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Synthesis, spectral analysis, antimicrobial evaluation and molecular docking studies of some novel 3,5-dichloro-2,6-diarylpiperidin-4-ones

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ABSTRACT

*A new series of compounds namely, 3,5-Dichloro-2,6-diarylpiperidin-4-ones(**11-17**) has been synthesized and characterized using various spectral analysis (IR, ^{1}HNMR,^{13}CNMR&Mass). In addition, the title compounds were screened for their antimicrobial activities against a spectrum of clinically isolated microbial organisms. Compoundswith fluoro, chloro, methoxy or methyl functions at the para position of the phenyl rings attached to C-2 and C-6 carbons of the piperidone moiety along with the chlorosubstituents at C-3 and C-5positions of the piperidone ring exerted potent biological activities against antimicrobial strains at a minimum inhibitory concentration. The molecular docking studies have widened the scope of developing a new class of antimicrobial agents.*

Key words: piperidin-4-ones, antibacterial activity, antifungal activity, molecular docking

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INTRODUCTION

Small heterocyclic compounds act as highly functionalized scaffolds and were known pharmacophores of a number of biologically active and useful molecules. Bioactive heterocyclic ring systems having 2,6-diaryl-piperidine-4-one nucleus with different substituents at 3- and 5-positions of the ring have aroused great interest due to their wide variety of biological properties such as antiviral, antitumour [1,2] central nervous system [3] local anesthetic [4] anticancer [5] antimicrobial activity [6] and their derivative piperidine are also biologically important and act as neurokinin receptor antagonists [7] analgesic and anti-hypertensive agents[8]. Due to an increase in the number of immunocompromised hosts, [9] over the past decades, the incidence of systemic microbial infections has been increasing dramatically. The increasing incidence of bacterial resistance to a large number of antibacterial agents such as glycopeptides (vancomycin, inhibition cell walls synthesis), sulfonamide drugs (inhibitors of tetrahydrofolate synthesis), b-lactam antibiotics (penicillins and cephalosporins), nitroimidazoles and quinolones (DNA inhibitors), tetracyclins, chloramphenicol and macrolides (erythromycin, inhibiting protein synthesis) is becoming a major concern [10]. For the past several years, vancomycin has been considered the last line of defense agent against Gram-positive infections and no alternative drugs for treating diseases that have become resistant to vancomycin [11]. Patients undergoing organ transplants, anticancer chemotherapy or long treatment with antimicrobial agents and patients with AIDS are immuno suppressed and very susceptible to life threatening systemic fungal infections like Candidiasis, Cryptococcosis and Aspergillosis. Antifungal azoles, fluconazole and itraconazole which are strong inhibitors of lanosterol 14a-demethylase (cytochrome P45014DM) and orally active have been widely used in antifungal chemotherapy. Reports are available on the developments of resistance to currently available antifungal azoles in Candida sp., as well as clinical failures in the treatment of fungal infections [12-15]. Furthermore, most of the present antifungal drugs are not effective against invasive Aspergillosis and the only drug of choice in such patients is the injectable amphotericin B. These observations places new emphasis on the need of as well as search for alternative new and more effective antimicrobial agents with a broad spectrum.

Widespread interest in the chemistry of piperidones, pyrans and thiopyrans in a large number of natural products has attracted due to their biological activities [16]. Structure–activity relationship (SAR) studies from piperidoneheterocycles indicated that nature and position of substituents were considerably important factors to effect the biological actions.So far, only a few reports [17-20] are available with chloro substitution at position 3 of the piperidone ring system.Baliah*et al*. have reviewed the importance of piperidin-4-ones as intermediates in the synthesis of several physiologically active compounds [21]. In corollary of the interesting biological and pharmaceutical properties and synthetic utility, there is substantial interest in piperidones; this substructure containing compounds are widely present in numerous alkaloids and synthetically derived molecules of biological importance [22].In the course of broad programme in developing biologically active molecules, our research group previously reported the synthesis of 2,6-diarylpiperidin-4-one derivatives and evaluated their biological importance [23-25]and recently reported the synthesis of 3-chloro-2,6-diarylpiperidin-4-ones [26] by adopting the literature precedent [19]. In continuation of our research on the synthesis and the biological screening of chloro substituted 2,6-diarylpiperidin-4-ones, herein we have synthesized a new series of compounds with two chlorine atoms substituted in the piperidin-4-one ring system namely, 3,5-dichloro-2,6-diarylpiperidin-4-ones. In order to extend our knowledge in structure-activity relationship, all the newly synthesized compounds are tested for their in vitro antibacterial and antifungal activities and the influence of some structural variations by varying the substituents at the phenyl ring in the synthesized compounds towards their biological activities is evaluated. Also the *in silico* antimicrobial activities for all the newly synthesized compounds were evaluated using molecular docking studies.

MATERIALS AND METHODS

TLC was performed to assess the reactions and the purity of the products. All the reported melting points were taken in open capillaries and were uncorrected. IR spectra were recorded in KBr (pellet forms) on a Nicolet-Avatar–330 FT-IR spectrophotometer and noteworthy absorption values (cm^{-1}) alone are listed. ^{1}H and ^{13}C NMR spectra were recorded at 500MHz and 125MHz respectively on Bruker AMX 500 NMR spectrometer using $CDCl_3$as solvent. The ESI +ve MS spectra were recorded on a Bruker Daltonics LC-MS spectrometer.

Microbiology

All the clinically isolated bacterial strains namely *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhii*, *Escherichia coli*, *Vibreocholerae*, *Klebsiella pneumonia*and fungal strains namely *Aspergillusniger, Aspergillusflavus*, *Mucor*, *Canidaalbicans, Rhizopus,Canida 6*obtained from Faculty of Medicine, Annamalai University, Annamalainagar-608 002, Tamil Nadu, India. The minimum inhibitory concentration (MIC) in µg/mL was determined by the serial dilution method [27]. The respective test compounds (**11-17**) were dissolved in DMSO to obtain 1 mg/mL stock solution. Seeded broth (broth containing microbial spores) was prepared in nutrient broth (NB) from 24-h-old bacterial cultures on nutrient agar (HiMedia, Mumbai) at 37 ± 1°C, while fungal spores from 1- to 7-day-old Sabouraud agar (HiMedia, Mumbai) slant cultures were suspended in Sabouraud dextrose broth (SDB). Ciprofloxacin was used as the standard drug for bacterial studies and Fluconazole as the standard drug for fungal studies.

Computational Methods

Docking calculations were carried out using DockingServer(**www.dockingserver.com**)[28]. Gasteiger partial charges were added to the ligand atoms. Non-polar hydrogen atoms were merged and rotatable bonds were defined. Docking calculations were carried out on corresponding protein model. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of AutoDock tools [29]. Affinity (grid) maps, 0.375 Å spacing were generated using the Autogrid program [30]. AutoDock parameter set- and distance-dependent dielectric functions were used in the calculation of the van der Waals and the electrostatic terms, respectively.Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method [31].

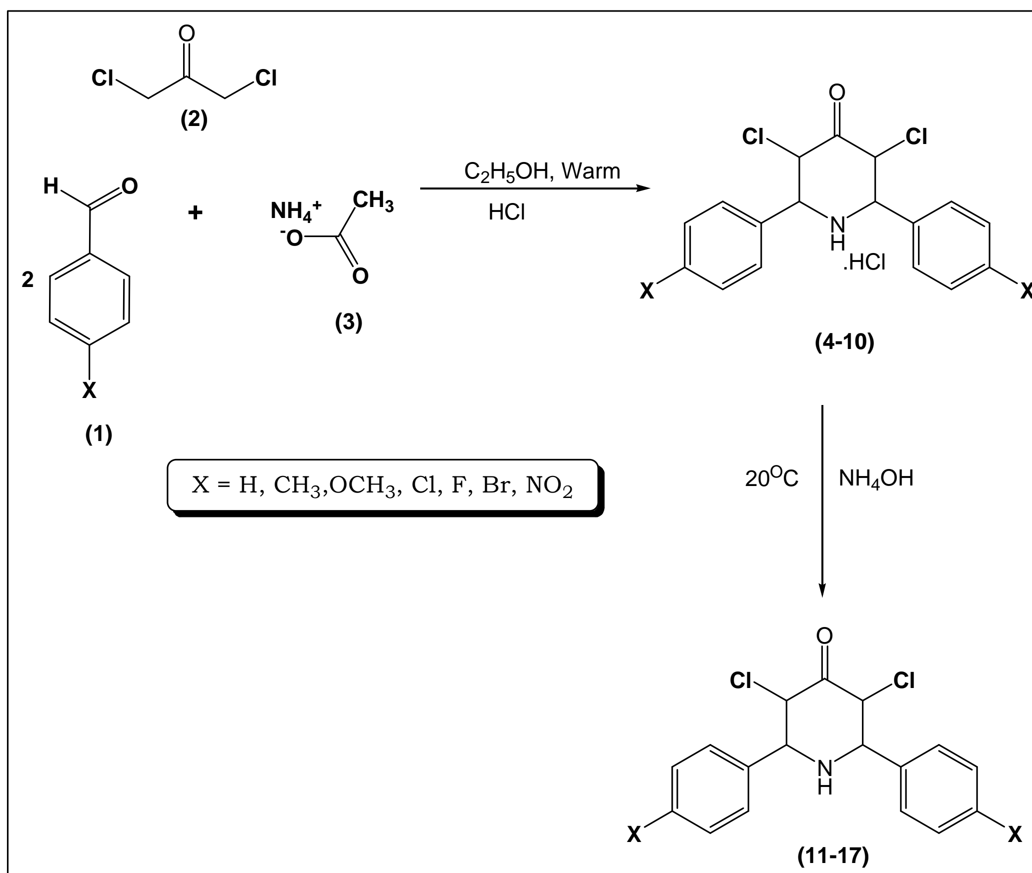
RESULTS AND DISCUSSION

Chemistry

General procedure for the synthesis of 3,5-dichloro-2,6-diarylpiperidin-4-ones (11-17)

A mixture of ammonium acetate (1 mmol), the respective substituted benzaldehyde(2 mmol) and 1,3-dichloroacetone (1 mmol) were dissolved in ethanol(80 mL) and the solution was heated on a hot plate with gentle swirling until the colour of the mixture changed to orange. The mixture was cooled and poured into diethyl ether (100 mL) and concentrated hydrochloric acid (14 mL) was added. The precipitated hydrochloride salt of the product was collected by filtration and recrystallized from the ethanol-ether mixture. The hydrochloride salt was then dispersed in acetone and aqueous ammonia was added drop wise until a clear solution was obtained. The clear solution was poured into

cold water and the solid precipitation was collected and recrystallized from ethanol.The synthetic route is outlinedin**Scheme1**.



Scheme 1:Synthetic route for the target compounds (11-17)

The yields and melting points of the newly synthesized target compounds were tabulated and given in Table 1.

Table 1:Physical data for the newly synthesized compounds 11-17

Compound	X	Yield (%)	Mp (°C)
11	H	81	92-96
12	CH_3	70	124-128
13	OCH_3	69	146-150
14	Cl	63	82-86
15	F	72	148-150
16	Br	60	150-152
17	NO_2	71	165-168

The structure of the target compounds were elucidated by IR spectral analysis. Further, the structural assignments of the synthesized compounds were made by using mass, ^{1}H and ^{13}C NMR spectral analysis.The IR spectrum of compound 3,5-dichloro-2,6-diphenylpiperidin-4-one (**11**)showed a strong absorption band at 3510 cm^{-1} which is assigned as N-H stretching frequency. AromaticC-H stretching vibrations are observed in the range of 3383-3336 cm^{-1} and aliphatic C-H stretching vibrations are observed in the range of 3035-2854 cm^{-1}. The absorption band appeared at 1744 cm^{-1} is due to C=O stretching frequency.Mass spectrum of compound **11**shows Molecular ion peak at m/z = 320 which is consistent with the proposed molecular structure of the compound.

In the ^{1}H NMR spectrum of compound **11**, the H2and H6 protons are appeared at 4.04-4.06 ppm and the H3 and H5 protons are appeared at 4.73-4.75 ppmrespectively. The aromatic protons are appeared at 7.32-7.52 ppm and the NH proton is appeared at 2.19 ppm.In the^{13}C NMR spectrum of compound **11**, the C2 and C6 carbons of the piperidone ring are observed at 68.3 ppm. The carbon signal resonates at 68.1 ppm is corresponds to the C3 and C5 carbon of the piperidone ring. The *ipso* carbons of the phenyl ring appeared at 138.6ppm and the aromatic protons are observed in the range of 127.7-129.0 ppm. The carbonyl group carbon of the piperidone ringappeared at 192.3 ppm. The spectral data for all the compounds (**11-17**) were given below.

3,5-Dichloro-2,6-diphenylpiperidin-4-one (**11**): MS (m/z) $M^{+\cdot}$ = 320.2; IR (KBr) (cm^{-1}): 3510 (N-H stretching), 3383-3336 (aromatic C-H), 3035-2854 (aliphatic C-H), 1744 (C=O); ^1H NMR (ppm) : 4.72 (d, 1H, H_3, J=10), 4.75 (d, 1H, H_5, J=10), 4.04 (d, 1H, H_2 J=10), 4.06 (d, 1H, H_6, J=10), 2.19 (s, 1H, H_1,),7.32-7.52 (m, 10H, H_{arom}); ^{13}C NMR (ppm): 68.1 (C-3 and C-5), 68.3 (C-2 and C-6), 127.7 -129.0 (aromatic), 138.6 (*ipso*), 192.3 (C=O).

3,5-dichloro-2,6-bis(p-methylphenyl)piperidin-4-one(**12**): IR (KBr) (cm^{-1}): 3480 (N-H stretching), 3344-3323 (aromatic C-H), 3027-2949 (aliphatic C-H), 1743 (C=O); ^1H NMR (ppm): 4.14 (d, 1H, H_3, J=10), 4.17 (d, 1H, H_5, J=10), 4.06 (d, 1H, H_2 J=10), 4.08 (d, 1H, H_6, J=10), 2.25 (s, 3H), 2.19 (s, 1H, H_1,), 7.17-7.31 (m, 8H, H_{arom}); ^{13}C NMR (ppm): 18.54 (CH_3), 68.06(C-3 and C-5), 68.35(C-2 and C-6), 127.6 -129.4 (aromatic), 138.9 and 135.8 (*ipso*), 192.4 (C=O).

3,5-dichloro-2,6-bis(p-methoxyphenyl)piperidin-4-one(**13**): IR (KBr) (cm^{-1}): 3402 (N-H stretching), 3347-3325 (aromatic C-H), 3035-2837 (aliphatic C-H), 1743 (C=O); ^1H NMR (ppm): 4.66 (d, 1H, H_3, J=10), 4.68 (d, 1H, H_5, J=10), 3.96 (d, 1H, H_2 J=10), 3.98 (d, 1H, H_6, J=10), 3.83 (s, 3H, OCH_3), 2.18 (s, 1H, H_1), 7.40-7.42and 6.92-6.94 (m, 8H, H_{arom}); ^{13}C NMR (ppm): 55.25 (OCH_3), 67.7(C-3 and C-5), 68.5(C-2 and C-6), 113.8 -129.0 (aromatic), 159.5 and 160.0 (*ipso*), 192.4 (C=O).

3,5-dichloro-2,6-bis(chlorophenyl)piperidin-4-one(**14**): IR (KBr) (cm^{-1}): 3531 (N-H stretching), 3134-3052 (aromatic C-H), 2923-2850 (aliphatic C-H), 1742(C=O); ^1H NMR (ppm): 4.64 (d, 1H, H_3, J=10), 4.66 (d, 1H, H_5, J=10), 4.01 (d, 1H, H_2 J=10), 4.03 (d, 1H, H_6, J=10), 2.19 (s, 1H, H_1), 7.42-7.46and 7.37-7.39 (m, 8H, H_{arom}); ^{13}C NMR (ppm):67.5(C-3 and C-5), 67.9(C-2 and C-6), 128.4-129.4 (aromatic),135.0 and 136.9 (*ipso*), 191.5(C=O).

3,5-dichloro-2,6-bis(p-fluorophenyl)piperidin-4-one (**15**): IR (KBr) (cm^{-1}): 3512 (N-H stretching), 3380-3330 (aromatic C-H), 3041-2854 (aliphatic C-H), 1739 (C=O); ^1H NMR (ppm): 4.66 (d, 1H, H_3, J=10), 4.68 (d, 1H, H_5, J=10), 4.02 (d, 1H, H_2 J=10), 4.04 (d, 1H, H_6, J=10), 2.19 (s, 1H, H_1), 7.47-7.51 and 7.08-7.14(m, 8H, H_{arom}); ^{13}C NMR (ppm): 67.4(C-3 and C-5), 68.1(C-2 and C-6), 115.4-129.6 (aromatic), 162.0 and 163.9 (*ipso*), 191.7 (C=O).

3,5-dichloro-2,6-bis(p-bromophenyl)piperidin-4-one(**16**): IR (KBr) (cm^{-1}):3402 (N-H stretching), 3383-3336 (aromatic C-H), 3035-2854 (aliphatic C-H), 1744 (C=O); ^1H NMR (ppm): 4.65 (d, 1H, H_3, J=10), 4.67 (d, 1H, H_5, J=10), 4.00 (d, 1H, H_2 J=10), 4.02 (d, 1H, H_6, J=10), 2.19 (s, 1H, H_1), 7.40-7.44and 7.34-7.37(m, 8H, H_{arom}); ^{13}C NMR (ppm): 67.3(C-3 and C-5), 68.2(C-2 and C-6), 127.6 -129.4 (aromatic), 138.9 and 135.8 (*ipso*), 191.6 (C=O).

3,5-dichloro-2,6-bis(p-nitrophenyl)piperidin-4-one(**17**): IR (KBr) (cm^{-1}): 3480 (N-H stretching), 3344-3261 (aromatic C-H), 3027-2949 (aliphatic C-H), 1744 (C=O); ^1H NMR (ppm): 4.64 (d, 1H, H_3, J=10), 4.66 (d, 1H, H_5, J=10), 4.02 (d, 1H, H_2 J=10), 4.04 (d, 1H, H_6, J=10), 2.20 (s, 1H, H_1), 7.45-7.49and 7.37-7.41 (m, 8H, H_{arom});^{13}C NMR (ppm): 67.7(C-3 and C-5), 68.3(C-2 and C-6), 113.8 -129.0 (aromatic), 159.5 and 163.9 (*ipso*), 191.4 (C=O).

Antibacterial activity

In this study, the newly prepared compounds **11-17** were tested for their antibacterial activity against different bacterial strains. The bacterial species investigated were*Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhii*, *Escherichia coli*, *Vibreocholerae*, *Klebsilla pneumonia.*The antibacterial potency of the synthesized compounds was compared with Ciprofloxacin, a standard drug, using their minimum inhibitory concentration (MIC) by serial dilution method; the values are summarized in **Table 2**. Close surveys of the MIC values indicate that all the compounds exhibited a varied range (12.5–200µg/mL) of antibacterial activity against all the tested bacterial strains. From the zone of inhibition of the compounds tested for antibacterial activity, **11** and **14** against *S. aureus*, **14** against *B. Subtilis,* **15** against *S. typhi* and *E. coli* exhibit better activity. Similarly, compounds **14, 15** and **17** against *V. Cholerae*and compound**15** against *K. pneumonia*exhibit better activitywhile rest of the compounds show moderate to poor activity. But, the compounds **13** against *S. aureus*, **17** against *B. Subtilis***13** and **14** against *E. coli*and compounds **11** and **13** against*K. pneumonia*have negligible activity. However, the antibacterial activity of compound **13, 15** and **17** against *S. typhi*are found to be good when compared to other compounds. Similarly, compounds**14, 15**and **17** against *V. Cholerae,* are found to be good when compared to other compounds. The compound **14**against *S. aureus*, *B. Subtilis*and *V. Cholerae*and compound **15** against *S. typhi,E. coli,V. Cholerae* and *K. pneumonia*exhibit significant inhibition of MIC at 12.5 µg/mL.Likewise, the compounds **11**against *S. aureus*, **13**against *S. typhi*and **17**against*S. typhi* and *V. Cholerae*exert significant activity at a minimum concentration of 12.5 µg/mL. Among the tested compounds (**11-17**), compound **11**against *E. coli*and compound**16**against *K. pneumonia*did not show any inhibition even at a maximum concentration of 200 µg/mL.

Table 2:*In vitro* antibacterial activities of 11-17 against clinically isolated bacterial strains

Compound	Minimum inhibitory concentration (MIC) in µg/mL					
	S. aureus	*B. subtilis*	*S. typhi*	*E. coli*	*V. cholerae*	*K. pneumonia*
11	12.5	25	25	-	25	100
12	25	50	50	50	50	25
13	100	50	12.5	200	25	100
14	12.5	12.5	25	100	12.5	25
15	50	25	12.5	12.5	12.5	12.5
16	50	25	25	25	25	-
17	25	100	12.5	50	12.5	50
Ciprofloxacin	12.5	12.5	12.5	25	12.5	25

'—' no inhibition even at a higher concentration of 200 µg/mL

Antifungal activity
In the case of antifungal activity, compound **13** against *A. niger* andcompound**16** against *A. flavus*exhibit excellent activity. However, they show moderate activity against rest of the tested organisms. Besides, compound **11** exhibits significant activity against*A. flavus, C. albicans*and *Rhizopus*compound **12** exhibits significant activity against*A. niger, C. albicans*and *Rhizopus,* compound **13** exhibits significant activity against*A. niger* and compound **16** exhibits significant activity against*A. flavus*with a growth inhibition value of 12.5µg/mL.The compounds **11** against *A. niger,* **12** against*A. flavus,* **13**against *Mucor,* **13**and **17** against*C. albicans,* **14**against *Rhizopus*and **11**against *Candida 6*show only a negligible activity with the inhibition concentration value of 100 µg/mL.Among the compounds (**11-17**) against the tested fungal strains, the compound**12** against *Candida 6,*compound **13**against *Rhizopus,*compound **15** against *Mucor* and compound**17**against *Candida 6*did not show any inhibition even at a maximum concentration of 200 µg/mL.The remaining compounds showed their growth inhibition against the various tested fungal strains at the range of 25-50µg/mLand which can be assigned as less to moderate activity. The antifungal potency of the synthesized compounds was compared with Fluconazole, a standard drug, using their minimum inhibitory concentration (MIC) by serial dilution method. The results are summarized in **Table 3.**

Table 3:*In vitro* antifungal activities of 11-17 against clinically isolated fungal strains

Compound	Minimum inhibitory concentration (MIC) in µg/mL					
	A. niger	*A. flavus*	*Mucor*	*C. albicans*	*Rhizopus*	*Candida 6*
11	100	25	50	25	25	100
12	25	100	50	25	25	-
13	12.5	50	100	100	-	50
14	50	25	50	25	100	25
15	25	25	-	25	50	25
16	25	12.5	25	25	25	50
17	50	25	50	100	50	-
Fluconazole	12.5	25	12.5	12.5	25	25

'—' no inhibition even at a higher concentration of 200 µg/mL

Molecular docking studies
Molecular docking study is a well-established technique to determine the interaction of two molecules and find the best orientation of ligand would form a complex with overall minimum energy.From the *invitro* antibacterial results, the molecular docking was carried out for the synthesized compound **11**with 7AHL protein is bounded well as compared to other proteinsshowed good binding energy toward the target protein ranging from -7.08to -5.99 kcal/mol. The docking results revealed that compound **14** showed minimum binding energy of -7.08kcal/mol, which is due to dipole-dipole and hydrogen bond interaction with amino acids of targeted protein. It was observed that the most active compound of the series, i.e., compound **14**was predicted to be most active *in silico* too. The other compounds like **14**and **16** having significant antibacterial activity are also found to have good docking scores.

The acting force of this binding mode is mainly depends on hydrogen bonding, electrostatic forces, van-der Waals forces and hydrophobic interaction due to non-polar residue interaction and water structure effect alteration. Docked ligand molecule **14** with the secondary structure of the structure of *alpha-hemolysin*of *Staphylcoccus aureus*in solid and ribbon model is depicted in **Figure 1**. The surface cavity with target molecule **14** at the active pocket of the protein structure is depicted in **Figure 2**.The 2D plot of hydrogen bond forming amino acids with target ligand and

the HB plot of interacted residues in protein and molecular interactions of *S. aureus*with compound **14**is depicted in **Figure 3&4** respectively.

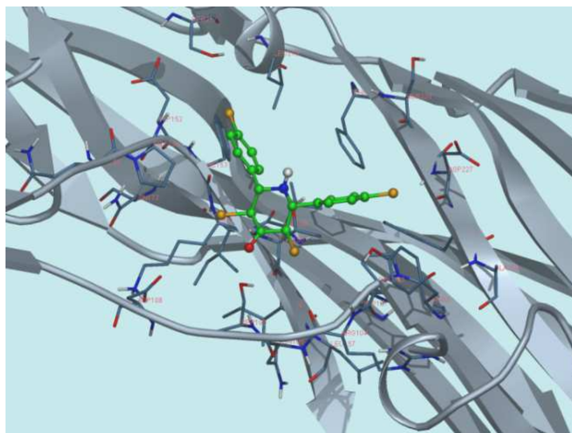


Figure 1. Docked ligand molecule 14 with7AHL protein in solid and ribbon model

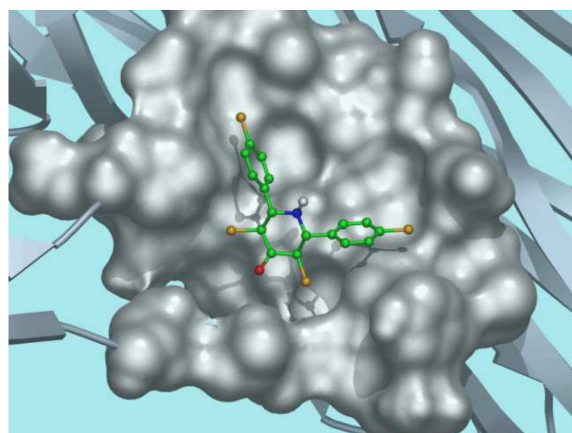


Figure 2. The surface cavity with target molecule 14 at the active pocket of the 7AHL protein

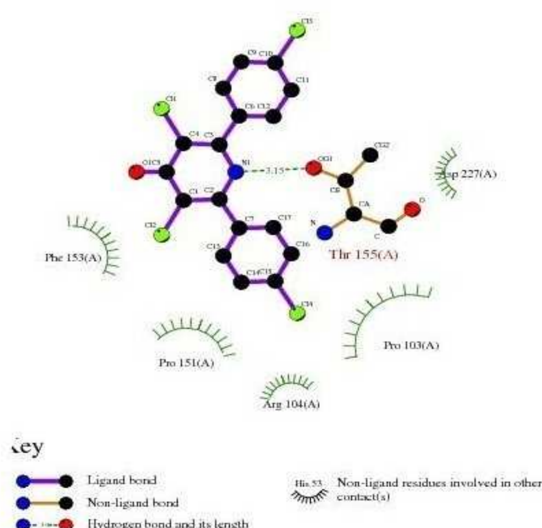


Figure 3. 2D plot of hydrogen bond forming amino acids of the 7AHL protein with target ligand for compound 14

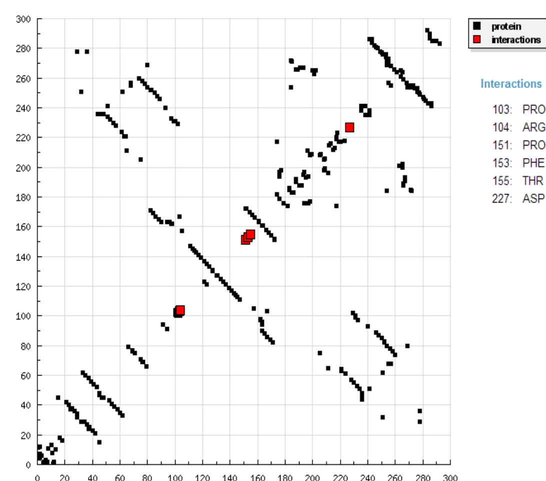


Figure 4. HB plot of the compound 14 showing interactions with different amino acids of the 7AHL protein

Table 4:Molecular docking results of the target molecules with *alpha-hemolysin* from *Staphylococcus aureus*(PDB ID:7AHL)

Compound	Binding Energy (kcal/mol)	Docking Energy (kcal/mol)	InhibitionConstant (µM)	Intermolec. Energy (kcal/mol)
11	-6.22	-6.77	27.62	-6.84
12	-6.77	-7.19	12.84	-7.26
13	-5.99	-6.95	42.05	-7.24
14	-7.08	-7.68	6.49	-7.68
15	-6.54	-7.11	16.13	-7.17
16	-6.71	-6.20	10.60	-6.22
17	-6.97	-6.86	1.98	-8.67

The *invitro* antifungal MIC values are correlated well with binding energies obtained through molecular docking with *Dihydrofolate Reductase* (PDB ID:**1AI9**) of *Candidaalbicans*[www.rcsb.org(DOI:10.2210/pdb1ai9/pdb)].Docked ligand molecule **14** with the secondary protein structure of Crystal structure of *Dihydrofolate Reductase*in solid and ribbon model is depicted in **Figure 5**. The minimum fungal inhibition potency against *C. albicans*of compounds **14**, **15** and **12** showed excellent docking energies. Their binding energies are -9.41, -8.31 and -8.30 kcal/mol respectively. From the comparative analysis, the above compounds **14**, **15** and **12** shows good *in vitro* antifungal activity which is further supported by their *in silico*analysis. The results are summarized in **Table 5**.

Table 5:Molecular docking results of the target molecules with *Dihydrofolate Reductase* from *Candida albicans* (PDB ID: 1AI9)

Compound	Binding Energy (kcal/mol)	Docking Energy (kcal/mol)	Inhibition Constant (µM)	Intermolec. Energy (kcal/mol)
11	-7.59	-8.28	2.71	-8.29
12	-8.30	-8.99	1.12	-8.99
13	-7.90	-9.04	1.61	-9.13
14	-9.41	-10.09	12.36	-10.07
15	-8.31	-9.06	1.04	-9.06
16	-7.48	-8.18	3.29	-8.38
17	-7.18	-8.29	4.25	-8.29

From the comparative analysis, the above compounds **14**, **15** and **12**shows good *in vitro* antifungal activity which is further supported by their *in silico*analysis. The above mentioned compounds utilize their amino head group to interact with the crucial amino acid residues such as Thr 58 through hydrogen bonds.The surface cavity with the molecule **14** at the active pocket of the protein structure is depicted in **Figure 6**. The 2D plot of hydrogen bond forming amino acids with target ligand**14**and the HB plot of interacted residues in protein and molecular interactions of *C. albicans* with compound **14**is depicted in **Figure 7& 8** respectively.Therefore, it is pleasing to state that the docking studies have widened the scope of developing a new class of antimicrobial agents.

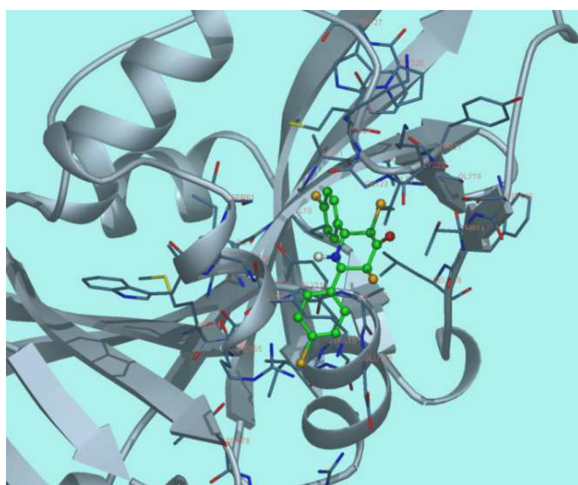


Figure 5. Docked ligand molecule 14 with 1AI9 protein in solid and ribbon model

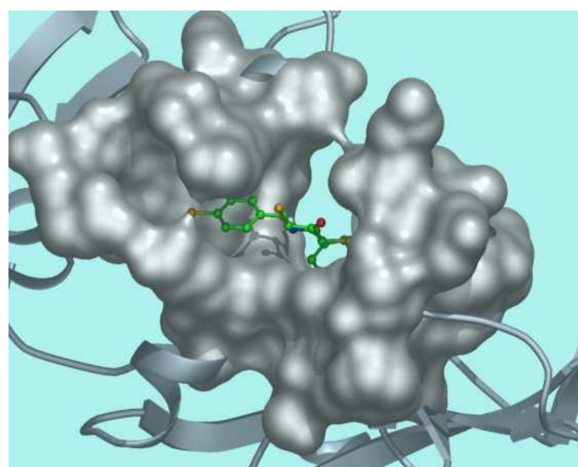


Figure 6. The surface cavity with target molecule 14 at the active pocket of the 1AI9 protein

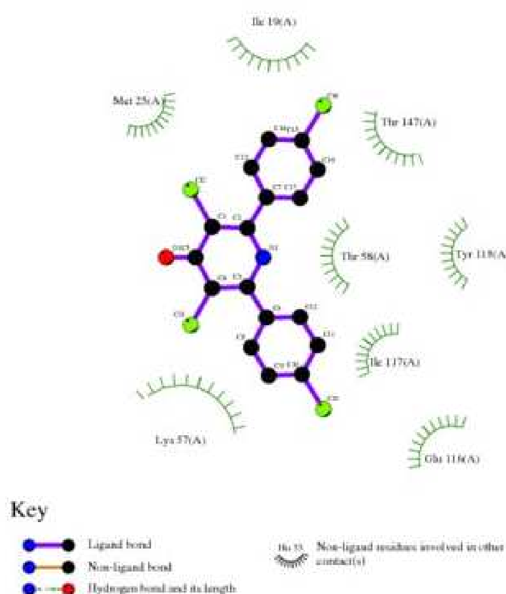


Figure 7. 2D plot of hydrogen bond forming amino acids of the 1AI9 proteinwith target ligand for compound 14

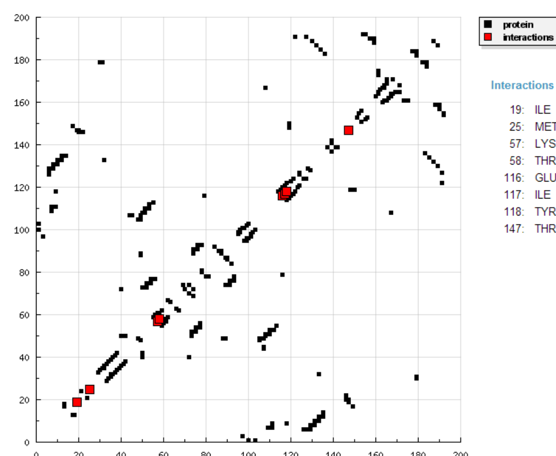


Figure 8. HB plot of the compound 14 showing interactions with different amino acids of the 1AI9 protein

CONCLUSION

A novel series of 3,5-Dichloro-2,6-diarylpiperidin-4-ones (**11-17**) were synthesized in good yields and their structures were characterized using various spectral analysis viz., IR, ^{1}H NMR, ^{13}CNMR & Mass. The antimicrobial activity results indicated that some of the tested compounds showed the most promising antibacterial and antifungal activities. These observations may promote a further development of our research in this field. Further development of this group of compounds may lead to compounds with better pharmacological profile than standard drugs and serve as templates for the construction of better drugs to combat bacterial and fungal infection. After studying the docking poses and binding modes of the docked compounds, the necessity of hydrogen bond formation for enhancing the activity of this class of compounds can be highly advocated.

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