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SYNTHESIS, MOLECULAR DOCKING STUDIES AND ANTIMICROBIAL ACTIVITY OF SUBSTITUTED CINNAMIDES

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ABSTRACT

A series of substituted cinnamide derivatives were synthesized by the condensation of 4-benzylidene-2-phenyl-1,3-oxazol-5(4H)-one with cyclohexylamine in presence of ethyl alcohol at room temperature. The chemical structures of synthesized compounds were confirmed by means of IR, ^{1}H NMR, mass spectral and elemental analysis. All the compounds were screened for antimicrobial activity against bacterial strains Staphylococcus aureus (gram positive), Escherichia coli (gram negative) and fungal strains Penicillium chrysogenum, Penicillium notatum and Aspergillus niger by cup plate method and also in silico and molecular docking studies using XP GLIDE. Out of these compounds N-cyclohexyl-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-(phenylformamido) prop-2-enamide (5) exhibited good antimicrobial activity against all the strains tested, which was comparable to standard drugs Ciprofloxacin and Fluconazole. Compound 5 also showed better docking score (-8.397) than standard drug ciprofloxacin (-4.74) predicted by XP GLIDE module of Schrodinger suite against FAB protein. All the derivatives obey Lipinski rule of five and has good bioactive scores.

KEY WORDS

Cinnamide, Antimicrobial activity, Docking, in silico screening.

INTRODUCTION

During the past few decades there is a dramatic increase of multi drug resistant pathogenic strains which potentiates the difficulties to treat with existing antibiotics and also slow down the development of new synthetic antimicrobial agents. Hence it is imperative to search for new compounds for treating pathogens. It is well known from literature Cinnamide derivatives (C_6H_5-CH=CH-CO-NH-R) are the versatile molecules constitutes an important class of organic compounds. In recent years, cinnamic acid derivatives such as cinnamides are reported to possess variety of biological activities such as antioxidant [1,2], antimicrobial [3], antitumor [4], antitubercular, anti-inflammatory [5,6,7], antifungal activity [8] and are often used as promising precursor for the development of new, highly effective drugs. However, the reactive center (vinyl fragment) of cinnamides was significantly affected by substituent present at various positions of the benzene nucleus [9-10]. Curcumin and dehydrozingerone are reported be potent scavengers of oxygen free radicals and also possess good anti-inflammatory activity [11]. In view of this,it has been planned to synthesize new substituted cinnamide derivatives and screened for antimicrobial activity and molecular docking studies against FAB protein[12] (β-ketoacyl-acyl carrier protein synthase III)

retrieved from the Protein Data Bank (PDB) incorporated with inhibitor followed by *in silico* studies.

MATERIALS AND METHODS

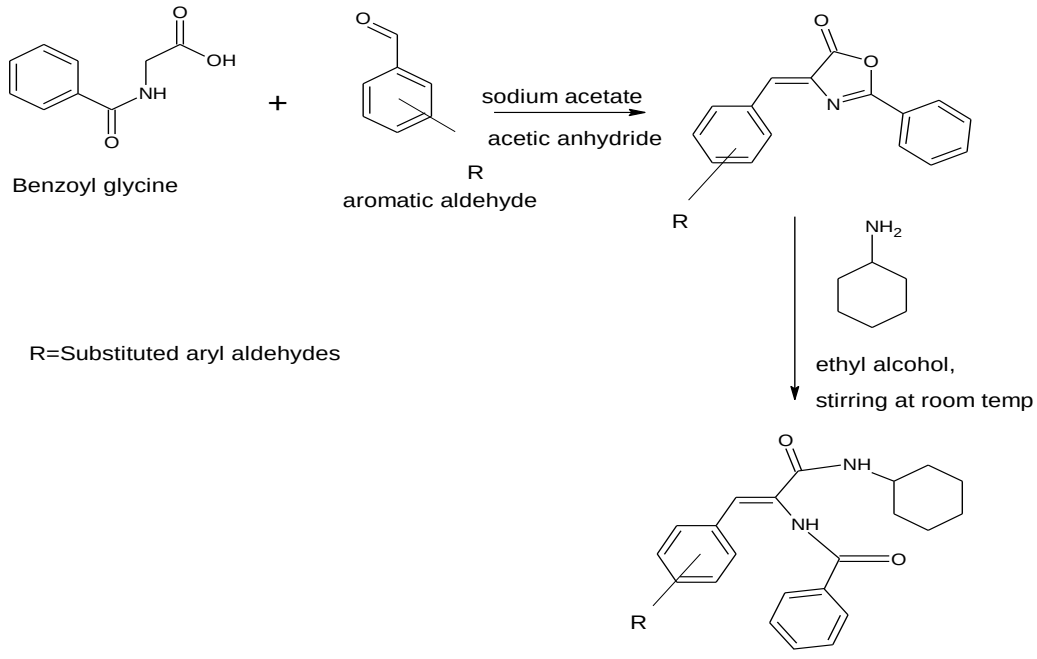
All the melting points reported in this series were determined in open capillaries using Thermonik Precision Melting Point Cum Boiling Point Apparatus C-PMB and are uncorrected. Homogeneity of the compounds was checked by using pre-coated Thin Layer Chromatography (TLC) plates. The IR spectra were recorded using KBr pellets technic on FTIR Brucker. ^{1}H-NMR spectra were recorded on Bruker Advance 400 MHz spectrophotometer using Tetramethylsilane (TMS) as an internal standard. Chemical shift (δ) values are reported in δ (ppm). Mass spectra were recorded on an Apex Mass spectrophotometer. All the solvents and chemicals used were procured from Sigma Aldrich, used without further purification. The molecular docking was done by using XP GLIDE module of Schrodinger suite.

Synthesis of 4-benzylidene-2-phenyl-1,3-oxazol-5(4*H*)-one: 4-Benzylidene-2-phenyloxazol-5-one was prepared by condensing benzaldehyde with benzoyl glycine in presence of acetic anhydride and anhydrous sodium acetate accordance with the previously reported method [13]. The various 4-benzylidene-2-substituted-phenyl-1,3-oxazol-5(4*H*)-one were prepared by similar method.

General method of synthesis of title compounds (1-14): Equimolar ratio of 4-benzylidene-2-substitutedphenyl-1,3-oxazol-5(4*H*)-one and cyclohexylamine in the presence of ethanol was stirred for half an hour at room temperature and kept a side for overnight. The reaction was monitored by TLC and the solid formed was collected, washed with water and recrystallized from methanol. All the compounds **(1-14)** were prepared similarly by various substituted oxazolones with cyclohexylamine.

Physicochemical data of N-cyclohexyl-3-(substituted phenyl)-2-(phenylformamido) pro-2-enamides (1-14):

Scheme



R=Substituted aryl aldehydes

(1-14)

N-cyclohexyl-3-phenyl-2-(phenylformamido)pro-2-enamide (1): Yield:78%; M.P: 168-170 °C; IR(KBr) cm^{-}**:** 3310.50 (N-H), 2932.81 (N-H Aliphatic), 2855.06 (Ar-H), 1648.08 (C=O), 1560 (C=C); 1H NMR (400 MHz, DMSO-d6):δ 1.10-1.76 (m, 11H, cyclohexyl ring), 7.11-7.86(m,10H,Ar-H), 7.98 (s, 1H,Ar-CH), 8.00 (s, 1H, CONH), 9.82 (s, 1H, NHCO-Ar); Mass **(**m/z**):** 349 (M+H)+ 348(M-H)- Elemental Analysis**:** Calculated: C,75.83; H,6.94; N, 8.04;Found: C, 75.78; H, 6.87; N, 8.01.

N-cyclohexyl-3-(2-hydroxyphenyl)-2-(phenylformamido)pro-2-enamide(2): Yield 75 %; M.P:170-172 ℃; IR(KBr) cm^{-}:3314.50 (N-H), 2924.81(N-H Aliphatic), 2850.06 (Ar-H), 1660.08 (C=O), 1560(C=C); 1H NMR (400 MHz, DMSO-d6) : δ 1.10-1.76 (m,11H, cyclohexyl ring), 7.13-8.20 (m, 9H, Ar-H), 7.91 (s, 1H, Ar-CH), 8.00 (s, 1H, CONH), 9.80 (s, 1H, NHCO-Ar), 9.97(s, 1H, Ar-OH)); Mass (m/z): 364 (M+H) +,363 (M-H)-; Elemental Analysis: Calculated: C, 71.41; H, 5.99; N, 8.33; Found: C, 71.40; H,5.96;N,8.31.

N-cyclohexyl-3-(4-hydroxyphenyl)-2-(phenylformamido)pro-2-enamide(3): Yield 77%; M.P:170-172℃; IR (KBr) cm^{-}**:** 3300.50 (N-H),2930.81 (N-H Aliphatic), 2857.06 (Ar-H), 1730.08 (C=O), 1561 (C=C); 1H NMR (400 MHz, DMSO-d6) : δ 1.10-1.76 (m, 11H, cyclohexyl ring) , 7.12-8.00 (m, 9H, Ar-H), 7.90 (s, 1H, Ar-CH), 8.00-8.01 (s,1H,CONH-),9.82(s,1H,NHCO-Ar), 9.97(s,1H,Ar-OH); Mass **(**m/z**) :** 364(M),363 (M-H)-; Elemental Analysis **:**Calculated: C, 71.41; H, 5.99; N, 8.33;Found: C, 71.40; H, 5.96; N, 8.31.

N-cyclohexyl-3-(4-hydroxy-3-methoxyphenyl)-2-(phenylformamido)pro-2-enamide(4):Yield75%;M.P:170-172℃;IR(KBr)cm-:3320.50(N-H),2930.81(N-HAliphatic), 2855.06 (Ar-H), 1660.08 (C=O),1565(C=C); 1H NMR (400 MHz, DMSO-d6) :δ 1.16-1.85 (m,11H,cyclohexylring), 7.27 7.52 (m,8H,ArH),7.81(s,1H,ArCH),7.88 (s, 1H, CONH), 9.76(s,1H,NHCO-Ar),11.39(s,1H,Ar-OH), 3.32 (s,3H,OCH_3); Mass(m/z) : 394(M),393(M-H)-; Elemental Analysis: Calculated: C, 70.03; H, 6.64; N, 7.10Found: C, 70.01; H, 6.61; N, 7.07.

N-cyclohexyl-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-(phenylformamido)prop-2enamide (5): Yield73%;M.P:168-170℃;IR (KBr)cm-:3318.50(N-H), 2924.81 (N-H Aliphatic), 2850.06 (Ar-H), 1710.08 (C=O),1560 (C=C); 1H NMR (400 MHz, DMSO-d6): δ 1.10-1.76 (m,11H, cyclohexylring),7.16-7.94(m,7H,Ar-H),7.90(s,1H,ArCH),8.00(s,1H,CONH),9.81(s,1H,NHCO-Ar),11.39(s,1H,Ar-OH),3.80(s,6H,$(OCH_3)_2$); Mass(m/z): 424(M),423(M-H)-;Elemental Analysis: Calculated: C, 67.91; H, 6.65; N, 6.60 Found: C, 67.89; H, 6.63; N, 6.58.

N-cyclohexyl-3-(4-methoxyphenyl)-2-(phenylformamido)prop-2-enamide (6): Yield 76%; M.P:166-168℃; IR(KBr) cm-:3334.50(N-H),2934.81 (N-HAliphatic), 2850.06 (Ar-H), 1680.08 (C=O), 1568(C=C); 1H NMR (400 MHz, DMSO-d6) :δ 1.10-1.76 (m, 11H, cyclohexylring),7.10-7.91 (m,9H,Ar-H),7.93(s,1H, Ar-CH),8.11-8.20(s,1H,CONH),9.81(s,1H,NHCO-Ar),3.79(s,3H, OCH_3); Mass (m/z) : 378(M),377(M-H)-; Elemental Analysis: Calculated: C, 72.99; H, 6.92; N, 7.40 Found: C, 72.96; H, 6.89; N, 7.37.

N-cyclohexyl-3-(3,4-dimethoxyphenyl)-2-(phenylformamido)prop-2-enamide(7): Yield 75%; M.P:168-170℃; IR (KBr) cm-:3330.50(N-H),2925.81(N-H Aliphatic), 2857.06 (Ar-H), 1649.08 (C=O), 1565(C=C); 1H NMR (400 MHz, DMSO-d6) :δ 1.14-1.75 (m, 11H, cyclohexyl ring), 7.12-7.94 (m, 8H, Ar-H), 3.51-3.74(s, 6H, $(OCH_3)_2$), 8.06-8.26 (s, 1H,CO NH)9.78(s, 1H, NHCO-Ar),8.00(s,1H,Ar-CH);Mass(m/z):408(M),407(M-H)-;ElementalAnalysis:Calculated: C, 70.57; H, 6.91; N, 6.86 Found: C, 70.54; H, 6.88; N, 6.84.

N-cyclohexyl-2-(phenylformamido)-3-(3,4,5-trimethoxyphenyl)prop-2-enamide(8): Yield75%;M.P:168-170℃;IR(KBr)cm-:3314.50(N-H),2934.81(N-HAliphatic), 2850.06 (Ar-H), 1740.08 (C=O),1561(C=C); 1H NMR (400 MHz, DMSO-d6) :δ 1.10-1.76 (m,11H, cyclohexyl ring), 7.11-7.90 (m,7H, Ar-H), 3.81(s,9H,$(OCH_3)_3$), 8.05-8.20 (s,1H,CO NH),9.81(s,1H,NHCO-Ar),7.90(s,1H, Ar-CH); Mass (m/z) : 438(M),437(M-H)-; Elemental Analysis: Calculated: C, 68.47; H, 6.90; N, 6.39 Found: C, 68.44; H, 6.87; N, 6.35.

N-cyclohexyl-3-(4-methylphenyl)-2-(phenyl formamido) prop-2-enamide (9): Yield78%; M.P:170-172℃; IR (KBr) cm-:3333.50 (N-H),2914.81(NH Aliphatic),2855.06 (Ar-H), 1670.08 (C=O),1555(C=C); 1H NMR (400 MHz, DMSO-d6): δ 1.10-1.76 (m,11H, cyclohexyl ring), 7.16-7.95(m,9H, Ar-H),2.33(s,3H, CH_3),8.05-8.23(s,1H, CONH) 9.81(s,1H, NHCO-Ar),7.90(s,1H, Ar-CH); Mass (m/z): 362(M),361(M-H)-; Elemental Analysis: Calculated: C, 76.21; H, 7.23; N, 7.73 Found: C, 76.18; H, 7.20; N, 7.71.

N-cyclohexyl-3-[4-(dimethyl amino) phenyl]- 2-(phenyl formamido) prop-2-enamide (10): Yield 77 %; M.P:166-168℃; IR (KBr) cm-:3324.50 (N-H), 2925.43 (N-H Aliphatic),2852.05 (Ar-H), 1763.66 (C=O), 1526.76 (C=C); 1H NMR (400 MHz, DMSO-d6) :δ1.10-1.76(m,11H, cyclohexylring),7.13-8.20(m,9H,Ar-H),8.20(s,1H,CONH), 3.08(s,6H,N$(CH_3)_2$),9.67(s,1H,NHCO-Ar),8.02(s,1H, Ar-CH);Mass(m/z):391(M),390(M-H)-; Elemental Analysis: Calculated:C,73.63; H,7.47; N,10.73 Found: C, 73.60; H, 7.44; N, 10.70.

3-(4-chlorophenyl)-N-cyclohexyl-2-(phenylformamido)prop-2-enamide (11): Yield 76%; M.P: 170-172℃; IR (KBr) cm-: 3334.50 (N-H), 2930.81 (N-H Aliphatic), 2847.06 (Ar-H), 1740.08 (C=O),1561 (C=C); 1H NMR (400 MHz, DMSO-d6) :δ 1.10-1.76 (m,

11H, cyclohexylring), 6.82-7.77 (m, 9H, Ar-H), 8.12-8.21(s,1H, CONH), 9.80 (s, 1H, NHCO-Ar), 7.90 (s, 1H, Ar-CH); Mass (m/z):382(M), 381 (M-H)-; Elemental Analysis: Calculated: C, 69.01; H, 6.05; N, 7.32 Found: C, 69.00; H, 6.01; N, 7.30.

3-(4-cyanophenyl)-N-cyclohexyl-2-(phenyl formamido)prop-2-enamide (12): Yield 78%; M.P:170-172°C; IR (KBr) cm-:3324.50 (Ar N-H), 2914.81 (N-H Aliphatic), 2850.06 (Ar-H), 1668.08 (C=O), 1551(C=C); 1H NMR (400 MHz, DMSO-d6):δ 1.10-1.76 (m, 11H, cyclohexylring), 6.81-7.77 (m, 9H, Ar-H), 8.07-8.24 (s, 1H, CONH), 9.81 (s, 1H, NHCO-Ar), 7.92 (s, 1H, Ar-CH); Mass (m/z): 387 (M), 386 (M-H)-; Elemental Analysis: Calculated: C, 73.97; H, 6.21; N, 11.25 Found: C, 73.94; H, 6.17; N, 11.21.

3-(4-nitrophenyl)-N-cyclohexyl-2-(phenyl formamido) prop-2-enamide (13): Yield 76%; M.P:174-176°C;IR (KBr) cm-:3314.50 (N-H), 2924.81 (N-H Aliphatic), 2847.06 (Ar-H), 1649.08 (C=O), 1565(C=C); 1H NMR (400 MHz,DMSO-d6):δ1.10-1.76(m,11H, cyclohexylring), 6.72-7.73 (m, 9H, Ar-H), 8.12-8.20 (s, 1H, CONH), 9.80(s, 1H, NHCO-Ar), 7.91 (s,1H, Ar-CH); Mass (m/z) : 393(M),392(M-H)-; Elemental Analysis: Calculated: C, 67.16; H, 5.89; N, 10.68 Found: C, 67.13; H, 5.85; N, 10.59.

3-(3-nitrophenyl)-N-cyclohexyl-2-(phenylformamido)prop-2-enamide (14):Yield75%;M.P:172-174°C;IR(KBr)cm-:3334.50(N-H),2928.81(N-HAliphatic), 2850.06 (Ar-H), 1710.08 (C=O),1561(C=C); 1H NMR (400 MHz, DMSO-d6) :δ 1.10-1.76 (m,11H, cyclohexylring),7.68-8.18(m,9H,Ar-H),8.01-8.22(s,1H,CONH),9.8(s,1H,NHCO-Ar),7.90(s,1H, Ar-CH); Mass (m/z) : 393(M),392(M-H)-; Elemental Analysis: Calculated:C, 67.16; H, 5.89; N, 10.68 Found: C, 67.12; H, 5.85; N, 10.65.

ANTIMICROBIAL ACTIVITY

Cultures of gram-positive bacteria: Staphylococcus aureus and Gram-negative bacteria: Escherichia coli were used to investigate the antimicrobial activity of the compounds **(1-14).** The antimicrobial activity was assayed biologically using agar well diffusion method [14]. In this method, wells of standard diameter are made in the nutrient agar medium, containing standard bacterial inoculum. The test compounds were introduced into the wells and diameter of the zone of inhibition was measured by antibiotic zone reader. The standard drugs used were ciprofloxcin and fluconazole.

MOLECULAR DESCRIPTORS AND DRUGLIKENESS

In-silico ADME: In the present study molecular properties of compounds **(1-14)** were calculated by using Molinspiration online tool [15] and SwissADME[16] in order to predict the compounds drug likeness score. The %ABS was calculated according to the formula [17].

%ABS = 109-(0.345 x TPSA).

Some physicochemical parameters of the synthesized compounds were predicted and listed in Table 2and 3. The predicted values revealed that the compounds obeyed Lipinski rule of five by possessing not more than 5 hydrogen bond donors (OH and NH groups), not more than 10 hydrogen bond acceptors (notably N and O) and not more than 15 rotatable bonds (rotb), a partition coefficient log P was found to be not more than 5 for some compounds. However, descriptors such as log P and solvent accessible surface area contributed towards the activity of the molecules, TPSA is another key property that has been linked to bioavailability. It was found that passively absorbed molecules with a TPSA more than 140 are thought to have low oral availability. TPSA obtained for the tested compounds were below 140 predict good oral bioavailability. Drug likeness scores of the synthesized compounds were predicted using molsoft website. This result is adding support to the biological activities observed for these compounds. Ability to predict the percent oral absorption was the primary goal in the design, optimization, and selection of potential candidates in the development of oral drugs.

BIOACTIVITY SCORE PREDICTION

The bioactivity scores of the compounds **(1-14)** were calculated for their GPCR ligand, kinase inhibitor, protease inhibitor and enzyme inhibitor activities. (Table 4). For average organic molecules the probability is that if the bioactivity score is more than 0 then it is active, if 0.5 to 0 then moderately active. Kinase inhibitor and enzyme inhibition scores of 0.26 and 0.08 obtained for compound **5** tested supported the presence of moderate anti-inflammatory and analgesic activity. The protease inhibitor score of compounds **5** was predicted as 0.02 and for compound **4**, 0.03 that is comparable with score of standard protease inhibitor, ritonavir (0.47). Good protease inhibitor scores obtained predicted the efficiency of these compounds as good antimicrobials and might possess protease inhibitor activities

MOLECULAR DOCKING

Molecular docking of compounds **(1-14)** with the 3D X-ray crystal structure of *E.coli* FAB protein (β-ketoacyl-acyl carrier protein synthase III) retrieved from the PDB (Protein Data Bank) incorporated with inhibitor was accessed to predict active site residue. The 3D structure of target (PDB ID: 5BNM) was imported in to maestro v 9.0 and receptor grid of 20x20x20 A° was generated for the 5BNM around the centroid of respective active site using ***XP GLIDE*** (Schrodinger). All the ligands, standard drug were embedded in to the generated grid of FAB protein to access their binding affinities.

RESULTS AND DISCUSSION

Chemistry

4-benzylidene-2-Substitutedphenyl-1,3-oxazol-5(4*H*)-one derivatives were synthesized by the nucleophilic addition of benzoyl glycine with different aromatic aldehydes and simultaneous elimination of water molecule under acidic conditions, showed good yields, purity and acts as a precursor for the synthesis in next step. The title compounds N-cyclohexyl-3-(substituted phenyl)-2-(phenyl formamido) pro-2-enamides **(1-14)** were synthesized by condensing cyclo hexylamine to the substituted oxazolones as depicted in scheme. The IR spectral data of titled compounds **(1-14)** displaced bands in the region of 3314-3350cm^{-1} due to N-H streching, 2847-2851cm^{-1} due to the aromatic C-H stretching, 1649-1680cm^{-1} due to C=O stretching and bands at 1550-1561cm^{-1} due to C=C stretching. The ^{1}H-NMR spectra of the compounds showed multiplet at δ 1.10-1.76 due to cyclohexyl protons, multiplet at δ 7.11-7.86 due to aryl protons, singlet at δ 7.98 due to Ar-CH=, singlet at δ 8.00 due to –CONHN-, singlet at δ9.82 due to =C-NHCO. The mass spectrum of compounds **1, 7**, and **10** showed the characteristic molecular ion peak(M±H) at m/z349,408and391 respectively. The Elemental analysis of the compounds were found to be within the limits of ±0.4% of theoretical values.

Anti-microbial activity

The anti-microbial data of title compounds was tabulated (Table 1) reveals that all derivatives showed good antimicrobial activity and antifungal activity. Among the compounds, **5** exhibited good antimicrobial activity. The phenolic groups containing methoxy substituents in ortho position showed good zone of inhibition in mm towards *E.coli* and *S.aureus*. All the derivatives also showed good anti-microbial activity.

Molecular Docking

Further the study was continued with the molecular docking studies with FAB protein coded with 5BNM and the data reveals all the derivatives elicited better docking score than the standard drug ciprofloxacin (-4.74) predicted by using ***XP GLIDE***. Among the series, **5** exhibited highest docking score indicating higher affinity towards the target. It might be due to the complete fitting of molecule within the hydrophobic cavity of target protein. Compound **5** showed hydrophobic interaction with PHE 213, MET 207, ILE 250, VAL 212, ALA 216, ALA 246, PHE 304, CYS 112, PHE 157, LEU 189, TRP 32, ILE 155, ILE 156, side chain hydrogen bonding of carbonyl group with ASN 247. The 2D binding mode of interaction with FAB is given in (Figures 1-4) and this data provides the possible pose and type of interactions within the protein environment.

***In silico* ADME**

All the compounds obeyed Lipinski rule of five is important for assessing of compounds oral bioavailability. It is clear from the (Table 2) that log P values of all the compounds found to be in the acceptable criteria (3.96-5.90) and TPSA (Total polar surface area) (<140) is another key property that has been linked to bioavailability. It was found that all the compounds showed goodTPSA predicts good oral bioavailability.The results of *in silico* data indicates that, these compounds may have the potential to become a lead compound.

Table 1: Antimicrobial activity and docking sores of title compounds (1-14)

		Diameter of zone of inhibition(mm)					Molecular docking
Compound Code	**Compound**	***E.coli***	***S.aureus***	***P.notatum***	***P.crysogenum***	***A.niger***	***Docking score***
1	C6H5	18	18	22	22	20	-7.912
2	2-OH C6H4	14	14	18	16	16	-7.641
3	4-OH C6H4	14	14	18	16	16	-7.587

4	4-OH ,3-OCH3 C6H3	20	19	18	16	16	-7.953
5	4-OH ,3,5 -(OCH 3)2 C6H2	22	22	20	24	24	-8.397
6	4-OCH3 C6H4	8	NA	NA	10	NA	-7.082
7	3,4 -(OCH 3)2 C6H3	12	12	14	14	12	-7.555
8	3,4,5 -(OCH 3)3 C6H2	18	16	14	14	12	-7.938
9	4-CH3	5	NA	NA	NA	NA	-7.044
10	4-N, N (CH 3)2C6H4	9	9	8	7	8	-7.341
11	4-Cl C6H4	16	16	14	14	12	-7.668
12	4-CN C6H4	20	20	18	18	20	-7.951
13	4-NO2 C6H4	16	18	14	16	16	-7.668
14	3-NO2 C6H4	13	12	12	12	10	-7.577
Fluconazole		-	-	23	23	21	-
Ciprofloxacin		20	19	-	-	-	-4.74

NA-Not Active**,**

a. Concentrationof 100 µg/ml for Test compounds and standards (ciprofloxacin and Fluconazole respectively)

b. Control -DMSO

c. Activity is measured as zone of inhibition in mm

Table 2: Molecular property prediction of the title compounds (1-14) using molinspiration.com.

Compound Code	Compound	MW[a]	LogP[b]	TSPA[c]	noN[d]	noHNH[e]	Nrotb[f]	Vol[g]	nAtoms[h]
1	C6H5	348.45	4.6	58.2	4	2	5	335.64	26
2	2-OH C6H4	343.65	4.1	78.42	5	3	5	343.65	27
3	4-OH C6H4	343.65	4.12	78.42	5	3	5	343.65	27
4	4-OH, 3-OCH3 C6H3	369.2	3.94	87.66	6	3	6	369.2	29
5	4-OH ,3,5 -(OCH 3)2 C6H2	394.75	3.96	96.89	7	3	7	394.75	31
6	4-OCH3 C6H4	361.18	4.66	67.43	5	2	6	361.18	28
7	3,4 -(OCH 3)2 C6H3	408.5	4.25	76.66	6	2	7	386.73	30
8	3,4,5 -(OCH 3)3 C6H2	438.52	4.23	85.9	7	2	6	412.27	32
9	4-CH3	362.47	5.05	58.2	4	2	5	352.9	27
10	4-N, N(CH 3) 2C6H4	391.51	4.7	61.43	5	2	6	381.54	29
11	4-Cl C6H4	382.89	5.28	58.2	4	2	5	349.17	27
12	4-CN C6H4	387.48	4.57	81.99	5	2	6	369.3	29
13	4-NO2 C6H4	393.44	4.56	104.02	7	2	6	358.97	29
14	3-NO2 C6H4	393.44	4.54	104.02	7	2	6	358.97	29

a. Molecular weight.
b. Log P – Partition coefficient.
c. TPSA-Topological polar surface area.
d. NON- No. of hydrogen bond acceptors.
e. NOHNH- No. of hydrogen bond donors.
f. Nrotb- No. of rotatable bonds.
g. Volume.
h. N atoms.

Table 3: Molecular property prediction of the title compounds (1-14) using SWISSADME.

Compound code	Lipinski rule of five	BBB	Bioavailability	Ghose filter	Muegge filter	Veber filter
1	YES	YES	0.55	YES	YES	YES
2	YES	YES	0.55	YES	YES	YES
3	YES	NO	0.55	YES	YES	YES
4	YES	NO	0.55	YES	YES	YES
5	YES	NO	0.55	YES	YES	YES
6	YES	YES	0.55	YES	YES	YES
7	YES	YES	0.55	YES	YES	YES
8	YES	NO	0.55	YES	YES	YES
9	YES	YES	0.55	YES	YES	YES
10	YES	YES	0.55	YES	YES	YES
11	YES	YES	0.55	YES	YES	YES
12	YES	NO	0.55	YES	YES	YES
13	YES	NO	0.55	YES	YES	YES
14	YES	YES	0.55	YES	YES	YES

Table4: Bioactivity scores of title compounds (1-14)

Compound code	GPCR Ligand	Ion Channel Modulater	Kinase Inhibitor	Nuclear Recepter Ligand	Protease Inhibiter	Enzyme Inhibiter
1	-0.06	-0.41	-0.31	-0.56	0.05	-0.11
2	-0.03	-0.37	0.28	-0.41	0.05	0.07
3	-0.02	-0.36	0.26	-0.42	0.06	-0.06
4	-0.08	-0.41	0.28	-0.48	0.03	0.11
5	-0.09	-0.39	0.26	-0.48	0.02	0.08
6	-0.1	-0.45	-0.32	-0.54	-0.01	-0.15
7	-0.11	-0.44	-0.3	-0.53	-0.04	-0.15
8	-0.11	-0.41	-0.28	-0.55	-0.05	-0.14
9	-0.1	-0.46	-0.34	-0.58	-0.01	0.17
10	-0.06	-0.4	-0.25	-0.51	-0.01	-0.13
11	-0.06	-0.4	-0.32	-0.57	0.01	-0.14
12	-0.04	-0.54	-0.29	-0.51	-0.1	-0.18
13	-0.19	-0.42	-0.41	-0.61	-0.09	-0.21
14	-0.2	-0.43	-0.4	-0.61	-0.09	-0.22

Fig 1: 2D interaction of 5 with active site of 5BNM target

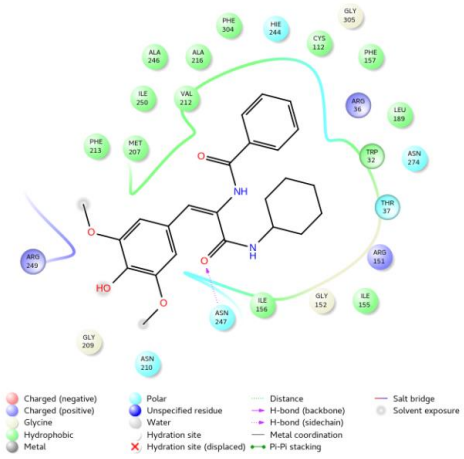


Fig 2:2D interaction of 4 with active site of 5BNM

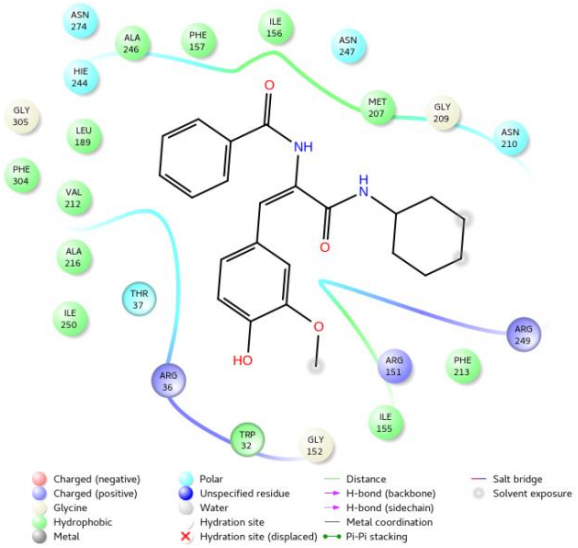


Fig 3: 2D interation of 8 with active site of 5BNM target

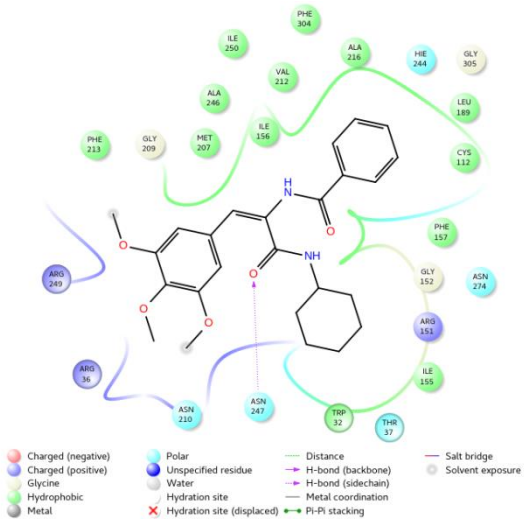
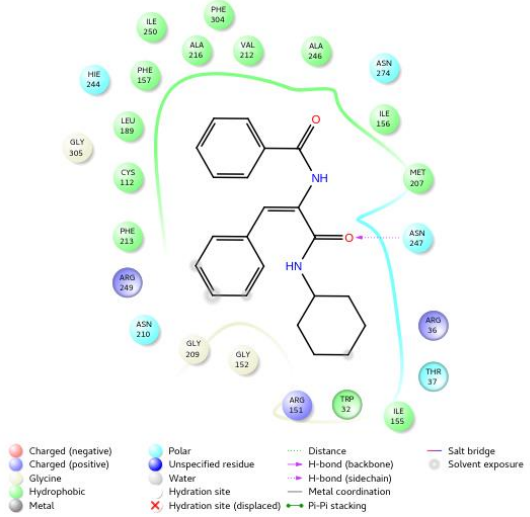


Fig 4: : 2D integration of 1 with active site of 5BNM target



CONCLUSION

In the present study we developed a facile synthetic route for the synthesis of new Cinnamide derivatives, screened for antimicrobial activity and further interaction with the target was explored by docking studies. Among all the compounds, compound **5** exhibited good antibacterial and antifungal activities. The molecular docking implying FAB showed maximum docking score for the compound **5.** The compound **5** could be considered as a lead compound for further development of potent antimicrobial agent and it supported by molecular docking results.

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