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Phytochemical Evaluation, Antimicrobial Activity of Selected Indigenous Plant Ethanolic Extracts and ADMET Properties of its Phytocompounds

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

The scientific investigation was made to study the phytochemical and antimicrobial analysis of ethanoic extract of some indigenous plants and ADMET properties of its phytocompounds. We investigated 27 active phytochemical components in ethanolic extracts of four medicinal plants:

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Andrographis paniculata, Centella asiatica, Psidium guajava, and Solanum trilobatum. The extracts were subjected to a standard procedure of qualitative phytochemical screening. The phytocompounds in the leaf extracts of the selected plants were identified using IR and GC-MS spectroscopy. The extracts were then tested for in vitro antibacterial activity against Gram-positive (*Staphylococcus aureus and Enterococcus*) and Gram-negative bacteria (*Pseudomonas aeruginosa and Escherichia coli*), as well as antifungal activity against *Candida albicans* and *Aspergillus flavus*, using Agar-diffusion methods and reference drugs *Amikacin* and *Nystatin*. *Psidium guajava* ethanol extract was found to be the most efficient against *Enterococcus*, with an inhibition area of 19 mm when compared to *Amikacin*. *Centella asiatica* showed a 13 mm zone of inhibition against *Candida albicans*, which is comparable to *Nystatin's* 15 mm zone. Molecular docking experiments revealed that *Andrographis paniculata's* Stigmasterol (-9.3 kcal/mol) is a good inhibitor of *Staphylococcus* (PDB:3FYM), and Lupeol (-9.6 kcal/mol) is a promising inhibitor of *Candida albicans* (PDB:4HOF). Both showed binding energies equivalent to common antibiotics *amikacin* (-7.2 kcal/mol) and *nystatin* (-8.6 kcal/mol).

Keywords: GC-MS analysis; ADMET; molecular docking; E. coli; Pseudomonas aeruginosa; Enterococcus; Staph aureus; Candia albicans; Aspergillus flaves.

1. INTRODUCTION

Infectious diseases are a leading cause of death worldwide, accounting for almost half of all fatalities, while infections account for 50-75% of hospital deaths [1]. Bacterial infections are a primary cause of recurring contaminations and mortality. Infectious disorders produce toxins into the body, which can injure or even kill tissues [2]. Synthetic medications have poor potency against specific pathogenic germs, stressing the need for alternate treatments. The development of novel antipathogenic medicines is so critical. Screening local medicinal plants for potential chemotherapeutic antibacterial and antifungal compounds is a promising strategy. Herbal therapies advised by herbalists for disorders such as itching, eczema, scabies, and skin ailments include numerous medicinal plant preparations [3-5]. Plant-based medications, whether obtained directly from plants or modified through synthesis, are widely used around the world. These medications contain phytochemicals, plant-derived substances that include both primary and secondary metabolites. Primary metabolites are substances with a large volume but low value, whereas secondary metabolites, which are formed from primary metabolites, have a smaller volume but higher value. Secondary metabolites are particularly interesting because of their antibacterial, antibiotic, insecticidal, and hormonal activities [6]. Indian medicinal plants have antibacterial qualities that prevent the growth of harmful bacteria and fungus [7].

Psidium guajava (Guava) is rich in bioactive substances such as polyphenols, flavonoids, and polysaccharides [8,9]. *P. guajava* leaf extract has antimicrobial properties due to flavonoid compounds such as quercetin-3-O-α-L-arabinofuranoside, quercetin-3-O-β-D-arabinofuranoside, quercetin-3-O-β-D-glucoside, quercetin-3-O-β-D-galactoside, and quercetin-3-O-β-D-arabinofuranoside. The extract also contains Squalene, which is renowned for its antifungal effects and is widely used in the beauty industry [10] and [11]. *Solanum trilobatum* L. (Solanaceae) is a popular ingredient in Ayurvedic and Siddha medicine in India. Pharmacological studies have indicated a wide range of biological activities, including anti-bacterial, anti-fungal, anti-tumor, anti-oxidant, anti-inflammatory, and anti-diabetic effects [12-15].

Centella Asiatica is regarded as an important ethnomedicine in the traditional Indian Ayurvedic system. The plant contains a variety of bioactive compounds, including triterpenes, glycosides, genins, flavonoids, and phenols. Triterpene centellosides, including asiaticoside, madecassoside, asiatic acid, and madecassic acid, are currently undergoing clinical trials [16,17]. *Andrographis paniculata* contains a wide variety of phytoconstituents, such as flavonoids, terpenoids, tannins, saponins, alkaloids, and phenolic compounds, which are spread throughout the plant. The plant's secondary metabolites are notable for their antibacterial, antibiotic, insecticidal, and hormonal effects. *Andrographis paniculata* has been recognized for its numerous medicinal qualities, which include antibacterial, antifungal, antiviral, choleretic, and hypoglycemic actions [18,19]. The main antibacterial compounds found in *Andrographis paniculata* are diterpenoids and flavonoids [20]. Based on the information given above, we have

phytochemical evaluation, ADMET properties, and antibacterial activity against selected Indigenous plant ethanolic extracts.

2. MATIRIALS AND METHODS

2.1 Collection and Authentication of Plant Material

Andrographis paniculata, Centella asiatica, Psidium guajava, and Solanum trilobatum leaves were harvested in Agastheswaram Taluk, Kanyakumari district, Tamilnadu, India, in October and November of 2023. Dr. C. Babu, a botany professor at Pioneer Kumaraswamy College in Nagercoil, identified and authenticated these plant specimens. The leaves were thoroughly cleaned before being air-dried at room temperature for 7-8 days. The dried plant leaves were finely crushed and stored in airtight containers.

2.2 Extract Preparation

To prepare the extract, 50 grams of dry leaves from *Andrographis paniculata, Centella asiatica, Psidium guajava,* and *Solanum trilobatum* were placed in a Soxhlet extractor and dissolved in 250 ml of ethanol. The extraction process using the Soxhlet loop continued until the solvent became colorless [21]. Following concentration at room temperature, allowing for solvent evaporation, the resulting extracts were stored in airtight containers. Additionally, the residual solvent was preserved in a refrigerator at 4°C for potential future use [22].

2.3 Phytochemical Analysis

Phytochemical tests were conducted on the leaves of *Andrographis paniculata, Centella asiatica, Psidium guajava*, and *Solanum trilobatum* using established standard methods as previously described [23]. The individual extracts underwent a comprehensive analysis through qualitative and quantitative chemical tests to determine their composition profiles. The extraction of crude powder was performed using various solvents, and the identification of phytoconstituents in each extract was carried out using standard procedures. A range of tests, including those for the presence of Protein, Carbohydrate, Phenol, Tannins, Flavonoids, Saponins, Glycosides, Steroids, Terpenoids, Alkaloids, and Reducing Sugar, was conducted to assess the chemical constituents in the samples.

2.4 Gas Chromatography Mass Spectrum (GC-MS) Analysis

GCMS analysis was performed on plant extracts of Andrographis paniculate, Centella asiatica, Psidium guajava and Solanum trilobatum from Heber Analytical Instrumentation Facility (HAIF), Bishop Heber College, Trichy 620 017 to assess their phytochemical composition. Analyzes were performed using GCMS equipment (GC MS QP2020; SHIMADZU), which includes an autosampler, injector, gas chromatograph (GC2010), and mass spectrometer. The GCMS system consisted of a SHRxi-5Sil-MS capillary standard non-polar column (dimensions: 30.0m, diameter: 0.25mm, film thickness: 0.25µm, which is composed of 100% Dimethyl polysiloxane). Using an electron ionization energy system, the ionization energy was 70 eV. Helium gas (99.99%) was used at a rate of 1.20ml/min and an injection volume of 5µl (split ratio: 10). For a total of 21 minutes, the GC was run at 50°C (isothermal for 2 minutes), increasing to 280°C for 10 minutes. Mass spectra were collected at 70eV at 0.3 seconds and the scanning range was between 50-500m/z. We calculated the percentage of each component by dividing its average peak area by its total peak area. We analyzed the mass spectra and chromatograms using Shimadzu's GC-MS real-time software [24].

2.5 Identification of Components

We have interpreted GC-MS mass spectra via way of means of the usage of statistics from the National Institute Standard and Technique (NIST14) [25] and WILEY8 [26] which include greater patterns. Molecular formulas, names, molecular weights, and structures of each component of the test material have been decided via way of means of comparing the spectrum of the unknown component with the spectrum of the known components from NIST14 and WILEY8 libraries.

2.6 Antimicrobial Bioassay

Preparation of plates: The medium is prepared and sterilized following the manufacturer's instructions. Discs, with a 6 mm diameter, are crafted on Petri plates and sterilized in a hot air oven. On a flat horizontal surface, the medium is poured to a depth of 4 mm into Petri dishes (25 ml in an 85 mm circular dish; 60 ml in a 135 mm circular dish). These poured plates are

refrigerated at +4°C for one week before use. During preparation, the pH of the medium is checked to ensure it falls within the range of 7.2 to 7.4.

***In vitro* antimicrobial activity:** The disc diffusion method [27 & 28] assessed the in vitro antibacterial activity of ethanolic extracts from four medicinal plants (*Andrographis paniculata, Centella asiatica, Psidium guajava*, and *Solanum trilobatum* leaves) *against Escherichia coli Pseudomonas aeruginosa, Enterococcus*, and *Staph aureus*, as well as fungi such as *Candida albicans* and *Aspergillus flavus*. The test organisms were inoculated on solidified agar plates using a micropipette, spread out, and left to dry for 15 minutes. Bacteria/fungi from a broth culture were then spread on the agar plate surface using a sterile cotton swab. Ethanol extracts were placed on sterile filter sheets (6 mm diameter) using sterile forceps. The antibacterial activities were evaluated against standard solutions (Amikacin for bacteria and Nystatin for fungi) used as controls. For fastidious organisms, plates were incubated for 16 to 18 hours at 35 to 37°C in a CO2 aerobic atmosphere. Zone sizes were measured using Vernier calipers after a 24-hour incubation period at 37°C. The zones of inhibition were interpreted according to tables, and each sample was examined three times.

2.7 Molecular Docking Studies

Preparation of ligands: We selected 27 phytocompounds as ligands and therapeutic medicines (Amikacin & Nystatin) as references, both of which have been demonstrated to be likely inhibitors. The PubChem database was used to derive the 3D structures of the ligands and standards. (https://pubchem.ncbi.nlm.nih.gov).

Preparation of target receptor: In this study, *E. coli* [PDB: 1QFG], *Pseudomonas Aeruginosa* [PDB: 1GZT], *Staphylococcus aures* [PDB: 3FYM], *Enterococcus* [PDB: 6QXS], were selected as bacterial targets protein receptor, and *Candia Albicans* [PDB: 4HOF], *Aspergillus Flaves* [PDB: 1R51] were selected as fungal targets proteins receptor. The crystal structures were recovered from the protein data bank (RCSB) (http://www.rcsb.org/pdb) are shown in Fig 1.

Molecular docking analysis: In this study, AutoDock Vina was employed to dock molecules with specified grid coordinates and sizes for each receptor. Ligands were treated as flexible under rigid conditions during their interaction with macromolecules. The AutoDock Vina program was executed through a configuration file opened in Notepad. PDBQT files were prepared, and grid box size and center were set for ADT on Proteins (1QFG, 1GZT, 3FYM, 6QXS, 4HOF & 1R51). Kollman charge and polar hydrogen atoms were added to these proteins. The grid size was established at 14 × 14 × 14 (x, y, and z) points, with specific coordinates for each protein. Negative Gibbs Free Energy scores (kcal/mol) were predicted based on AutoDock Vina scoring for ligand-binding affinities [29]. Post-docking analysis using PyMOL and Discovery Studio provided information on binding site sizes, locations, hydrogen-bond interactions, hydrophobic interactions, and bonding distances within a 5 Å interaction radius from the docked position. Compounds were docked into the active sites of 1QFG, 1GZT, 3FYM, 6QXS, 4HOF & 1R51 proteins, their binding poses were observed, interactions with proteins were investigated, and the most energetically favorable conformation of each ligand was selected.

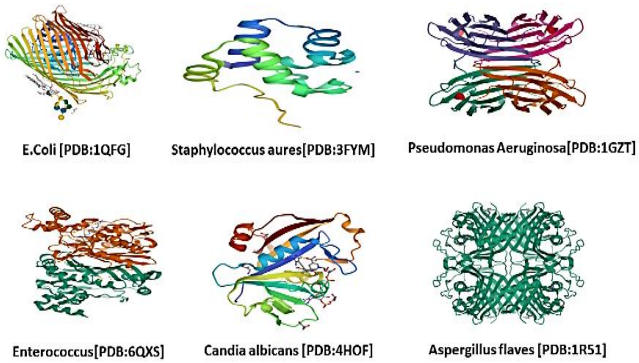

Fig. 1. 3D structures of different Bacterial and Fungal Strains recovered from Protein Data Bank

2.8 ADMET Studies

To estimate individual ADME behaviors of the selected antibiotics, Swiss ADME software of Swiss Institute of Bioinformatics (http://www.sib.swiss) and pkCSM software of University of Melbourne (http://biosig.unimelb.edu.au/pkcsm/prediction) were accessed through a web server that displays Swiss ADMET's Submission page in Google. Molecular inputs are categorized by a simplified molecular-input line-entry system called SMILES, and the results are presented for each molecule in a table and excel spreadsheet. A calculation was performed on Windows 10 Pro, Version 2021[30,31].

3. RESULTS AND DISCUSSION

In the present study, leaf extracts *of Andrographis paniculate, Centella asiatica, Psidium guajava,* and *Solanum trilobatum* were analyses for antimicrobial properties. The use of phytochemical tests, which are cost-efficient and fast, is recommended for the quality control of antimicrobial secondary metabolism. Our study found that phytochemicals were present in ethanol extracts of *Andrographis paniculate, Centella asiatica, Psidium guajava,* and *Solanum trilobatum.*

3.1 Qualitative Phytochemical Analysis of Ethanol Extracts of Four Medicinal Plant

Plants contain chemical substances that possess antimicrobial properties. The most important of these substances are alkaloids, terpenoids, steroids, fatty acids, and phenols. Table 1 shows qualitative phytochemical studies conducted on ethanolic extracts of leaves from *Andrographis paniculate, Centella asiatica, Psidium guajava*, and *Solanum trilobatum*. The phytochemical analysis data revealed that alkaloids, terpenoids, steroids, fatty acids, and phenolic compounds were present. The ethanol extracts of *four medicinal plants* contained high concentrations of terpenoids. *Andrographis paniculate, Centella asiatica,* and *Solanum trilobatum* extracts contained high concentrations of alkaloids. In extracts from Andrographis paniculate, steroids were found in high concentrations. Extracts of *Psidium Guajava* were found to contain very low levels of alkaloids. The phenolic compound was found in high concentrations in *Andrographis paniculate, Psidium Guajava* and *Solanum trilobatum* extracts. Four extracts were found to contain saponin in medium amounts, while extracts from Andrographis paniculate and Psidium Guajava contained very small amounts of flavonoids.

3.2 GC-MS Analysis of Plant Extract

GC-MS is the best tool for determining the functional groups that are involved in the bioactivity of Terpenoids, Steroids, Fatty Acids, Phenolic Compounds, Alkaloids, Saponins, and Flavonoids. We analysed the ethanolic extracts of *Andrographis paniculate, Centella asiatica, Psidium guajava*, and *Solanum trilobatum* using Gas Chromatography - Mass Spectroscopy, as shown in Fig 2 and followed by identify the active phytocompounds and their structure are presented in Fig 3. In Psidium Guajava plant ethanol extract, contain seventy-five phytocompounds are identified by GC-MS. Among seventy-five compounds in the Psidium guajava extract, eight phytocompounds showed to be antimicrobial in nature. The presence of antimicrobial chemicals such like Caryophyllene, Nerolidyl acetate, Curcuphenol, Caryophyllenyl alcohol, Megastigmastrieone, phytol, Hexadecanoic acid, and Neophytadiene was discovered by GC-MS analysis of Psidium guajava extracts are shown in Table 2. In the Solanum trilobatum ethanol extracts, thirty compounds were known and five of these compounds appeared antimicrobial like Lauric acid, Isochiapin B, Phytol, saturated fatty acid and Neophytadiene are shown in Table 3. In Centella Asiatica plant, GC-MS has detected 40 phytocompounds in this plant extracts. Among the 40 compounds in Centella Asiatica, seven of which are antibacterial in nature, such as 2,4-di-tert-butyl phenol, Capsidiol, Loliolide, 5, Hydroxy7,8-dimethoxyflavone, Loliolide, Phytol, Hexadecanoic acid and Neophytadiene are shown in Table 4. In Andrographis paniculate, by using GC-MS 40 phytocompounds of Andrographis paniculata were discovered. Seven antimicrobial compounds have been found among the 40 components in ethanol extract, including Lauric acid, Lupeol, Stigmasterol, and Phytol. Andrographolide, hexadecanoic acid, and Neophytadiene shown in Table 5.

Table 1. Phytochemical analysis of four ethanol plant extracts

Phytochemicals	Result for Ethanolic Extractants			
	Psidium Guajava	***Solanum trilobatum***	***Centella asiatica***	***Andrographis paniculata***
Protein	++	+++	+++	++
Carbohydrate	+++	++	+++	+
Phenol	++	++	-	+++
Tannins	++	+++	+++	-
Flavonoid	+	+	_	++
Saponins	++	+++	++	++
Glycosides	+	++	+	++
Steroids	+	+	+	++
Terpenoids	+++	+++	+++	+++
Alkaloids	+	++	++	+++
Reducing sugar	+	+++	++	-

Note: *+ → present in small concentration; ++ → present in moderately high concentration; +++ → present invery high concentration; - → absent*

Table 2. Antimicrobial compounds are present in ethanol extract of *Psidium gujava* by GC-MS analysis

S. No	Retention Time	Peak Area%	Name of the Compound	Molecular formula	Molecular weight	Name of the Phytocompounds
1.	16.585	3. 85	Caryophyllene	$C_{15}H_{24}$	204	sesquiterpene
2.	19.411	1.11	Nerolidyl acetate	$C_{17}H_{28}O_2$	264	sesquiterpene
3.	19.782	0.39	Curcuphenol	$C_{15}H_{22}O$	218	sesquiterpene
4.	19.826	0.35	Caryophyllenyl alcohol	$C_{15}H_{26}O$	222	sesquiterpene
5.	20.698	0.69	Megastigmatrienone	$C_{13}H_{18}O$	190	terpene
6.	25.222	0.7	Phytol	$C_{20}H_{40}O$	296	Diterpene
7.	26.65	4.9	Hexadecanoic acid	$C_{16}H_{32}O_2$	256	saturated fatty acid
8.	24.486	2.61	Neophytadiene	$C_{20}H_{38}$	278	Diterpene

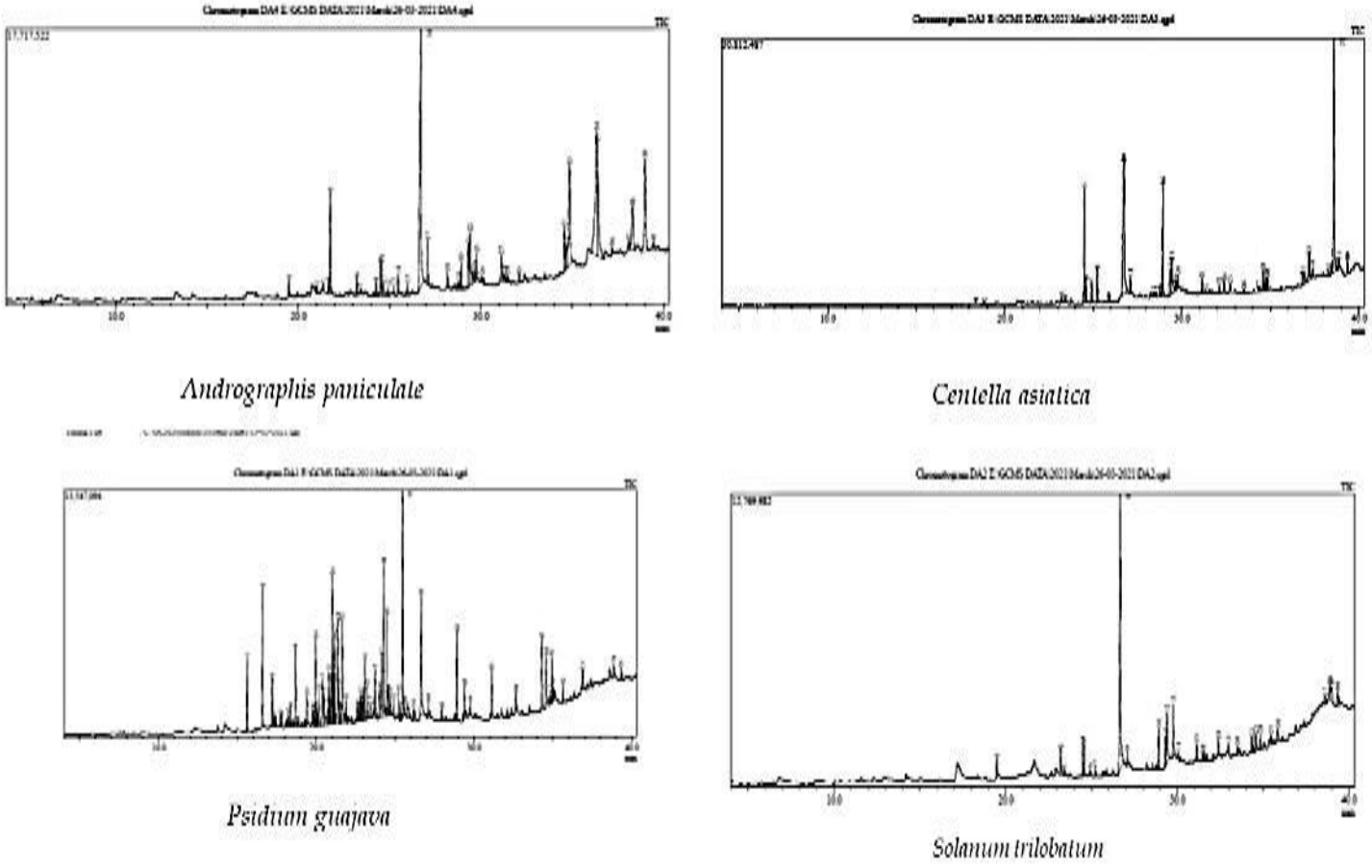

Fig. 2. GC-MS Chromatogram for ethanolic extracts of four plants

Table 3. Antimicrobial compounds in ethanol extract of *Solanum Trilobatum* by by GC-MS analysis

S. No	Retention Time	Peak Area%	Name of the Compound	Molecular formula	Molecular weight	Name of the Phytocompounds
1.	19.48	2.47	Lauric acid acid	$C_{12}H_{24}O_2$	200	saturated fatty acid
2.	24.484	2.93	Neophytadiene	$C_{20}H_{38}$	278	Diterpene
3.	28.922	3.62	Phytol	$C_{20}H_{40}O$	296	Diterpene
4.	26.673	40.44	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256	saturated fatty acid
5.	32.974	1.17	Isochiapin B	$C_{19}H_{26}O_6$	350	sesquiterpene lactone

Table 4. Antimicrobial compounds in ethanol extract of *Centella Asiatica* by by GC-MS analysis

S. No	Retention Time	Peak Area%	Name of the Compound	Molecular formula	Molecular weight	Name of the Phytocompounds
1.	18.355	0.19	2,4-di-tert-butyl Phenol	$C_{14}H_{22}O$	206	hydrocarbon
2.	32.705	0.77	Capsidiol	$C_{15}H_{24}O_2$	236	sesquiterpenoid
3.	37.172	3.23	5-Hydroxy-7,8-	$C_{17}H_{14}O_5$	298	heterocyclic compound
4.	23.417	0.38	Loliolide	$C_{11}H_{16}O_3$	196	monoterpenoid
5.	24.489	7.92	Neophytadiene	C20H38	278	Diterpene
6.	28.543	0.19	Phytol	$C_{20}H_{40}O$	296	Diterpene
7.	26.72	21.84	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256	saturated fatty acid

Table 5. Antimicrobial compounds in ethanol extract of *Andrographis paniculata* by GCMS analysis

S. No	Retention Time	Peak Area%	Name of the Compound	Molecular formula	Molecular weight	Name of the phytocompounds
1	19.48	0.85	Lauric acid	$C_{12}H_{24}O_2$	200	Saturated fatty acid
2.	24.485	1.12	Neophytadiene	$C_{20}H_{38}$	278	Diterpene
3.	24.908	0.4	Phytol	$C_{20}H_{40}O$	296	Diterpene
4.	26.704	19.75	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256	saturated fatty acid
5.	38.11	0.68	Lupeol	$C_{30}H_{50}O$	426	Diterpene
6.	38.989	9.38	Stigmasterol	$C_{29}H_{48}O$	412	Phytosterol
7.	36.341	14.93	Andrographolide	$C_{20}H_{30}O_5$	350	lapdane diterpenoid

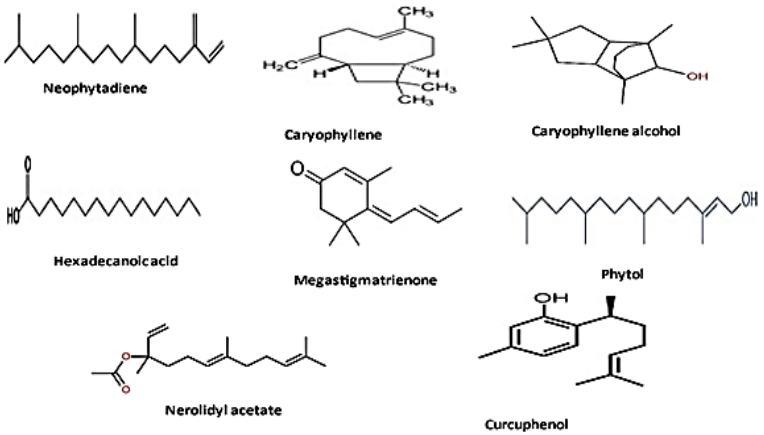

Fig (a). Two-dimensional structure for Psidium Gujava

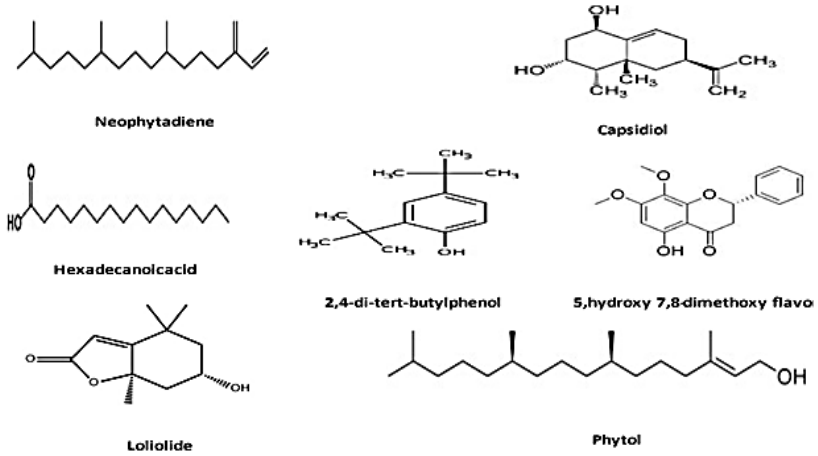

Fig (b). Two-dimensional structure for Centella Asiatica

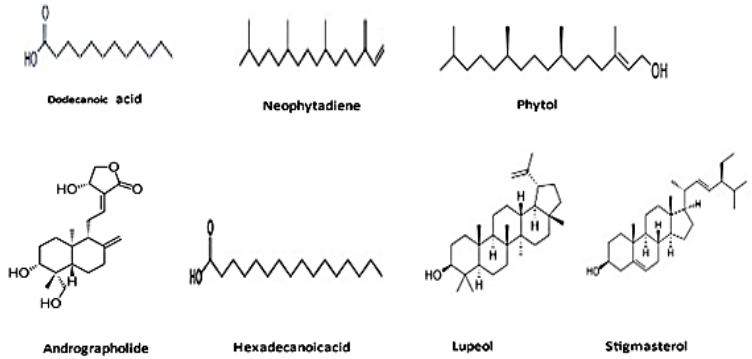

Fig (c). Two-dimensional structure for Andrographis Paniculata

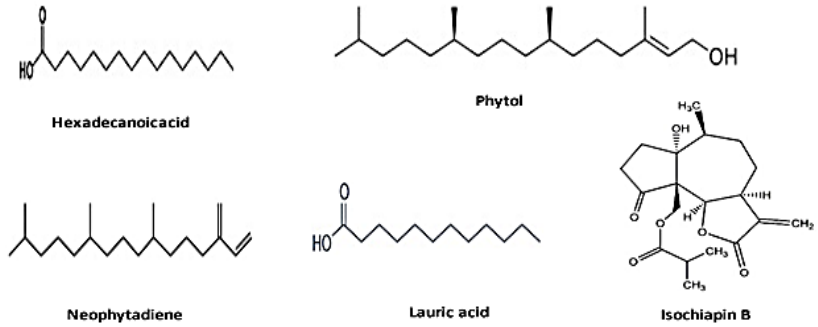

Fig (d). Two-dimensional structure for Solanum Trilobatum

Fig 3. Identified antimicrobial phytocompounds in the ethanol extract of four medicinal plant leaves by using GC-MS analysis

3.3 Antimicrobial Activity Testing

The in vitro antimicrobial activity of four ethanol plant extracts was assessed using the Kirby–Bauer assay method, and the results are presented in Table 6. Comparative analysis with the reference drug Amikacin showed that all four plant leaf extracts exhibited similar antibacterial activity against E. coli, Enterococcus, Pseudomonas aeruginosa, and Staph aureus, though varying degrees of inhibition were observed. Among the ethanol extracts, *Psidium guajava* demonstrated the highest inhibitory potency against *Enterococcus* bacterial strain (19mm), followed by *solanum trilobatum* (16mm), *Centella asiatica* (17mm), and *Andrographis paniculata* (16mm). Notably, *Psidium guajava* exhibited the largest zone of inhibition (19mm) compared to the reference drug Amikacin (19mm). Overall, the 95% ethanol extracts, especially from *Psidium guajava*, displayed the most robust antimicrobial activity among the herb extracts tested in this study .Similarly, from this result revealed that antifungal activity of ethanolic extracts of four plant leaves had good antifungal activity against *Candida albicans, Aspergillus flaves*, and also had highest fungal activity inhibition were absorbed in *Centella asiatica*(13mm) against *Candia albicans* as compared to that of reference drug Nystatin (15mm) than other fungal. On the basis of the mean diameter of the zone of inhibition surrounding the disc in millimetres, the antimicrobial potential of ethanolic extracts in four plants were assessed. A millimeter scale was used to assess the zones of inhibition of the tested microorganisms by the extracts. All the potent zone of inhibition activity in four plants against pathogens are represented in graphically shown in Fig 4.

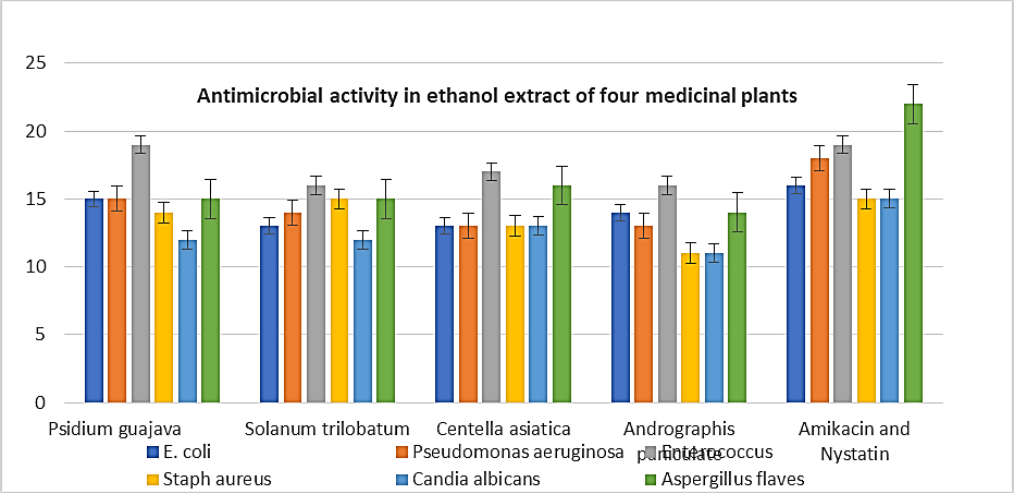

Fig. 4. Antimicrobial activity in ethanol extract of four medicinal plants by Disc diffusion method

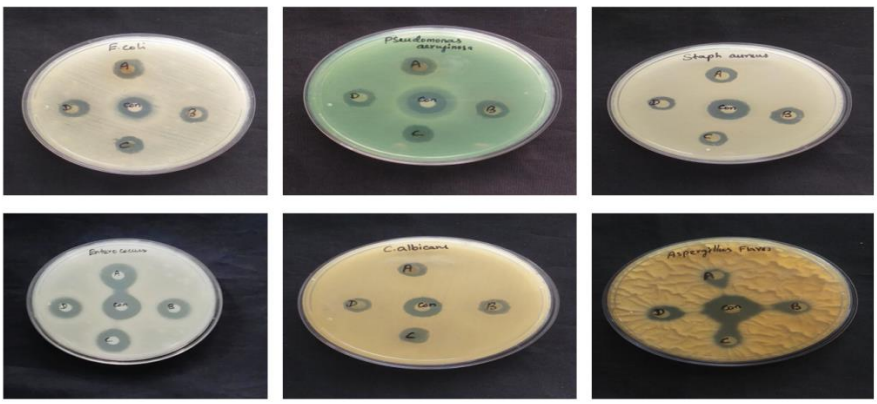

Fig. 5. Antimicrobial screening result in ethanol extract of four plants

Table 6. Antimicrobial screening results of ethanol extracts of four plant measuring the zone of inhibition in millimeters

		Antimicrobial Activity					
		Bacterial Activity				Fungal Activity	
Sl No	**Plant Extracts**	***E. coli***	***Pseudomonas aeruginosa***	***Enterococcus***	***Staph aureus***	***Candida albicans***	***Aspergillus flaves***
1	*Psidium guajava*	15mm	15mm	19mm	14mm	12mm	15mm
2	*Solanum trilobatum*	13mm	14mm	16mm	15mm	12mm	15mm
3	*Centella asiatica,*	13mm	13mm	17mm	13mm	13mm	16mm
4	*Andrographis paniculate*	14mm	13mm	16mm	11mm	11mm	14mm
5	*Reference -Amikacin*	16mm	18mm	19mm	15mm	-	-
	Nystatin	-	-	-	-	15mm	22mm

Table 7. Binding energy table for four medicinal plants with different target proteins by Molecular Docking

Sl.NO	**Plants**	**Phyto Compounds**	**Binding energy value**					
			E. coli	***Pseudomonas Aeruginosa***	***Staphylo coccus aures***	***Entero coccus***	***Candia albicans***	***Aspergillus flaves***
1.	Psidium Gujava	Carryophyllene	-5.3	-5.7	-7.9	-6.2	-6.5	-6.6
		Nerolidyl acetate	-4.6	-4.7	-6.7	-6.0	-6.5	-5.4
		Curcuphenol	-5.6	5.9	-7.0	-6.2	-6.4	-5.9
		Caryophyllenyl Alcohol	-5.3	-5.9	-7.8	-6.6	7.2	-6.7
		Megastigma-Trienone	-5.6	-5.5	-7.1	-5.9	-6.9	-6.3
		Phytol	-2.7	-4.3	-6.3	-5.3	-5.7	-4.1
		Hexadecanoic acid	-3.9	-4.0	-5.5	-4.5	-5.3	-3.8
		Neophytadiene	-3.9	-5.1	-6.5	-6.3	-6.2	-4.7
2.	Solanum Triolobatum	Lauric acid	-3.6	-4.1	-5.2	-4.6	-4.9	-4.9
		Isochiapin B	-5.6	-6.4	-8.1	-7.1	-6.7	-6.8
		Phytol	-2.7	-4.3	-6.3	-5.3	-5.7	-4.1
		Hexadecanoic acid	-3.9	-4.0	-5.5	-4.5	-5.3	-3.8
		Neophytadiene	-3.9	-5.1	-6.5	-6.3	-6.2	-4.7
3.	Centella Asiatica	2,4-di-tert-butylphenol.	-5.6	-5.4	-7.0	-6.3	-7.3	-6.1
		Capsidiol	-5.1	-6.3	-6.9	-6.5	-6.1	-6.5
		5-Hydroxy-7,8-dimethoxyflavone	-6.0	-7.2	-8.5	-7.5	-7.8	-7.4

Sl.NO	Plants	Phyto Compounds	Binding energy value					
			E. coli	***Pseudomonas Aeruginosa***	***Staphylo coccus aures***	***Entero coccus***	***Candia albicans***	***Aspergillus flaves***
		Loliolide	-4.8	-5.6	-6.5	-5.3	-6.2	-6.2
		Phytol	-2.7	-4.3	-6.3	-5.3	-5.7	-4.1
		Hexadecanoic acid	-3.9	-4.0	-5.5	4.5	-5.3	-3.8
		7.Neophytadiene	-3.9	-5.1	-6.5	-6.3	-6.2	-4.7
4.	Andrographis	Lauric acid	-3.6	-4.1	-5.2	-4.6	-4.9	-4.9
	Paniculata	Lupeol	-5.3	-8.9	-7.5	-8.2	-9.6	-8.5
		Stigmasterol	-4.8	-7.8	-9.3	-8.6	-6.7	-7.5
		Phytol	-2.7	-4.3	-6.3	-5.3	-5.7	-4.1
		Hexadecanoic acid	-3.9	-4.0	-5.5	-4.5	-5.3	-3.8
		Neophytadiene	-3.9	-5.1	-6.5	-6.3	-6.2	-4.7
		Andrographolide	-5.6	-7.4	-8.7	-7.5	-7.4	-7.3
	Reference	Amikacin	-4.8	-6.2	-7.2	-7.1	-	-
	Drug	Nystatin	-	-	-	-	-8.6	-7.5

3.4 Molecular Docking

The utilization of Computer-Aided Drug Design (CADD) as a computational strategy has gained renewed interest in drug discovery and design due to its ease, speed, cost-effectiveness, and exceptional success rate in screening molecules for biological and chemical interactions, outperforming traditional methods [32]. This approach accelerates the design of small-molecule ligands, identification of lead compounds, and optimization of drug candidates, contributing to the development of novel therapeutic agents. Molecular docking, a crucial method in computational drug discovery, plays a significant role in predicting the interaction of small compounds with target receptors [33]. This method is preferred for its accurate predictions of binding affinities, intermolecular interactions, and ligand conformations at receptor binding sites [34]. The molecular docking study conducted on twenty-seven phytoconstituents from four medicinal plants against four target proteins aimed to assess the efficacy of these compounds in inhibiting target protein activity. The MolDock scores of the phytoconstituents from the four plants are presented in Table 7.

From the results, In Bacterial activity represents a good number of ligands displayed comparable activity to those of standards. Binding affinities for the reference drug Amikacin show antibacterial activity is -4.8 kcal/mol for E. coli, -6.2kcal/mol for *pseudomonas aeruginosa*, -7.2kcal/mol for *staphylococcus aures*, -7.1kcal/mol for *enterococcus* target proteins while those of the ligands were docking score between – 2.7 kcal/mol to – 8.6 kcal/mol for four selected medicinal plants. In *Psidium gujava*, out of the eight phyto ligands the best binding interaction is -7.9 kcal/mol are obtained in docking of disease proteins of *Staphylococcus* aures by Caryophyllene and it involving the four hydrophobic bond interactinon (PHE X:92, LEU X:20, ILE X:50 and LEU X:54) are shown in Fig.(6a). Similarly, ethanolic extract of *solanum trilobatum*, out of the five phyto ligands the best binding interaction is -8.1 kcal/mol are obtained in docking the disease proteins of *Staphylococcus aures* by Isochiapin B and involving two H-bond interactions (THR X:46&GLN X:19) are shown in Fig(6b). In *Centella asiatica*, out of the seven phyto ligands the best binding interaction is -8.5kcal/mol from docking the disease proteins of *Staphylococcus aures* against 5-Hydroxy-7,8-dimethoxyflavone and involving two H-bond interaction (ASN X:18 & THR X:46), six hydrophobic interaction (LYS X:45, ILE X:14, LEU X:20, PHE X:92, ALA X:7 & ILE X:50) are shown in fig (6c). In *Andrographis paniculate*, out of the seven phyto ligands the best binding interaction is -9.3 kcal/mol and it involving the one H-bond interaction (THR X:121) and five hydrophobic interactions (LYS X:32, LEU X:28, LEU X:54, LEU X:20&ILE X:50) are obtained in docking the disease proteins of *Staphylococcus aures* by Stigmasterol are shown in Fig(6d).

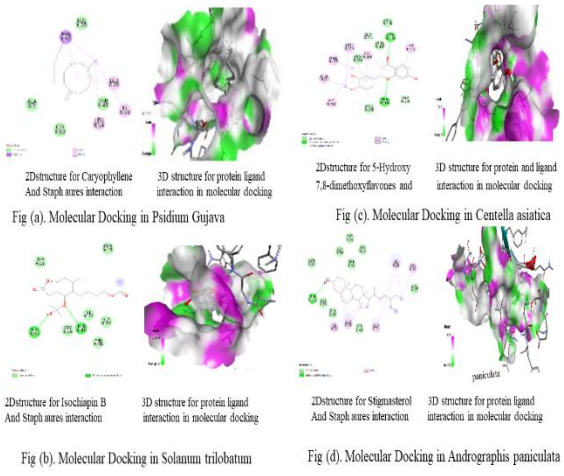

Fig. 6. Antibacterial activity in ethanol extract of four medicinal plants by Molecular Docking analysis

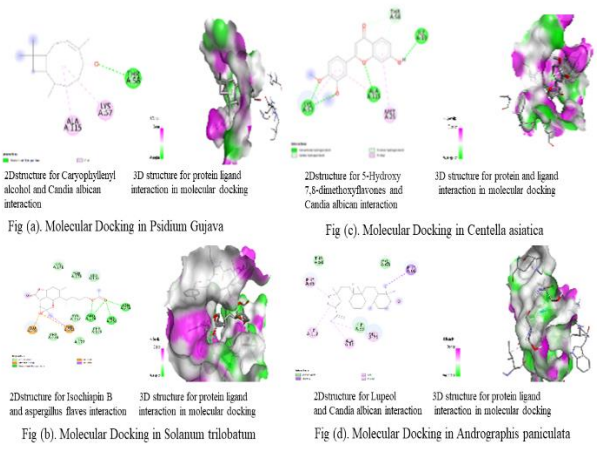

Fig. 7. Antifungal activity in ethanol extract of four medicinal plants by Molecular Docking analysis

In antifungal activity, Binding affinities for reference drug Nystatin is -8.6kcal/mol for *Candia albicans* and -7.5kcal/mol for *aspergillus flaves* target proteins while those of the ligands were docking score between – 3.8 kcal/mol to – 9.6kcal/mol for four selected medicinal plants. In *Psidium gujava*, the maximum inhibitions are obtained from Caryophyllenyl alcohol docked with *Candia albicans* target protein is -7.2kcal/mol and involving one H-bonding interaction (THR A:58) and two hydrophobic interaction (LYS A:57&ALA A:115) are shown in Fig(7a).Similarly, *Solanum trilobatum* have the maximum binding energy is-6.8kcal/mol are obtained from Isochiapin B by *aspergillus flaves* target protein and involving three H-bond interactions (ASN A:254, HIS A:256&ARG A:176), one hydrophobic interaction (PHE A:258) and two electrostatic bond interaction (PHE A:258&GLU A:259) are shown in Fig(7b).In *Centella asiatica*, the maximum binding energy is-7.8kcal/mol and it involving three H-bond interaction (ILE A:19, ALA A:115&LYS A:57) and three hydrophobic interactions (MET A:25, ALA A:115&LYS A:57) are obtained from 5-Hydroxy-7,8-dimethoxyflavone against *Candia albicans* target protein by docking are shown in Fig(7c).Finally *Andrographis paniculate*, the maximum binding energy is-9.6kcal/mol are docking are obtained from Lupeol by *Candia albicans* target protein and it involving the five hydrophobic bond interactions (PHE A:66, MET A:25, ALA A:11, ILE A:112&PHE A:36) are shown in Fig(7d).

This study furnishes Carryophyllene as significant potential inhibitors of Staphylococcus aures bacteria Protein (3FYM) and Caryophyllenyl alcohol as significant potential inhibitors of Candia albicans fungal Protein (4HOF) in Psidium gujava, Similarly Isochiapin B as significant potential inhibitors of *Staphylococcus aures* bacteria Protein (3FYM) and Isochiapin B as significant potential inhibitors of *aspergillus flaves* fungal protein (1R51) in Solanum trilobatum, 5-Hydroxy-7,8-dimethoxyflavone as significant potential inhibitors of Staphylococcus aures bacteria Protein (3FYM) and 5-Hydroxy-7,8-dimethoxyflavone as significant potential inhibitors of *Candia albicans* fungal Protein (4HOF) in *Centella asiatica* and Stigmasterol as significant potential inhibitors of *Staphylococcus aures* bacteria Protein (3FYM) and Lupeol as significant potential inhibitors of *Candia albicans* fungal Protein (4HOF) in *Andrographis paniculate* as compared to that reference drug Amikacin for bacteria activity and Nystatin for fungal activity.

Order of highest Antibacterial activity in ethanol extract of selected four medicinal plants

Stigmasterol (-9.3) > 5-Hydroxy-7,8-dimethoxyflavone (-8.5) > Isochiapin B (-8.1) > Carryophyllene (-7.9)

Order of highest Antifungal activity in ethanol extract of selected four medicinal plants

Lupeol (-9.6) > 5-Hydroxy-7,8-dimethoxyflavone (-7.8) >Caryophyllenyl alcohol (-7.2) > Isochiapin B (-6.8)

3.5 Drug -likeness and Oral Bioavailability Analysis

The pharmacokinetic parameters of potential drug candidates must be evaluated in the early stages of drug discovery. Lipinski and colleagues suggest that drug-like compounds must follow the rule of five (RO5): molecular weight (MW) < 500 Da, number of hydrogen bond donors (HBD) < 5, number of hydrogen bond acceptors (HBAs) < 10, and octanol-water partition coefficient (LogP) < 5. Each violation is limited to one [35]. Table 8 demonstrate that the HA, MW, HBD, HBA, and Log P values of all selected compounds are within the allowed range as stated in the RO5, and no substance violated more than one regulation, although the standard medications utilized (Amikacin and Nystatin) had three violations respectively. The oral bioavailability and other physiochemical parameters of the specified drugs and standards were determined using the Swiss ADME web tool, as shown in Table 8. The bioavailability radar can quickly detect the main physicochemical properties and drug-likeness of the specified compounds and standards [36]. As illustrated in Fig. 8, the colored part (pink) represents the maximum needed area for each of the bioavailability properties. The octanol-water partition coefficient (XLOGP3) from Table 8 was used to calculate the LIPO (lipophilicity) of the compounds and reference drugs. Surprisingly, the selected chemicals such as Stigmasterol, Isochiapin B, Carryophyllene, and Caryophyllenyl alcohol were in the colored zone and fell inside the LIPO recommended range of -0.7 to +5.0. But 5-Hydroxy-7,8-dimethoxyflavone, Lupeol, and Stigmasterol broke from the rule. According to the Lipinski rule of five (RO5), a good drug candidate's SIZE (Molecular Weight)

Table 8. ADMET properties of the identified phytochemical compounds in four medicinal plants

Sl.No	Phyto Compounds	ADMET-Parameters																		
		Absorption				Distribution			Metabolism					Excertion		Toxicity				
		Water Solubility Log Mol/L) (Swiss Adme)	Intestinal Human Absorption (%) (Pkcsm)	Skin Permeability (Log Kp) (Pkcsm)	TPSA(Å²) (Swiss Adme)	VDSS (PKCSM)	BBB Permeability (Logbb) (Pkcsm)	CNS Permeability (Logps) (Pkcsm)	CYP1A2(Swiss Adme)	CYP2C19(Swiss Adme)	CYP2C9(Swiss Adme)	CYP2D6(Swiss Adme)	CYP3A4(Swiss Adme)	Total Clearance (Log Ml/(Pkcsm) Min/Kg)(Pkcsm)	Renal Oct2 Substrate(Pkcsm)	H ERG I Inhibitor (Pkcsm)	H ERG II Inhibitor (Pkcsm)	Skin Sensitization (Pkcsm)	Acute Oral Toxicity(Ld50 Ma/Kg) (Pkcsm)	Bioavailability Score (Swiss	Lipinski Rule (Swissadme)
1	PC1	-3.07 Soluble	93.379	-2.693	37.30	-0.631	0.057	-2.034	No	No	No	No	No	1.623	No	No	No	Yes	1.511	0.85	No Violation
2	PC2	-8.64 Poorly Soluble	95.782	-2.744	20.23	0	0.726	-1.714	No	No	No	No	No	0.153	No	No	No	No	2.563	0.55	1 Violation
3	PC3	-7.46 Poorly Soluble	94.97	-2.783	20.23	0.178	0.771	-1.652	No	No	No	No	No	0.618	No	No	Yes	No	2.54	0.55	1 Violation
4	PC4	-5.98 Moderately Soluble	90.71	-2.576	20.23	0.468	0.806	-1.563	No	No	Yes	No	No	0.618	No	No	Yes	No	2.54	0.55	1 Violation
5	PC5	-5.02 Moderately Soluble	92.004	-2.717	37.30	-0.543	-0.111	-1.816	Yes	No	Yes	No	No	1.763	No	No	No	Yes	1.44	0.85	1 Violation
6	PC6	-6.77 Poorly Soluble	92.85	-2.518	0.00	0.692	0.983	-1.299	No	No	Yes	No	No	1.764	No	No	Yes	Yes	1.473	0.55	1 Violation
7	PC7	-3.18 Soluble	95.357	-3.794	86.99	-0.286	-0.598	-2.691	No	No	No	No	No	1.183	No	No	No	No	2.162	0.55	No Violation
8	PC8	-3.07 Soluble	93.379	-2.693	37.30	-0.631	0.057	-2.034	No	No	No	No	No	1.623	No	No	No	Yes	1.511	0.85	No Violation
9	PC9	-3.13 Soluble	96.607	-3.401	89.90	0.275	-0.421	-2.869	No	No	No	No	No	1.124	No	No	No	No	2.07	0.55	No Violation
10	PC10	-5.98 Moderately Soluble	90.71	-2.576	20.23	0.468	0.806	-1.563	No	No	Yes	No	No	0.618	No	No	No	No	2.54	0.55	1 Violation
11	PC11	5.02 Moderately Soluble	92.004	-2.717	37.30	-0.543	-0.111	-1.816	Yes	No	Yes	No	No	1.763	No	No	No	Yes	1.44	0.85	1 Violation
12	PC12	-6.77 Poorly Soluble	92.85	-2.518	0.00	0.692	0.983	-1.299	No	No	Yes	No	No	1.764	No	No	No	Yes	1.473	0.55	1 Violation
13	PC13	-3.87 Soluble	94.845	-1.58	0.00	0.652	0.733	-2.172	No	Yes	Yes	Yes	No	1.088	No	No	No	Yes	1.617	0.55	1 Violation
14	PC14	-4.53 Moderately Soluble	93.999	-1.93	26.30	0.273	0.57	-2.133	No	Yes	Yes	No	No	1.752	No	No	No	Yes	1.631	0.55	No Violation
15	PC15	-4.53 Moderately Soluble	90.443	-1.617	20.23	0.885	0.423	-1.821	No	No	No	Yes	No	1.217	No	No	No	Yes	2.179	0.55	No Violation
16	PC16	-3.56 Soluble	94.205	-2.038	20.23	0.458	0.566	-2.439	No	No	No	No	No	1.034	No	No	No	Yes	1.683	0.55	No Violation
17	PC17	-2.59 Soluble	95.804	-1.636	17.07	0.263	0.59	-2.094	No	No	No	No	No	0.249	No	No	No	Yes	1.607	0.55	No Violation
18	PC18	-5.98 Moderately Soluble	90.71	-2.576	20.23	0.468	0.806	-1.563	No	No	Yes	No	No	0.618	No	No	Yes	No	2.54	0.55	1 Violation
19	PC19	5.02 Moderately Soluble	92.004	-2.717	37.30	-0.543	-0.111	-1.816	Yes	No	Yes	No	No	1.763	No	No	No	Yes	1.44	0.85	1 Violation
20	PC20	-6.77 Poorly Soluble	92.85	-2.518	0.00	0.692	0.983	-1.2999	No	No	Yes	No	No	1.764	No	No	Yes	Yes	1.473	0.55	1 Violation
21	PC21	-4.55 Moderately Soluble	92.034	-2.301	20.23	0.611	0.478	-0.848	No	No	No	Yes	No	0.759	No	No	No	Yes	2.351	0.55	No Violation
22	PC22	-3.0 Soluble	93.724	-2.918	40.46	0.255	0.084	-2.94	No	No	No	No	No	1.241	No	No	No	Yes	1.826	0.55	No Violation
23	PC23	-4.12 Moderately Soluble	94.748	-2.719	68.90	0.022	-0.29	-2.228	Yes	Yes	Yes	Yes	Yes	0.413	Yes	No	No	No	2.537	0.55	No Violation
24	PC24	-1.69 Very Soluble	95.935	-3.816	46.53	0.117	-0.189	-3.048	No	No	No	No	No	1.042	No	No	No	No	1.94	0.55	No Violation
25	PC25	-5.98 Moderately Soluble	90.71	-2.576	20.23	0.468	0.806	-1.563	No	No	Yes	No	No	0.618	No	No	Yes	No	2.54	0.55	1 Violation
26	PC26	5.02 Moderately Soluble	92.004	-2.717	37.30	-0.543	-0.111	-1.816	Yes	No	Yes	No	No	1.763	No	No	No	Yes	1.44	0.85	1 Violation
27	PC27	-6.77 Poorly Soluble	92.85	-2.518	0.00	-0.692	0.983	-1.299	No	No	Yes	No	No	1.183	No	No	Yes	Yes	1.473	0.55	1 Violation
28	RD1	-2.23 Highly Soluble	0	-2.735	331.94	-1.671	-2.05	-5.453	No	No	No	No	No	0.36	No	No	No	No	2.414	0.17	3 Violation
29	RD2	-5.26 Moderately Soluble	0	-2.735	319.61	-0.355	-2.09	-3.702	No	No	No	No	No	-1.357	No	No	No	No	2.518	0.17	3 Violation

Where, PC1 -Lauric acid PC2 -Lupeol PC3-Stigmasterol PC4-Phytol PC5-Hexadecanoic acid PC6-Neophytadiene PC7-Andrographolide PC8 -Lauric acid PC9-Isochiapin B PC10-Phytol PC11 -Hexadecanoic acid PC12-Neophytadiene PC13-Caryophyllene PC14-Nerolidyl acetate PC15-Curcuphenol PC16-Caryophyllenyl alcohol PC17-Megastigmatrienone PC18-Phytol PC19-Hexadecanoic acid PC20-Neophytadiene PC21-2,4-di-tert-butylphenol PC22-Capsidiol PC23-5, Hydroxy 7,8-dimethoxyflavone PC24-Loliolide PC25-Phytol PC26-Hexadecanoicacid PC27-Neophytadiene RD1-Amikacin RD2-Nystati

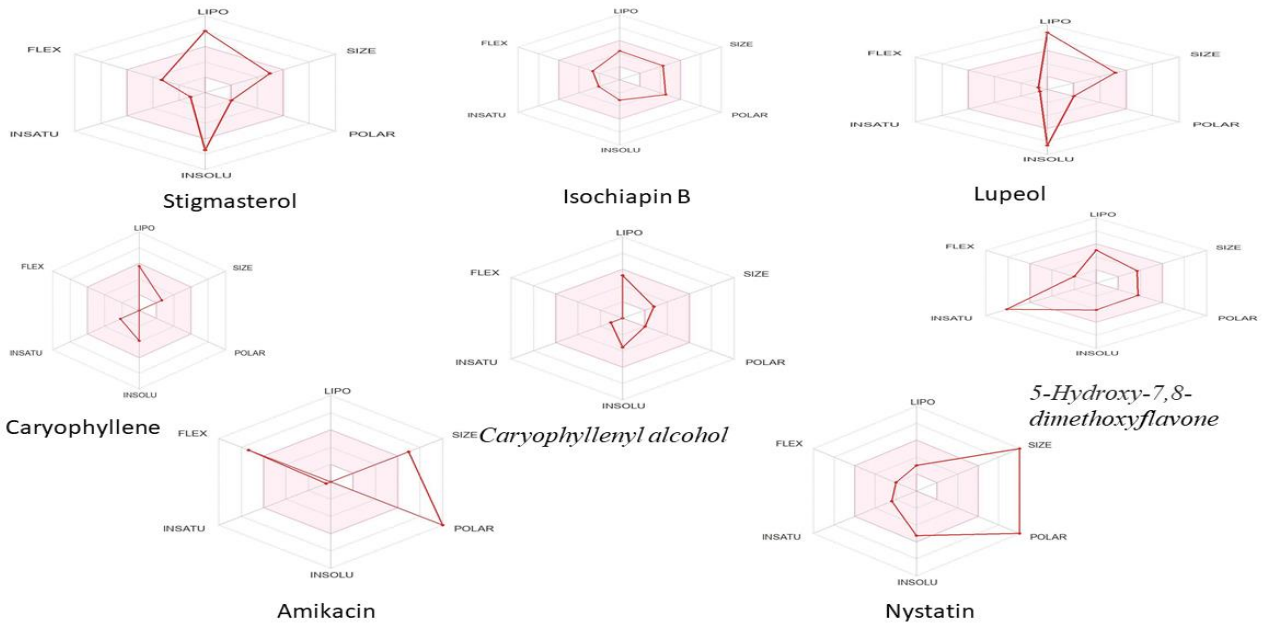

Fig 8. Bioavailability Radar images for best active binding energy compounds from four medicinal plants and standard components

should not exceed 500gmol-1, which applies to all compounds. The INSOLU (insolubility) requirement of the selected compounds as depicted in their ESOL (Log S) and ESOL Class revealed that Isochiapin B, Carryophyllene, and Caryophyllenyl alcohol are very soluble, 5-Hydroxy-7,8-dimethoxyflavone is moderately soluble, while Lupeol and Stigmasterol are poorly soluble, and reference drug amikacin is highly soluble while nystatin is moderately soluble, respectively. The Total Polarity Surface Area (TPSA), with proposed values ranging from 20 to 130 A°, was utilized to investigate the POLAR (polarity) of the selected compounds. Only C-1 and C-2 fit inside the ideal range, as indicated in Table 8 and Fig. 8, whereas the others fell apart.

3.6 ADMET Properties of the Selected Phytocompounds and Standards

The ADMET SAR2 online server was used to calculate the ADMET values (absorption, distribution, metabolism, excretion, and toxicity) shown in Table 8. ADMET qualities are critical in the early stages of drug discovery and development because high-quality drug candidates must exhibit acceptable efficacy against the therapeutic target as well as appropriate ADMET properties at a therapeutic dose [37]. Interestingly, all of the selected antibiotics have a higher probability of being absorbed than the reference drug in the human intestine, with HIA + values of 94.97%, 94.748%, 96.607%, 94.845%, 93.379%, and 94.205% for Stigmasterol, 5-Hydroxy-7,8-dimethoxyflavone, Isochiapin B, Carryophyllene, Lupeol, and Caryophyllenyl alcohol, respectively. The normal HIA absorption rate for Amikacin and Nystatin is 0%. Furthermore, specific phytocompounds such as Stigmasterol, Carryophyllene, Lupeol, and Caryophyllenyl alcohol have a high likelihood of crossing the blood-brain barrier, which is an important pharmacokinetic feature in drug discovery. Other selected drug candidates and the reference drug have negative BBB potential; however, this may not pose a threat in the meantime. Our focus in this study is not on outcome potential drug candidates that target brain receptors, such as antiepileptic, antipsychotic, and antidepressant drugs. Furthermore, a drug compound is expected to be in the aqueous solubility range of -1 to -5, with Log S values of -3.13, -3.87, and -3.56 for selected phytocompounds such as Isochiapin B, Carryophyllene, and Caryophyllenyl alcohol, -4.12 for 5-Hydroxy-7,8-dimethoxyflavone, and -7.46 for Stigmasterol. The log S value of the standard is -2.23 for Amikacin, which is very soluble, and -5.26 for Nystatin, which is moderately soluble. The selected phytocompounds are within the range, indicating that they have better absorption and distribution potential than the reference drugs. The range of cytochromes (CYPs) governs drug metabolism, with CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4 being crucial for the biotransformation of drug compounds. Microsomal enzymes (Cytochrome P450 inhibitors) were also used to predict the metabolic activities of the proposed medication candidates. Among the chosen medications and standards are non-inhibitors of all Cytochrome P450, such as Isochiapin B, Caryophyllenyl alcohol, Stigmasterol, Lupeol, Amikacin, and Nystatin, which increase their metabolism as possible therapeutic agents. The specific phytocompounds and reference medication are projected to be non-biodegradable, although they are not carcinogenic. The data from excretion experiments revealed that all of the selected phytochemical compounds and standard amikacin had positive total clearance values and could be eliminated completely. Considering the AMES toxicity of the selected phytocompounds and standards, i.e., their mutagenic capacities, all phytocompounds were found to be non-AMES-toxic except for Isochiapin.B. Furthermore, all of the selected chemicals and standards have type III oral acute toxicity, which means that they remain mildly poisonous despite causing no ocular irritation or corrosion. Nonetheless, type III toxicity can be rapidly advanced to type IV and converted (non-toxic) during the lead optimization era of drug discovery. A drug's capacity to decrease human hERG is truly harmful since it can block the potassium ion channel in the myocardium, disrupting the electric activity of the heart and perhaps causing early death [38, 39]. Interestingly, the majority of the selected phytocompounds and standards do not inhibit hERG, with compounds C-1 and C-2 having a higher likelihood of being non-inhibitors. In conclusion, based on the facts presented above, we were able to determine that Caryophyllene alcohol, derived from an ethanol extract of *Psidium gujava*, possesses the most antibacterial capabilities of every phytocompound tested. Furthermore, these phytocompounds are safe and excellent therapeutic candidates in the absence of the target receptor. The ADME and Docking tests validated that the selected phytocompounds closely match the *in vitro* antimicrobial investigations.

4. CONCLUSION

According to the findings, 27 powerful phytochemicals with antibacterial activities have been discovered in four medicinal plants. These chemicals are effective in suppressing the growth of human infections. In vitro tests found that of the four plants, *Psidium guajava* ethanol extracts had the strongest antibacterial activity, with reference amikacin showing equivalent inhibitory efficacy. In an antifungal investigation, *Centella asiatica* showed a maximal zone of inhibition against *Candida albicans* when compared to the reference medication Nystatin, confirming effective inhibitory efficacy. Docking experiments revealed that Stigmasterol (-9.3 kcal/mol), one of the discovered phytochemicals, is a potential good inhibitor against the bacterial strain Staphylococcus (PDB:3FYM), implying a role as a bacterial antibiotic from *Andrographis paniculata*. Similarly, the antifungal activity of Lupeol (-9.6 kcal/mol) appears as a possible good inhibitor of the fungal strain *Candida albicans* [PDB:4HOF], implying its involvement as a fungal antibiotic from *Andrographis paniculata*. This compares to conventional antibiotics like Amikacin (-7.2 kcal/mol) and Nystatin (-8.6 kcal/mol). Furthermore, the ADMET (Drug-likeness) investigations revealed that the phytocompounds had the highest drug-likeness qualities, implying that these compounds behave as drugs and have extraordinary biological activity.These findings can serve as a major tool for further assessing the plant's biological and pharmacological capabilities. When compared to reference drugs such as amikacin and Nystatin, the six highest docking score phytocomponents from ADMET, namely Isochiapin B, Carryophyllene, Caryophyllenyl alcohol, Stigmasterol, 5-Hydroxy-7,8-dimethoxyflavone, and Lupeol, demonstrated significant drug likeness properties based on Lipinski's rule-of-five. Furthermore, investigations on the ADMET profiles of certain phytocompounds demonstrate that they are easily absorbed by humans, do not inhibit Cytochrome P450, are not carcinogenic, and do not inhibit hERGs. However, during the Hit-Lead optimization stage of drug development, there is the possibility to enhance their potency, efficacy, pharmacokinetics, and reduce toxicity. In vitro studies, molecular docking, drug-likeness properties, and ADMET analysis indicate that the selected compounds have the potential to be used as drug leads for highly potent bioactive antimicrobial compounds found in plants such as *Psidium guajava, Andrographis paniculata, Solanum trilobatum,* and *Centella asiatica* when compared to reference drugs. These phytochemicals must be extracted before in-vivo investigations may be conducted for further investigation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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