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**DIHYDROFOLATE REDUCTASE AND DNA GYRASE INHIBITORS
FROM *Citrus sinensis* AND *Piper betle*: *IN SILICO* EXPLORATION**

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ABSTRACT

The current investigation was aimed at *in silico* studies of selected phytoconstituents in the peels of *Citrus sinensis* and leaves of *Piper betle* to examine their antimicrobial activity. In this study, a total of 52 phytoconstituents were selected and Clotrimazole was used as standard in assessing the antimicrobial activity. Primarily drug like properties and bioactivity score was calculated and then the compounds were subjected to ADMET studies. Further the molecular docking studies was performed to ascertain the binding fitness score using SWISSDOCK software towards Dihydrofolate reductase (DHFR) and DNA gyrase proteins. The results of the *in silico* screening reveals that the phytoconstituents exhibited prominent binding interactions with the selected proteins. Upon comparison with others Myricetin and 1,8 Cineole showed the strongest binding interactions with both DHFR and DNA gyrase respectively. Hence, the current exploration suggests that these phytoconstituents may furnish as leads in the development of antimicrobial agents.

**Keywords: *Citrus sinensis*, *Piper betle*, Docking, Dihydrofolate reductase, DNA Gyrase,
Antimicrobial**

INTRODUCTION

Researching novel compounds with antimicrobial capabilities to use against these microorganisms is necessary since resistant bacteria constitute a problem in the treatment of certain well-known illnesses. Long before humans ever set foot on the planet, plants had already been linked to it. Many recognized and unidentified chemical compounds that are vital to medications are found in plants [1]. Since the beginning of time, medicinal plants have distinguished themselves by acting as the savior in the treatment of numerous illnesses [2]. Modern science recognized the medicinal benefits of numerous plants and recorded all pertinent information for future use and reference in manuscripts and records for millennia to come.

Traditional medicine among various ethnic groups worldwide has been built on curative herbs and medicinal food plants from the dawn of humanity. Natural product structural motifs have shown to be a priceless source of fresh chemical information for medicinal chemistry and drug design [3]. Most investigations on phytoconstituents have shown their potency in terms of antioxidative activities, controlling gene expression, and altering cellular processes [4]. *Citrus sinensis* and *Piper betle* are two of the most prevalent kinds of plants that have therapeutic

characteristics and have a substantial biological impact.

One of the most significant citrus species and a common fruit crop, *Citrus sinensis* is estimated to produce about 120 million tonnes of fruit annually worldwide [5]. Orange peels are a fruit waste byproduct that may include beneficial phytonutrients with biological significance. Orange peel extract provides a wide range of medical benefits, including those for colic, upset stomach, cancer, as a diuretic, carminative, immuno-enhancing, stomachic, and tonic for the skin, immune system, and digestive system [6]; [7]. Additionally, it aids in the treatment and prevention of scurvy, colds, flu, and vitamin deficits as well as bacterial and viral infections.

The Piperaceae family member *Piper betle* is one of the most valued medicinal plants, and its leaves have been utilized for a variety of therapeutic purposes. The crop is widely grown in India and other Southeast Asian nations [8]. Its leaves are commonly used as a post-meal mouth refresher. According to reports from numerous studies, betel oil and extract have antibacterial and antioxidant properties in model systems [9]; [10]; [11].

Identification of the phytoconstituents of *C. sinensis* peels and *P. betle* leaf extracts, as well as assessments of the extracts' pharmacological effects, including their antibacterial effects, are available [12]; [13]. The search for phytoconstituents likely to serve as leads in the development of anti-microbe drugs and in-depth insights into the interactions of these phytoconstituents with receptors remain unreported. Therefore, the current study's objectives are to investigate the drug-like qualities of reported phytoconstituents in the chosen plants and to assess reported phytoconstituents using computational methods to assess their antimicrobial activity.

MATERIAL AND METHODS:

Preparation of Chemical compound Library:

Altogether, 52 phytochemicals reported in the selected plant materials were accounted, which were meant to act as ligands in the docking procedure. The structures of the 52 reported phytoconstituents were drawn using **Chemdraw Ultra 12.0**, the molecular formula and IUPAC names were noted referring **Pubchem**. The selected structures were depicted along with their IUPAC names (**Table 1**).

Prediction of Molecular properties:

Molinspiration was employed to predict a number of physicochemical attributes, the Lipinski's rule of five compounds was tested. The physical characteristics of a molecule, such as its molecular weight, volume, polar surface area (PSA), hydrogen bond acceptor/donor, log P, and the number of rotatable bonds, were calculated in order to determine how likely it is to be a drug. The estimated bioactivity score values demonstrate a chemical's overall potential to be a therapeutic candidate [14].

ADME properties:

To examine the ADME characteristics of substances, the Swiss ADME and PreADMET web tools were used to predict a number of metrics, including GI absorption, BBB permeability, skin permeability, and toxicity [15].

Docking Studies:

Preparation of Ligands and protein:

Chem Draw Ultra 12.0 served to draw the ligand structures, and Chem Draw 3D Pro was utilised to lessen the energy and save it in the form of mol 2 form. The ligand must be saved in PDB form in order to be transmitted it to Swiss Dock software. Using MGL tools, the ligand is transformed into PDB format. From Protein Data Bank, the necessary protein PDB i.e, PDB ID: 4HOF (dihydrofolate reductase)

and PDB ID: 6F86 (DNA Gyrase B) are downloaded.

Docking Procedure:

Swiss Dock server, was used to dock the chosen receptor and ligands. The result was obtained by providing an email address, which was then used to retrieve and download the result.

RESULTS AND DISCUSSION:

Prediction of Molecular properties:

Lipinski's rule of five analysis on phytoconstituents was carried out by Molinspiration. The findings demonstrated all compounds' high oral bioavailability by showing that they all adhered to Lipinski's rule of five and did not violate more than one requirement (Table 2).

Bioactivity scores of compounds:

Molinspiration was used to forecast the bioactivity ratings of compounds towards the selected receptors (www.molinspiration.com) [16]. All of the compounds were found to have biological score between -5.0 and 5.0, indicating a moderate to good level of activity against biological targets. These results are consistent with earlier studies on different phytochemicals, which claim that these compounds have drug-like characteristics and biological effects.

ADME Properties:

Computations of important Absorption, distribution and metabolic properties of all the derivatives were performed by Swiss ADME. Most of the ligands except L6, L9, L15, L28, L32, L35, L37, L38, L41, L42, L43, L46, L52 have high GI absorption. Most of the ligands do not have BBB permeability. Ligands L8, L27, L28, L36, L37, L38, L41, L46 contain PGP substrate. Ligands L1, L3, L7, L10, L11, L18, L20, L21, L23, L24, L27, L33, L35, L36, L45, L47 are metabolized by the enzyme CYP1A2. Ligands L9 is metabolized by CYP2C19. Ligands L6, L9, L32, L39, L41, L42, L43, L49, L50 are metabolized by CYP2C9. Ligands L3, L33, L45 are metabolized by CYP2D6. Ligands L3, L23, L25, L26, L27, L33, L35, L36, L39, L44, L45, L50 are metabolized by CYP3A4.

Docking exploration:

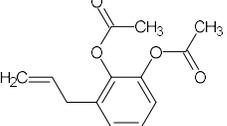
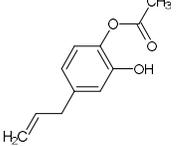
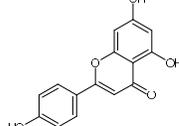
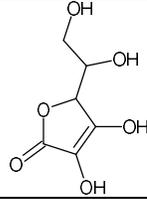
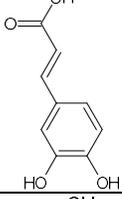
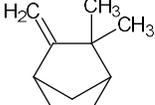
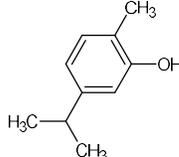
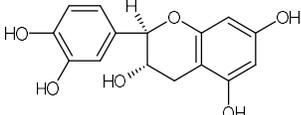
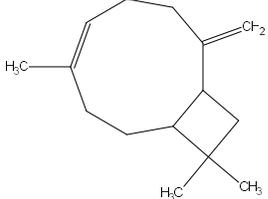
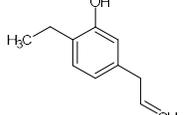
The atomic contact energy of molecules having macromolecular structure was calculated using Swiss dock [17]. Most of the substances binding interactions with target proteins have demonstrated potent hydrogen bonding and hydrophobic interactions.

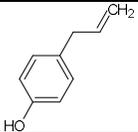
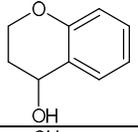
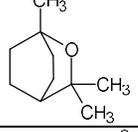
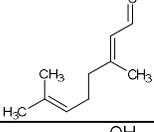
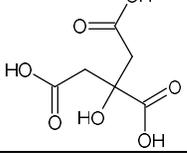
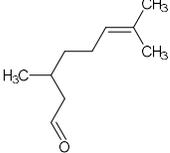
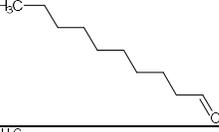
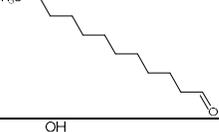
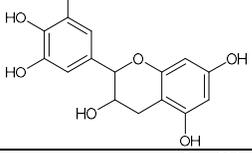
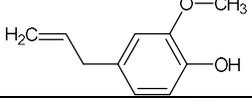
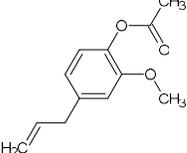
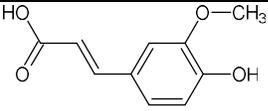
Dihydrofolate reductase (DHFR) is the intracellular target of four amino analogues of folic acid and is required to maintain the reduced folates necessary for donating carbon atoms, which are necessary for the de novo synthesis of purines, pyrimidines, and amino

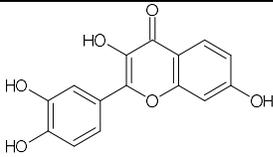
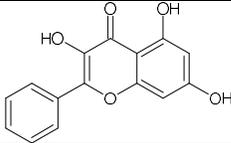
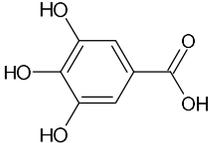
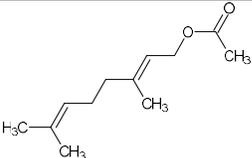
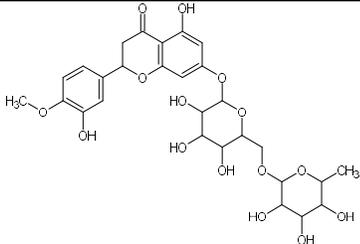
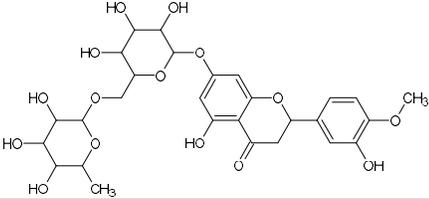
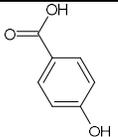
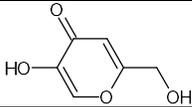
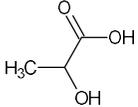
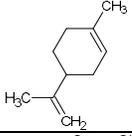
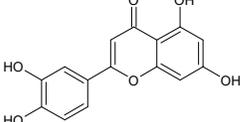
acids [18]. Dihydrofolate reductase (DHFR) inhibition reduces the amount of tetrahydrofolate that is accessible and prevents the production of thymidylate, purines, the amino acids methionine and glycine, and several other cell components which leads to inhibition of DNA synthesis and cell growth [19]; [20]. Currently our findings of molecular docking illustrated that when compared to all other ligands, L35(Myricetin), L36(Naringenin) exhibited the strongest binding affinity of -6.10Kcal/mol and -5.98Kcal/mol respectively with the dihydrofolate reductase receptor which is evidently more than the binding affinity of the Standard, Clotrimazole (-5.37 Kcal/mol) (Table 3).

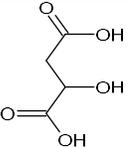
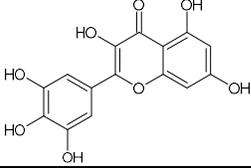
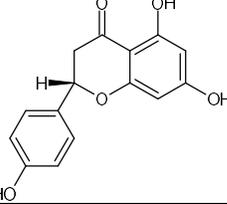
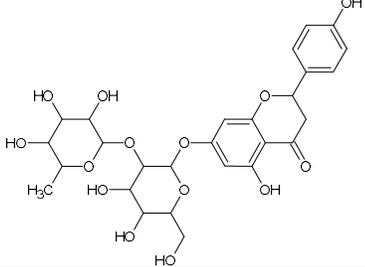
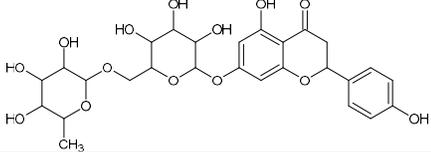
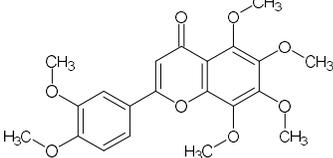
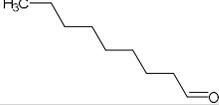
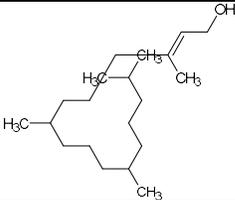
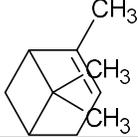
DNA gyrase B is an essential enzyme responsible for the homeostatic control of DNA supercoiling and the target of promising antibacterial compounds [21]. In current exploration (Table 3), when compared to all other ligands L13(1,8-cineole), L36(Naringenin) exhibited the strongest binding affinity of -5.80 Kcal/mol and -5.67 Kcal/mol respectively with the DNA gyrase receptor which is more than that of the standard, Clotrimazole (-5.27 Kcal/mol).

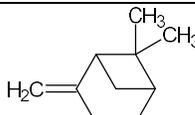
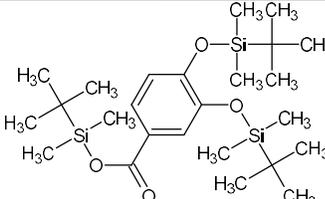
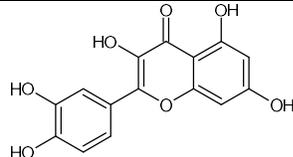
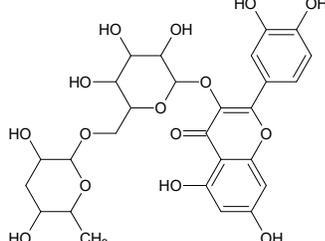
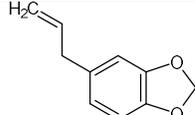
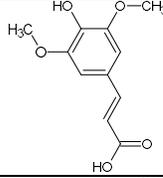
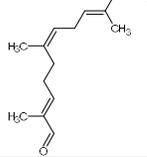
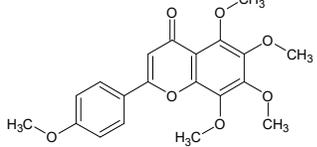
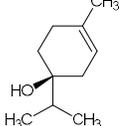
Table 1: Ligand Codes and IUPAC Names

S. No.	Ligand codes	Structure	IUPAC Name
1.	L1 Allyl pyrocatechol diacetate		(2-acetyloxy-3-prop-2-enylphenyl) acetate
2.	L2 Allyl pyrocatechol monoacetate		(2-hydroxy-4-prop-2-enylphenyl) acetate
3.	L3 Apigenin		5,7-dihydroxy-2-(4-hydroxyphenyl)chromen-4-one
4.	L4 Ascorbic acid		(2R)-2-[(1S)-1,2-dihydroxyethyl]-3,4-dihydroxy-2H-furan-5-one
5.	L5 Caffeic acid		(E)-3-(3,4-dihydroxyphenyl)prop-2-enoic acid
6.	L6 Camphene		2,2-dimethyl-3-methylidenebicyclo[2.2.1]heptane
7.	L7 Carvacrol		2-methyl-5-propan-2-ylphenol
8.	L8 Catechin		(2S,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol
9.	L9 Caryophyllene		(1R,4E,9S)-4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undec-4-ene
10.	L10 Chavibetol		2-methoxy-5-prop-2-enylphenol

11.	L11 Chavicol		4-prop-2-enylphenol
12.	L12 4-chromanol		3,4-dihydro-2H-chromen-4-ol
13.	L13 1,8-cineole		1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane
14.	L14 Citral		(2E)-3,7-dimethylocta-2,6-dienal
15.	L15 Citric acid		2-hydroxypropane-1,2,3-tricarboxylic acid
16.	L16 Citronellal		3,7-dimethyloct-6-enal
17.	L17 Decanal		Decanal
18.	L18 Dodecanal		Dodecanal
19.	L19 Epigallocatechin		(2R,3R)-2-(3,4,5-trihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol
20.	L20 Eugenol		2-methoxy-4-prop-2-enylphenol
21.	L21 Eugenyl acetate		(2-methoxy-4-prop-2-enylphenyl) acetate
22.	L22 Ferulic acid		(E)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enoic acid

23.	L23 Fisetin		2-(3,4-dihydroxyphenyl)-3,7-dihydroxychromen-4-one
24.	L24 Galangin		3,5,7-trihydroxy-2-phenylchromen-4-one
25.	L25 Gallic acid		3,4,5-trihydroxybenzoic acid
26.	L26 Geranyl acetate		(2E)-3,7-dimethylocta-2,6-dienyl acetate
27.	L27 Hesperetin		(2S)-5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-2,3-dihydrochromen-4-one
28.	L28 Hesperidin		(2S)-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-7-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxy-2,3-dihydrochromen-4-one
29.	L29 4-hydroxy benzoic acid		4-hydroxybenzoic acid
30.	L30 Kojic acid		5-hydroxy-2-(hydroxymethyl) pyran-4-one
31.	L31 Lactic acid		2-hydroxypropanoic acid
32.	L32 Limonene		1-methyl-4-prop-1-en-2-ylcyclohexene
33.	L33 Luteolin		2-(3,4-dihydroxyphenyl)-5,7-dihydroxychromen-4-one

34.	L34 Malic acid		2-hydroxybutanedioic acid
35.	L35 Myricetin		3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl) chromen-4-one
36.	L36 Naringenin		5,7-dihydroxy-2-(4-hydroxyphenyl)-2,3-dihydrochromen-4-one
37.	L37 Naringin		(2S)-7-[(2S,3R,4S,5S,6R)-4,5-dihydroxy-6-(hydroxymethyl)-3-[(2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl] oxyoxan-2-yl] oxy-5-hydroxy-2-(4-hydroxyphenyl)-2,3-dihydrochromen-4-one
38.	L38 Narirutin		(2S)-5-hydroxy-2-(4-hydroxyphenyl)-7-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl] oxymethyl] oxan-2-yl] oxy-2,3-dihydrochromen-4-one
39.	L39 Nobiletin		2-(3,4-dimethoxyphenyl)-5,6,7,8-tetramethoxychromen-4-one
40.	L40 Nonanal		Nonanal
41.	L41 Phytol		(E,7R,11R)-3,7,11,15-tetramethylhexadec-2-en-1-ol
42.	L42 α -pinene		2,6,6-trimethylbicyclo[3.1.1]hept-2-ene

43	L43 β-pinene		6,6-dimethyl-2-methylidenebicyclo[3.1.1]heptane
44	L44 Protocatechuic acid		6,6-dimethyl-2-methylidenebicyclo[3.1.1]heptane
45	L45 Quercetin		2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one
46	L46 Rutin		2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxochromen-4-one
47	L47 Safrole		5-prop-2-enyl-1,3-benzodioxole
48	L48 Sinapic acid		(E)-3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-enoic acid
49	L49 Sinensal		(2Z,6E)-2,6-dimethyl-10-methylidenedodeca-2,6,11-trienal
50	L50 Tangertin		5,6,7,8-tetramethoxy-2-(4-methoxyphenyl)chromen-4-one
51	L51 Terpinene 4-ol		(1S)-4-methyl-1-propan-2-ylcyclohex-3-en-1-ol

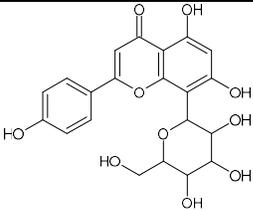
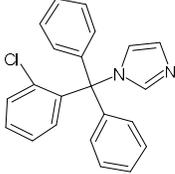
52	L52 Vitexin		5,7-dihydroxy-2-(4-hydroxyphenyl)-8-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]chromen-4-one
53	Standard Clotrimazole		1-[(2-chlorophenyl)-diphenylmethyl]imidazole

Table 2: Physicochemical properties of ligands

S. No.	Ligand Code	Mol Wt	ROB	HBA	HBD	TPSA	Log p	Volume	Violation
1.	L1	234.25	6	4	0	52.61	1.57	217.63	0
2.	L 2	192.21	4	3	1	46.53	1.59	181.12	0
3.	L 3	270.24	1	5	3	90.89	2.46	224.05	0
4.	L 4	176.12	2	6	4	107.22	-1.40	139.71	0
5.	L 5	180.16	2	4	3	77.75	0.94	154.50	0
6.	L 6	136.24	0	0	0	0.00	3.33	152.37	0
7.	L 7	150.22	1	1	1	20.23	3.81	158.57	0
8.	L 8	290.27	1	6	5	110.37	1.37	244.14	0
9.	L 9	204.36	0	0	0	0.00	5.17	229.95	1
10.	L 10	164.20	3	2	1	29.46	2.10	162.14	0
11.	L 11	134.18	2	1	1	20.23	2.28	136.59	0
12.	L 12	150.18	0	2	1	29.46	1.27	140.64	0
13.	L 13	154.25	0	1	0	9.23	2.72	166.66	0
14.	L 14	152.24	4	1	0	17.07	3.65	169.74	0
15.	L 15	192.12	5	7	4	132.1	-1.98	151.76	0
16.	L 16	154.25	5	1	0	17.07	3.60	175.95	0
17.	L 17	156.27	8	1	0	17.07	4.60	182.59	0
18.	L 18	184.32	10	1	0	17.07	5.61	216.20	1
19.	L 19	306.27	1	7	6	130.60	1.08	252.16	1
20.	L 20	164.20	3	2	1	29.46	2.10	162.14	0
21.	L 21	206.24	5	3	0	35.54	1.90	198.65	0
22.	L 22	194.19	3	4	2	66.76	1.25	172.03	0
23.	L 23	286.24	1	6	4	111.12	1.97	232.07	0
24.	L 24	270.24	1	5	3	90.89	2.65	224.05	0
25.	L 25	170.12	1	5	4	97.98	0.59	135.10	0
26.	L 26	196.29	6	2	0	26.30	3.91	212.09	0
27.	L27	302.28	2	6	3	96.22	1.94	255.81	0
28.	L28	610.57	7	15	8	234.30	-0.55	511.79	3
29.	L29	138.12	1	3	2	57.53	1.37	119.06	0
30.	L30	142.11	1	4	2	70.67	-0.89	117.43	0
31.	L31	90.08	1	3	2	57.53	-0.71	81.04	0
32.	L32	136.24	1	0	0	0.00	3.62	157.30	0
33.	L33	286.24	1	6	4	111.12	1.97	232.07	0
34.	L34	134.09	3	5	3	94.83	-1.57	108.28	0
35.	L35	318.24	1	8	6	151.58	1.39	248.10	1
36.	L36	272.26	1	5	3	86.99	2.12	230.26	0
37.	L37	580.54	6	14	8	225.06	-0.37	486.25	3
38.	L38	580.54	6	14	8	225.06	-0.37	486.25	3
39.	L39	402.40	7	8	0	85.61	3.37	353.27	0
40.	L40	144.26	7	1	1	20.23	3.64	171.63	0
41.	L41	296.54	13	1	1	20.23	6.76	349.38	1

42.	L42	136.24	0	0	0	0.00	3.54	151.81	0
43.	L43	136.24	0	0	0	0.00	3.33	152.37	0
44.	L44	154.12	1	4	3	77.75	0.88	127.08	0
45.	L45	302.24	1	7	5	131.35	1.68	240.08	0
46.	L46	610.52	6	16	10	269.43	-1.06	496.07	3
47.	L47	162.19	2	2	0	18.47	2.65	152.51	0
48.	L48	224.21	4	5	2	76.00	1.26	197.57	0
49.	L49	218.34	7	1	0	17.07	5.03	241.69	1
50.	L50	372.37	6	7	0	76.38	3.78	327.72	0
51.	L51	154.25	1	1	1	20.23	2.60	170.65	0
52.	L52	432.38	3	10	7	181.04	0.52	355.20	1
53.	Standard	344.85	4	2	0	17.83	5.47	309.52	1

Table 3: Binding interaction of ligands with Dihydro folate reductase and DNA Gyrase B receptors

S. No.	Ligand Code	Name of the ligand	DHFR		DNA Gyrase B	
			Estimated ΔG (kcal/mol)	Full Fitness (kcal/mol)	Estimated ΔG (kcal/mol)	Full Fitness (kcal/mol)
1.	L1	Allyl pyrocatechol diacetate	-4.97	-1115.46	-4.19	-1064.24
2.	L2	Allyl pyrocatechol monoacetate	-4.77	-1052.05	-4.15	-1155.42
3.	L3	Apigenin	-1.45	-1879.63	-4.92	-1321.30
4.	L4	Ascorbic acid	-5.30	-1932.66	-5.02	-1072.08
5.	L5	Caffeic acid	-4.90	-1978.70	-4.20	-1095.25
6.	L6	Camphene	-4.74	-1914.24	-1.46	-4242.16
7.	L7	Carvacrol	-3.86	-1930.43	-4.92	-1078.65
8.	L8	Catechin	-5.46	-1934.15	-5.11	-1061.62
9.	L9	Caryophyllin	-5.41	-1894.80	-5.02	-1024.69
10.	L10	Chavibetol	-4.95	-1917.87	-5.02	-1053.52
11.	L11	Chavicol	-3.53	-1917.06	-5.00	-1073.19
12.	L12	4-Chromanol	-5.38	-1093.42	-----	-----
13.	L13	1,8-Cineol	-3.64	-1907.33	-5.85	-1073.30
14.	L14	Citral	-4.29	-1924.95	-4.40	-834.03
15.	L15	Citric acid	-3.33	-1056.18	-3.91	-1052.63
16.	L16	Citronellol	-5.15	-1947.25	-4.65	-1476.16
17.	L17	Decanal	-3.92	-1935.89	-4.93	-1085.66
18.	L18	Dodecanal	-5.78	-1933.77	-5.15	-1101.11
19.	L19	Epigallocatechin	-----	-----	-4.19	-1064.24
20.	L20	Eugenol	-5.53	-1961.88	-4.61	-1046.22
21.	L21	Eugenyl acetate	-5.49	-1919.89	-5.45	-1045.93
22.	L22	Ferulic acid	-4.88	-1946.59	-4.98	-1056.46
23.	L23	Fisetin	-4.97	-1931.03	-4.98	-1056.46
24.	L24	Galangin	-4.12	-1915.36	-5.06	-1056.96
25.	L25	Gallic acid	-4.40	-1957.93	-4.34	-1097.65
26.	L26	Geranyl acetate	-4.95	-1923.07	-5.15	-1063.08
27.	L27	Hesperetin	-5.43	-1955.15	-5.10	-1080.42
28.	L28	Hesperidin	-5.01	-1923.01	-4.09	-1179.24
29.	L29	4-hydroxy benzoic acid	-4.15	-1087.06	-3.78	-1932.16
30.	L30	Kojic acid	-5.39	-1950.94	-4.09	-1062.65
31.	L31	Lactic acid	-4.77	-1092.12	-4.03	-1961.31
32.	L32	Limonene	-4.06	-2632.16	-3.60	-1046.87
33.	L33	Luteolin	-5.33	-1980.63	-1.04	-1011.93
34.	L34	Malic acid	-4.78	-1086.44	-3.46	-1967.31
35.	L35	Myricetin	-6.10	-1932.89	-4.74	-1058.49
36.	L36	Naringenin	-5.98	-1008.52	-5.67	-1810.40
37.	L37	Naringin	-4.85	-1072.05	-3.99	-1036.52
38.	L38	Narirutin	-4.33	-1055.09	-3.56	-1055.45

39.	L39	Nobiletin	-1.65	-1832.42	-2.39	-996.71
40.	L40	Nonanal	-2.47	-1914.94	-3.83	-1907.76
41.	L41	Phytol	-3.83	-1907.76	-4.04	-1912.41
42.	L42	α -pinene	-4.19	-1064.24	-----	-----
43.	L43	β -pinene	-----	-----	-5.03	-1066.23
44.	L44	Proto catechuic acid	-3.33	-1993.25	-4.11	-1958.55
45.	L45	Quercetin	-5.20	-1934.95	-5.60	-970.04
46.	L46	Rutin	-2.36	-1009.13	-5.45	-1745.32
47.	L47	Safrole	-4.30	-1078.03	-3.46	-951.53
48.	L48	Sinapic acid	-3.81	-1115.76	-5.10	-1945.31
49.	L49	Sinensal	-----	-----	-4.13	-1056.32
50.	L50	Tangeretin	-5.10	-1062.08	-4.73	-1053.30
51.	L51	Terpinen4-ol	-4.07	-1087.31	-5.01	-1945.18
52.	L52	Vitexin	-4.58	-1702.04	-----	-----
53.	L53	Standard	-5.37	-1874.36	-5.27	-997.46

CONCLUSION:

In this study, we explored the potential of a few phytochemicals that have been found in the most popular medicinal plants, *P. betle* and *C. sinensis* peels. The findings strongly suggested that these compounds could be used as effective antimicrobial agents and have significant anti-microbial potential in preventing infections against bacteria. The findings are expected to catch the interest of researchers working on developing drugs to treat microbial infections.

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