identified using HPLC. Though some of the identified molecules are already reported in other plants and *F. indica (Duchesnea indica)* (Kjersti *et al*., 2007; Dias *et al*., 2016; Miklasinska *et al*., 2018); however, from literature quests, Isorhamnetin-3-rutinoside, 5, 7-Dihydroxy-4' -methoxyflavone and Luteolin were first time reported in *F. indica.*

Further profiling was done using GC-MS/MS analysis. In the list of molecules, 1,2-Propanediol, 2-(2-Ethoxyethoxy) ethanol, Phenol 2-methoxy-4-(2-propenyl) and 2-Cyclohexen-1-one were reported previously in strawberry species. Most of these compounds exhibited miscellaneous activities not limited to antibacterial, antioxidant, and anticancer (Zabetakis *et al*., 1998; Federica *et al*., 2005; Saad *et al*., 2023). From a detailed literature mining, it was noted that compounds, including Beta-Himachalene, Bicyclo [5.2.0]nonane 2-methylene-4,8,8-trimethyl-4-vinyl, Bicyclo[2.2.2] octane-cis-2,3-diyl Carbonate, Alpha-Himachalene, cis-1,1,3,4-Tetramethylcyclopentane, and 1,3-Diphenyl-1-((trimethylsilyl) oxy)-1(Z)-heptene were reported for the first time in *F. indica*. After ADMET prediction analysis of the new bioactive compounds, most have good water solubility, druglikeness, and medicinal characteristics; however, their true role may be explored via *in-vitro* and *in-vivo* analysis. Some of these compounds were previously reported in plants (Singh & Agarwal,1988; Ayat *et al*., 2018). One study reported the ADMET properties of phytosterol derivatives from *Lagerstroemia speciosa* ethanolic seed extract (Raju & Eswaran, 2021), which showed the predicted compounds as non-toxic, non-carcinogenic, and non-mutagenic, with favorable pharmacokinetic properties.

In silico ligand-receptor interaction studies using molecular docking tools are useful for the elucidation of important medicinal molecules (Bouamrane *et al*., 2022). Based on high water solubility, druglikeness characteristics, and favorable medicinal chemistry, Alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate were assessed for possible interaction with bla-TEM beta-lactamase.

It was found that these two compounds strongly interacted with the bla-TEM; therefore, further studies are recommended to validate their therapeutic activity against bla-TEM producing multidrug-resistant foodborne pathogenic bacteria.

CONCLUSIONS

Fragaria indica extracts exhibited activity against bla-TEM producing foodborne pathogens. Ten bioactive compounds were for the first time identified in *Fragaria indica* leaf extract. ADMET and docking analysis revealed two compounds, including Alpha-Himachalene and Bicyclo[2.2.2]octane-cis-2,3-diyl carbonate as potential anti-infective molecules against bla-TEM producing foodborne pathogens.

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Conflict of interest

The authors declare no conflicts of interest.

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