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ANTIMICROBIAL SCREENING OF CRUDE EXTRACT OF PLUCHEA ARABICA: CHEMICAL COMPONENTS, DRUG LIKENESS, PHYSICOCHEMICAL PROPERTY AND MOLECULAR DOCKING ASSESSMENT

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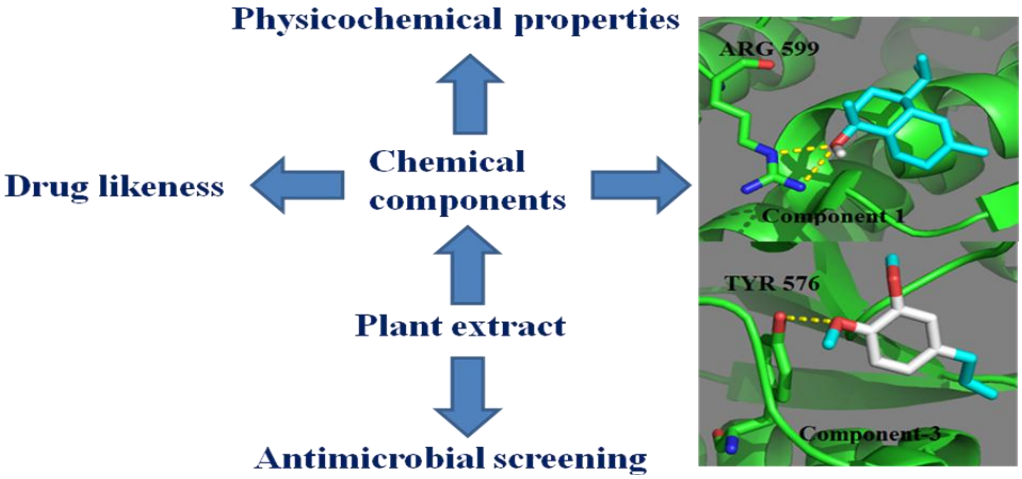
ABSTRACT

Objective: To explore the antimicrobial efficacy of the crude extract of Pluchea Arabica, drug likeness, physicochemical and molecular studies of its components.

Methods: The crude extract was obtained applying soxhelt extraction assembly and the antimicrobial screening was performed using disc diffusion method. The drug likeness and physicochemical were investigated by employing the available software on the web (www. molinspiration.com) and molecular docking studies was carried out by Auto Dock Tools-4.2.



Results: The methanol extract possess significant activity in comparison to the n-hexane extract. All the components following the Lipinski rule, out of all three components showed good bioactivity score in which two (1 & 3) mainly belongs to methanol extract and hydrogen bonding to the receptor also observed with these two component on molecular docking assessment.

Conclusion: The crude extract of Pluchea Arabica was screened for antimicrobial evaluation and its components were subjected for calculation of computational parameters and molecular docking studies. Methanol extract of this is found to possess better antimicrobial potential than the n-hexane and the computational studies strongly supported the experimental results.

KEYWORDS: *Pluchea arabica* extract, antimicrobial and computational studies.

INTRODUCTION

Resistance to present antimicrobial drugs has become a major public health concern globally[1]. The microbial diseases are amplified mainly due to indiscriminate use of antibiotics that leads to the antibiotic resistance[2-3]. Mutation and genetic exchange systems revoked the elimination of disease and are responsible for antimicrobial resistance[2-4]. Medicinal plants have been widely investigated as the rich source of antimicrobial agents. A variety of medicinal plants possess chemical compounds representing different biological and pharmacological potentials. Numerous studies has been carried out on biological and pharmacological potential of plants, such as antimicrobial, antioxidant, antitumor, anti-inflammatory, hypoglycemic, etc.[5-10]. Pluchea, corresponds to the family Asteraceae comprising eighty

species throughout the world mainly in African, American and Asian[11]. The plant has been found to exhibit the variety of traditional pharmacological applications[12-19]. The compounds found in the Pluchea are as follows- sesquiterpenoids, monoterpenes, lignan glycosides, triterpenoids, flavonoids, lignan glycosides, terpenic glycosides, tertiary bases, a large number of water-soluble quaternary bases, including pluchine 7-O-glucoside. The flavonoids include quercetin, isorhamnetin, hesperidin, a dihydroflavonol-taxilolin 3-arabinoside and an isoflavonoid-formononetin[20-31]. In a recent study antioxidant properties of Pluchea arabica showed the inhibition of DPPH radical at 89-93%. Recently the fresh twigs of *Pluchea arabica* (Boiss) were analyzed for the main components such as δ-cadinol, 9-(1-methylethylidene)-bicyclo[6.1.0]nonane, caryophyllene oxide, methyleugenol and β-caryophyllene[32]. It is crucial important to discover some new antimicrobial agents with different mode of action and less cytotoxicity considering the medicinally important natural resources which will help to replace the currently available antimicrobials[33].

Experimental

Extraction

The extraction of the compounds from *Pluchea arabica* was prepared using Soxhlet extraction assembly, methanol and n-hexane solvent. The Fresh twigs of *Pluchea arabica* were grounded and kept inside a thimble loaded into the soxhlet extractor for 15 hr in the solvent (300 mL) with refluxing at the boiling temperature of solvent. After completion dried under vacumm applying Heidolph laborata/Germany. The obtained extract was incubated at 40 ^{0} C for 24 hr, after that stored at 4 ^{0}C evaluation for antimicrobial activity.

Antimicrobial activity

Antimicrobial activity of the extract was employed against all the gram negative and gram positive pathogens by the reported method. The dilutions were obtained as 3.125, 6.25, 12.5, 25 and 50 µg/ml. Ciprofloxacin was taken as positive control and Methanol and n-hexane poured disk was used as negative control[39-47].

Physicochemical properties

The components were subjected for physicochemical properties such as miLogP, TPSA, Natoms, MW, nON, nOHNH, Nviolations, Nrotb, Volume using the online available software (www. molinspiration.com)[48-54].

Bioactivity score

The components were also subjected for the calculation of the bioactivity score of the components using the same software as for physicochemical properties at (www. molinspiration.com)[48-54].

Molecular docking studies

The docking analysis for all the component was performed using GlcN-6-P synthase, (PDB: 2VF5) following the procedure[55-56]. The structures were made using ChemDraw Ultra 8.0 and were optimized for energy to yield 3D.

RESULTS

Antimicrobial activity

The antimicrobial activity of the extract for both portions methanol and n-hexane was done as the zone of inhibition was mapped with antibiotic zone scale and the findings are reported in the **Table-1, Table-2 and Table-3.**

The phytochemical screening

The reported literature confirmed that the pluchea extract has been found to possess δ-cadinol (26.8%), 9-(1-methylethylidene)-bicyclo[6.1.0]nonane (10.8%), caryophyllene oxide (10.0%), methyleugenol (9.2%) and β-caryophyllene (6.9%) **Fgure-1** shows the structures of all the components[33].

Physicochemical properties[34-38]

Lipinski's rule of five explained the general criteria for the activity of the drug such as the MW of the drug should not exceed than 500, that, in general, it should not possess more than five OH and NH groups and not ten N and O, the log P must less than 5 and number of violation less than 4. The components were obtained in agreement with Lipinski's rule of five except components three that exhibited the partition coefficient 5.17, the detailed results are reported in **Table 4**.

Bioactivity score[34-38]

For a drug to be active it is the required condition that it should possess the bioactivity score more than 0.00, if it is up to -0.50 then moderate active and finally if it is less than -0.50 then it lies in the category of inactive drugs. The results for calculated bioactivity score are presented in **Table 5**. The results exhibited that the bioactivity score for component one and three and five are mostly lying under the zone of active and moderately active drugs but for component two and four mostly lying in inactive region, a little moderately active but nothing in active drugs range.

Molecular docking studies

The docking analysis for all the components of P. Arabica was performed using GlcN-6-P synthase, (PDB: 2VF5) The results for molecular docking studies are provided in **Figure-2, 3 and 4,** the results exhibited that the hydrogen bonding is found only in two components (component one and component three) of the extracts and both the components belongs to the methanol extract. The component one is forming hydrogen bond with ARG 599 and the component three with TYR 576 residue. The component three was found to exhibit resemblance with the standard drug ciprofloxacin with respect to the H-bond with TYR 576. Rest of the components belonging to n-hexane, have no hydrogen

bonding that provides strong recommendation to the obtained experimental results for antimicrobial assay.

Table: 1. Representing zone of inhibition for methanol extract of *Pluchea arabica* against gram positive and gram negative bacteria.

Compounds (µg/ml)	Effect of methanol extract on Microorganism			
	Gram positive		Gram negative	
	S. aureus	*S. epidermidis*	*P. mirabilis*	*E. coli*
50	19.30±.22	18.50±.34	15.32±.24	15.14±.11
25	17.14±.04	16.25±.22	10.42±.19	13.24±.12
12.5	11.12±.52	07.14±.40	-	11.52±.32
6.25	10.22±.32	-	-	11.08±.14
3.125	09.24±.18	-	-	9.14±.04

Table: 2. Representing zone of inhibition for n-hexane extract of *Pluchea arabica* against gram positive and gram negative bacteria.

Compounds (µg/ml)	Effect of n-Hexane extract on Microorganism			
	Gram positive		Gram negative	
	S. aureus	*S. epidermidis*	*P. mirabilis*	*E. coli*
50	12.30±.22	09±.34	08.32±.20	19.34±.11
25	10.14±.04	8.12±.22	-	9.18±.34
12.5	9.52±.52	-	-	7.24±.04
6.25	08.22±.32	-	-	-
3.125	-	-	-	-

Table: 3. Representing zone of inhibition for ciprofloxacin, methanol and hexane against gram positive and gram negative bacteria.

Microorganism			
	Ciprofloxacin (10 µg/ml)	Methanol	Hexane
S. aureus	21.46 ±.31	-	-
S. epidermidis	22.64±.54	-	-
P. mirabilis	22.24±.30	-	-
E. coli	23.82±.47	-	-

Table: 4. Representing the physicochemical properties of all the components found in *Pluchea arabica* and ciprofloxacin.

Physicochemical property score	Components					
	1	**2**	**3**	**4**	**5**	**Ciprofloxacin**
miLogP	4.97	2.41	**5.17**	5.00	4.14	-0.701
TPSA	20.23	18.47	0.00	0.00	12.53	74.569
Natoms	16	13	15	12	16	24.0
MW	222.37	178.23	204.36	164.29	220.36	331.347
nON	1	2	0	0	1	6
nOHNH	1	0	0	0	0	2
Nviolations	0	0	1	0	0	0
Nrotb	1	4	0	0	0	3
Volume	243.65	179.67	229.95	185.96	234.01	285.46

Table-5: Representing the bioactivity score of all the components found in *Pluchea arabica* and ciprofloxacin.

Bioactivity score	Components					
	1	**2**	**3**	**4**	**5**	**Ciprpfloxacin**
GPCR ligand	-0.09	-0.81	-0.34	-0.76	-0.08	0.12
Ion channel modulator	0.05	-0.38	0.28	-0.35	0.14	-0.04
Kinase inhibitor	-0.87	-1.06	-0.78	-1.23	-0.86	-0.07
Nuclear receptor ligand	0.39	-0.80	0.13	-0.63	0.62	-0.19
Protease inhibitor	-0.63	-1.14	-0.60	-1.00	0.00	-0.21
Enzyme inhibitor	0.40	-0.43	0.19	-0.30	0.57	0.28

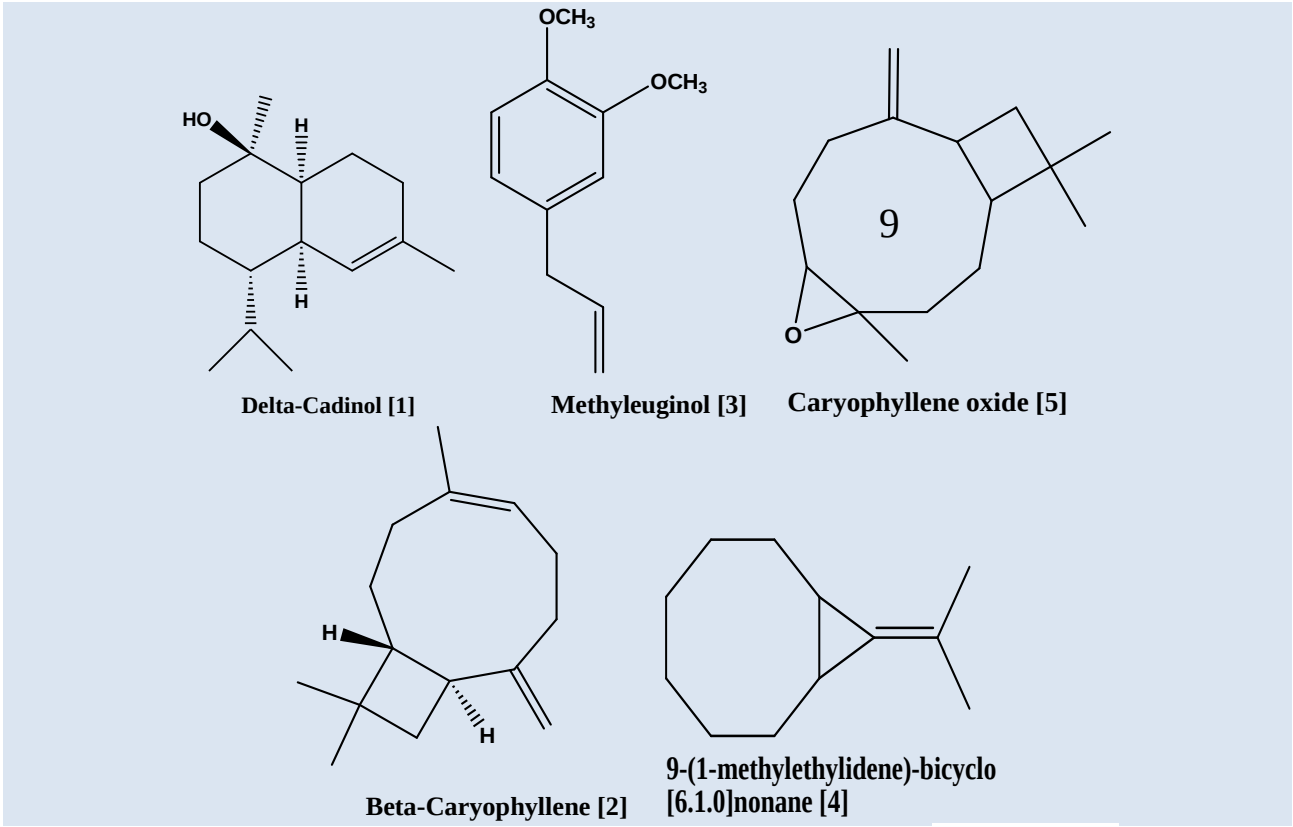
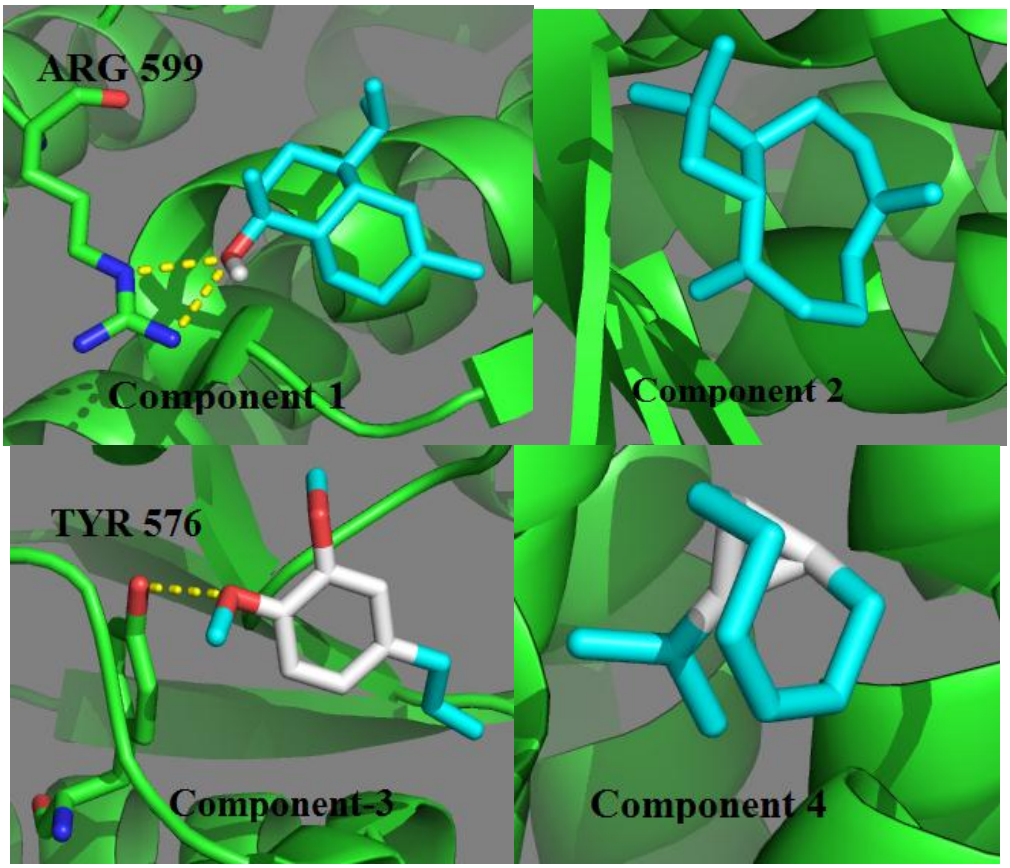


Figure-1- Exhibiting the structures of all the components found in *Pluchea arabica.*



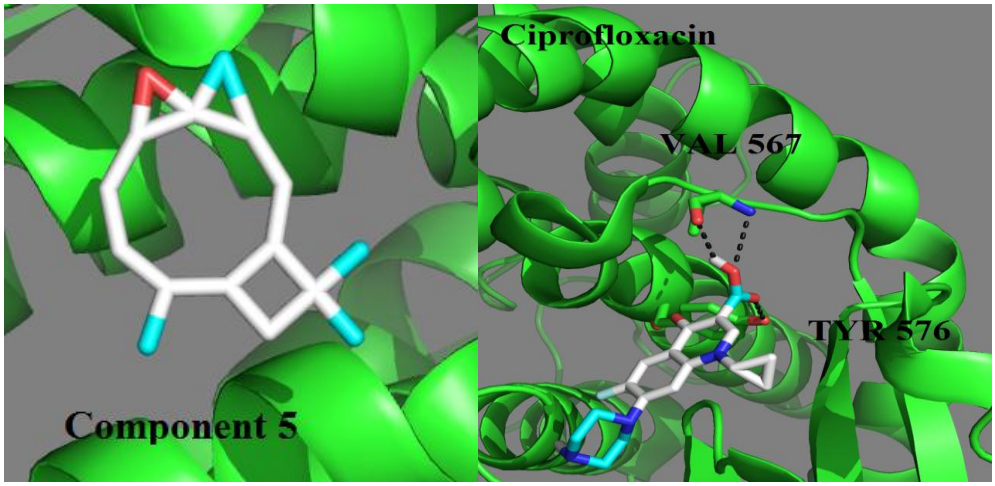


Figure-2- Representing the docked images of the synthesized compounds with the GlcN-6-P-synthase.

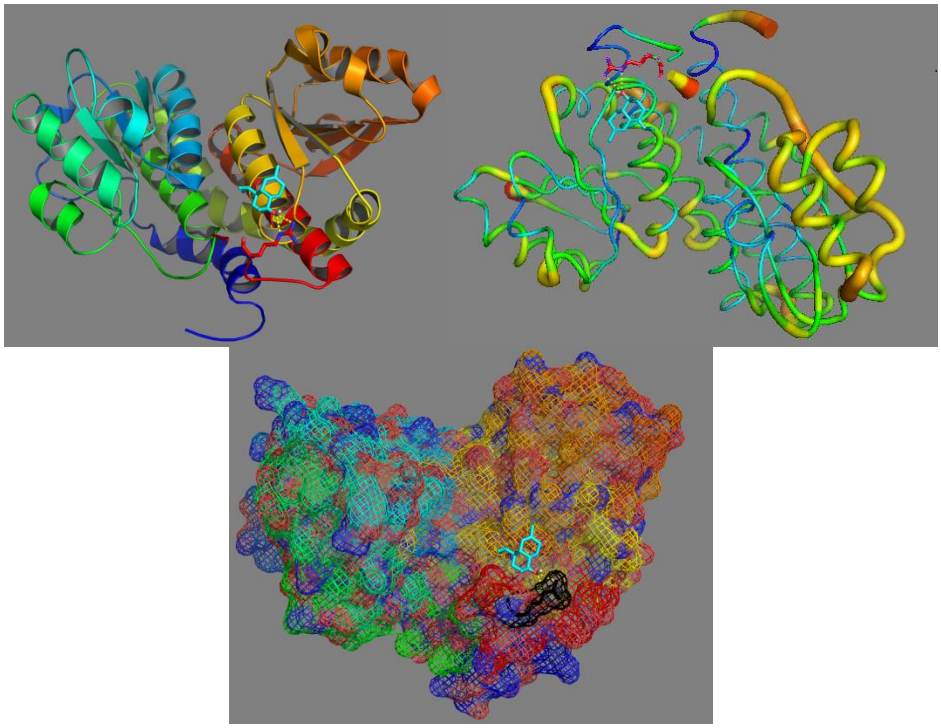
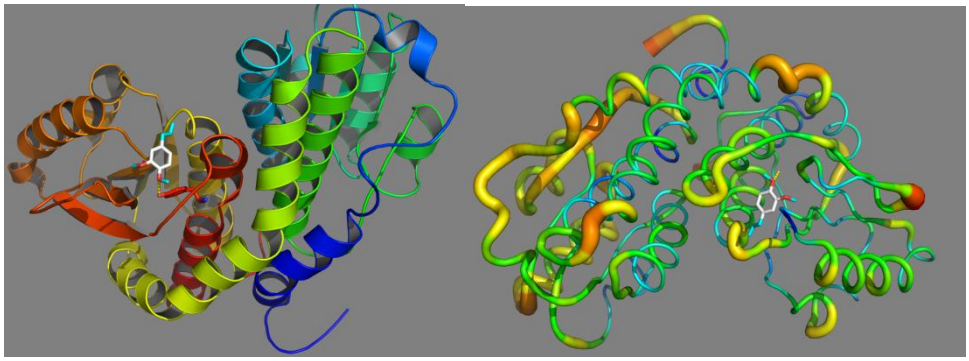


Figure-3- Exhibiting the different binding modes for component -1



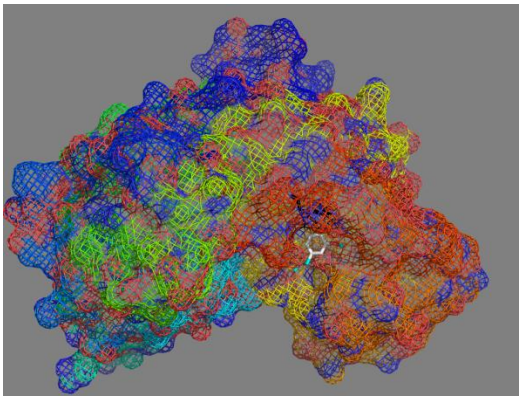


Figure-4- Exhibiting the different binding modes for component-3.

DISCUSSION

The crude extract of the plant pluchea arabica was obtained and subjected for antibacterial study. The results for antibacterial activity exhibited that methanol extract represented better antibacterial potential than n-hexane. Targeting the phytochemical screening were achieved on the basis of available literature which confirms the presence of components *δ*-cadinol and methyleugenol mainly in methanol extract[32-33]. The elevated bioactivity might be because of the composition of methanol extract. Though to confirm the results obtained by phytochemical and antibacterial analysis we carried out the virtual screening of all the components present in the extract of Pluchea Arabica, calculated the physicochemical parameters and bioactivity score and found that results strongly supported the studies. To find out more clear picture regarding the study molecular docking studies were also carried out which provided strong recommendation that the antibacterial potential of methanol extract of pluchea Arabica is having better antibacterial potential than the n-hexane extract as the formation of hydrogen bond to the receptor is only observed in case of the components belongs to methanol extract.

CONCLUSION

The extraction of plant *Pluchea arabica* was performed and subjected for biological potential. The obtained results showed that the methanol extract of the plant contained better antimicrobial potential than the n-hexane extract. On the basis of available literature the plant components of P. Arabica, aimed for virtual screening to calculate the bioactivity, physicochemical and docking properties. The computational findings were found in strong recommendation to experimental results. Our study, the screening for antimicrobial potential in addition to the computational studies can be used as lead finding for the development of antimicrobial agents from natural sources.

Conflict of Interest

There is no conflict of interests.

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