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Laccase Enzyme Catalyst Mediated Synthesis of Pyrimidines and its Antibacterial, Antifungal, Molecular Docking Studies

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The novel synthesis of pyrimidine derivatives (**1a-f**) by using green chemistry technique with laccase as an enzyme catalyst. FT-IR, ^{1}H NMR, and elemental analyses were used to describe the produced compounds (**1a-f**). Antibacterial, antifungal, and molecular docking investigations to characterize the produced pyrimidine derivatives (**1a-f**). In antibacterial testing, compound **1e**, showed considerable action towards *E. coli* (MIC 02 µg/mL) as associated to ciprofloxacin (MIC 04 µg/mL). When related to clotrimazole in antifungal assessment, compound **1d** was shown to be significant activity towards *C. albicans* (MIC 0.25 µg/mL) than clotrimazole (MIC 0.5 µg/mL). Molecular docking experiments further indicate that compound **1e** inhibited antibacterial and compound **1d** inhibited antifungal proteins more effectively than the control compounds ciprofloxacin and clotrimazole.

Keywords: Pyrimidine, Enzyme catalyst, Green chemistry, Antibacterial activity, Antifungal activity, Molecular docking.

INTRODUCTION

Because of its great atom economy, wide requests in combinatorial chemistry and diversity-oriented production, multicomponent reactions (MCRs) are becoming more important in medicinal and organic chemistry [1-6]. The Biginelli reaction is one of the most effective multicomponent procedures for obtaining multifunctionalized 3,4-dihydropyrimidin-2(1H)-ones (DHPMs) and similar heterocyclics [7]. Anticancer [8], antibacterial [9], anti-inflammatory [10], antiviral [11], and antihypertensive properties [12] are only a few of the biological actions of these pyrimidines. First one-pot cyclocondensation process of urea, benzaldehyde and ethyl acetoacetate was accomplished by simple heating the three component mixtures solubilized in ethanol at reflux temperature with a catalytic quantity of HCl. The product yields, on the other hand, are fairly poor (20-50%). Replacement of HCl catalyst with $ZrCl_4$ [13], $Ln(OTf)_3$ [14], $Sr(OTf)_2$ [15], [bmim][$FeCl_4$] [16], $FeCl_3$ [17], $Cu(OTf)_2$ [18], $InBr_3$ [19], $MgBr_2$ [20], BF_3 [21], [bmim] BF_4-immobilized Cu(II) acetyl acetonate [22], $ZnCl_2$ [23] and $In(OTf)_3$ [24], has resulted in better yields of up to 95% in Biginelli reactions. Environmental contamination, excessively acidic reaction conditions, inadequate yields, hazardous catalysts and difficult processes were all disadvantages of the technologies mentioned above.

In recent times, as the chemical and pharmaceutical industries have become more environmentally concerned, efficient, cost-effective, and clean operations have gotten more attention. While research into the use of green solvent [25] and ultrasonic or microwave irradiation [26] in the Biginelli reaction is ongoing, it is also critical to continue developing an effective, accessible, and ecologically friendly approach for constructing such a large framework. Numerous enzymes have a wide range of catalytic efficiency that is not limited to its native substrates.

Enzyme promiscuity [27] is a feature that may be readily manipulated and employed in MCRs. Enzymes surpass most typical chemical catalysts because they are environmentally safe, biocompatible, and their reactions take place in mild circumstances [28]. They may be retrieved and utilized in many transformations after being immobilised on solid supports [29]. Numerous enzymes, in addition to their intrinsic capacity to catalyze a main reaction, may also catalyse secondary reactions, which is known as 'catalytic promiscuity' [30,31]. Michael addition may be catalyzed by lipase [32], while aldol additions

can be catalyzed by arylmalonate decarboxylase [33]. As a result, enzymes are becoming a more viable replacement to chemical catalysts in MCRs.

The current article discusses the synthesis and characterization of pyrimidine derivatives (**1a-f**) by using novel green chemistry technique (Grindstone method) with laccase enzyme as a catalyst. The synthesized compounds was further assessed for antibacterial, antifungal and molecular docking assessments.

EXPERIMENTAL

Sigma-Aldrich chemicals provided all of the supplies. Melting points were measured in unadjusted open capillary tubes and are uncorrected. On a shimadzu 8201pc, the IR spectra (KBr) was documented in KBr (4000-400 cm^{-1}). A JEOL-300 MHz was used to retrieve the ^{1}H and ^{13}C NMR spectra. An Elemental analyzer model (Varian EL III) was utilized to record the Elemental analysis (C, H and N). Thin layer chromatography (TLC) on silica gel plates was used to govern the purity of the substances.

Synthesis of pyrimidine derivatives (1a-f): In a pestle and mortar, the reactants 1,3-cyclohexanedione (0.01mol), substituted benzaldehyde (0.01mol), urea (0.01mol) and laccase (0.01mol) were mashed together. TLC was used to observe the response. The resulting mixture was cored into ice-cold water once the TLC revealed that the reaction was complete. The white precipitate was collected by filtration and dried. To get pure product, the product was recrystallized in ethanol. Other pyrimidine derivatives (**1b-f**) were synthesized using the same approach.

4-Phenyl-3,4,7,8-tetrahydroquinazoline-2,5(1*H*,6*H*)-dione (1a): Yellow solid; *m.w.*: 242.27; m.p. 206 ºC; IR (KBr, ν_{max}, cm^{-1}): 3312.40 (NH), 3110.32 (Ph-CHstr), 2984.39 (Ar-H), 2932.40 (CH_2), 1723.60 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 9.10 (2H, s, NH), 7.33 (2H, m, Phenyl ring), 7.26 (1H, t, Phenyl ring), 7.23 (2H, m, Phenyl ring), 5.13 (1H, s, CH), 2.90 (2H, t, -CH_2), 1.90 (2H, t, -CH_2), 1.60 (2H, m, -CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.80 (1C, C=O), 150.40 (1C, C=O), 145.30 (1C, -C=C), 143.30, 126.90, 128.50, 126.70 (6C, Phenyl), 104.20 (1C, -C=C), 51.70 (1C, -CH), 34.20, 26.10, 30.40 (3C, CH_2). Elemental analysis of $C_{14}H_{14}N_2O_2$ calcd. (found) %: C, 69.41 (69.36); H, 5.82 (5.90); N, 11.56 (11.53).

4-(4-Chlorophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1*H*,6*H*)-dione (1b): Brown solid; *m.w.*: 276.72; m.p. 194 ºC; IR (KBr, ν_{max}, cm^{-1}): 3316.26 (NH), 3114.38 (Ph-CH *str.*), 2990.32 (Ar-H), 2946.20 (CH_2), 1720.20 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 9.40 (2H, s, NH), 7.37 (2H, m, Phenyl ring), 7.34 (2H, m, Phenyl ring), 5.10 (1H, s, CH), 2.96 (2H, t, -CH_2), 1.92 (2H, t, -CH_2), 1.62 (2H, m, -CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.60 (1C, C=O), 150.20 (1C, C=O), 145.10 (1C, -C=C), 141.40, 132.30, 128.60, 126.10 (6C, Phenyl), 103.30 (1C, -C=C), 50.40 (1C, -CH), 35.10, 24.36, 28.10 (3C, CH_2). Elemental analysis of $C_{14}H_{13}ClN_2O_2$ calcd. (found) %: C, 60.77 (60.70); H, 4.74 (4.81); N, 10.12 (10.15).

4-(4-hydroxyphenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1*H*,6*H*)-dione (1c): Dust white solid; *m.w.*: 258.27; m.p. 162 ºC; IR (KBr, ν_{max}, cm^{-1}): 3320.26 (NH), 3118.38 (Ph-CH *str.*), 2994.32 (Ar-H), 2950.20 (CH_2), 1724.20 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 11.20 (1H, s, OH), 9.30 (2H, s, NH), 7.06 (2H, m, Phenyl ring), 6.63 (2H, m, Phenyl ring), 5.20 (1H, s, CH), 2.90 (2H, t, -CH_2), 1.86 (2H, t, -CH_2), 1.64 (2H, m, -CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.80 (1C, C=O), 150.40 (1C, C=O), 146.10 (1C, -C=C), 156.50, 135.90, 126.10, 115.70 (6C, Phenyl), 104.30 (1C, -C=C), 52.10 (1C, -CH), 34.10, 26.80, 22.36 (3C, CH_2). Elemental analysis of $C_{14}H_{14}N_2O_3$ calcd. (found) %: C, 65.11 (65.18); H, 5.46 (5.42); N, 10.85 (10.80).

4-(3-Nitrophenyl)-3,4,7,8-tetrahydroquinazoline-2,5-(1*H*,6*H*)-dione (1d): Pale yellow solid; *m.w.*: 287.29; m.p. 186 ºC; IR (KBr, ν_{max}, cm^{-1}): 3322.20 (NH), 3116.42 (Ph-CH *str.*), 2996.10 (Ar-H), 2952.40 (CH_2), 1726.30 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 9.40 (2H, s, NH), 8.12 (2H, m, Phenyl ring), 7.62 (2H, m, Phenyl ring), 5.16 (1H, s, CH), 2.84 (2H, t, -CH_2), 1.90 (2H, t, -CH_2), 1.68 (2H, m, -CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.60 (1C, C=O), 151.20 (1C, C=O), 143.20 (1C, -C=C), 147.70, 144.20, 133.00, 129.40, 121.90, 120.70 (6C, Phenyl), 103.20 (1C, -C=C), 50.70 (1C, -CH), 35.20, 27.40, 21.60 (3C, CH_2). Elemental analysis of $C_{14}H_{13}N_3O_4$ calcd. (found) %: C, 58.53 (58.50); H, 4.56 (4.60); N, 14.63 (14.65).

4-(2-Hydroxyphenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1*H*,6*H*)-dione (1e): Brown solid; *m.w.*: 258.27; m.p. 132 ºC**;** IR (KBr, ν_{max}, cm^{-1}): 3328.20 (NH), 3122.42 (Ph-CH *str.*), 2990.42 (Ar-H), 2958.12 (CH_2), 1732.26 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 11.20 (1H, s, OH), 9.20 (2H, s, NH), 7.09 (2H, m, Phenyl ring), 6.83 (2H, m, Phenyl ring), 5.20 (1H, s, CH), 2.90 (2H, t, -CH_2), 1.94 (2H, t, -CH_2), 1.60 (2H, m, -CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 197.20 (1C, C=O), 150.10(1C, C=O), 145.60 (1C, -C=C), 154.00, 128.30, 128.10, 122.80, 121.10, 115.70 (6C, Phenyl), 104.60 (1C, -C=C), 45.50 (1C, -CH), 36.00, 28.10, 21.30 (3C, CH_2). Elemental analysis of $C_{14}H_{14}N_2O_3$ calcd. (found) %: C, 65.11 (65.14); H, 5.46 (5.50); N, 10.85 (10.82).

4-(3,4,5-Trimethoxyphenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1*H*,6*H*)-dione (1f): White solid; *m.w.*: 332.35; m.p. 168 ºC; IR (KBr, ν_{max}, cm^{-1}): 3324.56 (NH), 3118.48 (Ph-CH *str.*), 2980.69 (Ar-H), 2957.62 (CH_2), 1725.72 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 9.20 (2H, s, NH), 6.20 (2H, m, Phenyl ring), 5.13 (1H, s, CH), 3.83 (9H, s, -OCH_3), 2.94 (2H, t, -CH_2), 1.96 (2H, t, -CH_2), 1.67 (2H, m, -CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.90 (1C, C=O), 150.20 (1C, C=O), 146.10 (1C, -C=C), 152.70, 136.47, 137.61, 137.28, 104.30 (6C, Phenyl), 105.30 (1C, -C=C), 60.80 (1C, -OCH_3), 56.14 (2C, -OCH_3), 52.30 (1C, -CH), 36.04, 28.14, 21.30 (3C, CH_2). Elemental analysis of $C_{17}H_{20}N_2O_5$ calcd. (found) %: C, 61.44 (61.36); H, 6.07 (6.12); N, 8.43 (8.43).

Antibacterial activity: The synthesized compounds **(1a-f)** was evaluated antibacterial activity by *Klebsiella pneumoniae* (recultured), *Staphylococcus aureus* (ATCC-25923), *Pseudomonas aeruginosa* (ATCC-27853) and *Escherichia coli* (ATCC-25922) bacterial strains and technique analyzed by reported in the literature [34,35].

Antifungal activity: The synthesized compounds **(1a-f)** was evaluated antifungal activity by using *Microsporum audouinii*,

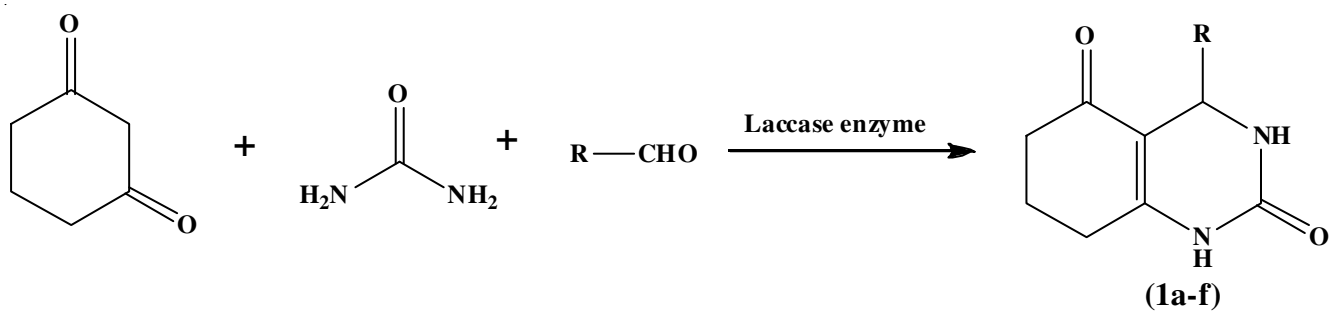
Aspergillus niger, *Cryptococcus neoformans* (recultured) and *Candida albicans* (fungal strains) and procedure analyzed by reported in the literature [36,37].

Molecular docking: Molecular docking experiments with Autodock vina 1.1.2 [38] were performed to examine the interaction and binding mechanism among compounds **1a**, ciprofloxacin, clotrimazole and the proteins 1KZN, 1FI4. The target proteins, namely Topimerase II DNA gyrase B (PDB ID: 1KZN) and mevalonate 5-diphosphate decarboxylase (PDB ID: 1FI4) were obtained from Protein Data Bank (http://www.rcsb.org). Chem3D Pro 12.0 and ChemDraw Ultra 12.0 were used to create the 3D structures of compounds **1a**, ciprofloxacin and clotrimazole. The AutoDock Tools 1.5.6 software suite was utilized to generate the input data for Autodock Vina. The 1KZN protein search grid was detected as dimensions size x,y,z: 22, 20, 20 with center x,y,z: 18.839, 26.702, 37.939 with 1.0 spacing. The 1FI4 protein search grid was defined as dimensions size x,y,z: 24, 22, 24 with center x,y,z: 21.935, 57.745, 20.018 with 1.0 spacing. The assessment for exhaustiveness was set to 8. For Vina docking, the other settings were enabled by default and were not stated. The significant compound is the one with the lowest binding affinity value, and the outcomes were visually assessed with the Discovery studio 2019 software.

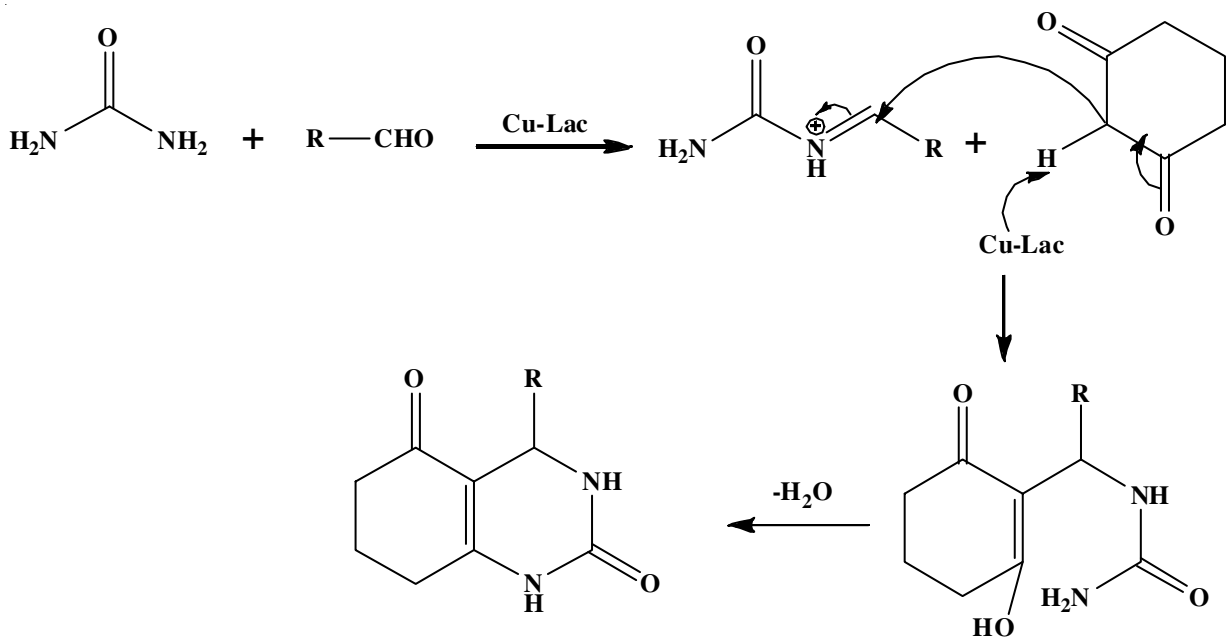
RESULTS AND DISCUSSION

The enzyme mediated synthesis of title compounds (**1a-f**) is illustrated in **Scheme-I**. The suggested mechanism for the development of pyrimidine derivatives is shown in **Scheme-II**. Compounds (**1a-f**) were synthesized by condensation method. The optimization of catalyst is shown in Table-1, while the optimization of reaction condition is shown in Table-2. Initially, the formation of pyrimidine derivative **1a** without enzyme catalyst with low yield about 4% and takes long reaction time about 90 min. Then the utilization of enzymes like protease from *Streptomyces griseus*, lipase from *Candida antarctica*, trypsin from bovine pancreas, laccase from *Trametes versicolor* increased the yield from 4 to 94% and also reduces the reaction time from 90 min to 5 min. Among these enzymes, laccase from *Trametes versicolor* produced higher yield of 94%. The formation of the title compound was characterized by spectral techniques like FT-IR, ^{1}H, ^{13}C NMR spectra and elemental analyses.

The IR spectra of the synthesized compounds (**1a-f**) displayed the absorption bands at 3312.40-3328.20, 3110.32-3118.48 and 1720.20-1732.26 cm^{-1} corresponding to the NH, phenyl and C=O moieties, respectively. The ^{1}H NMR spectra of compounds (**1a-f**) exhibited a sharp singlet at δ 9.10-9.40



Scheme-I: Synthetic route of compounds (**1a-f**)



Scheme-II: Suggested mechanism for the synthesis of compounds (**1a-f**)

TABLE-1
CATALYST OPTIMIZATION FOR COMPOUND **1a**

Catalyst	Yield (%)	Time (min)
No enzyme	04	90
Protease from *Streptomyces griseus*	46	8
Lipase from *Candida antarctica*	62	10
Trypsin from bovine pancreas	76	12
Laccase from *Trametes versicolor*	94	5

TABLE-2
OPTIMIZATION OF REACTION

Compound	-R	Yield (%)	Time (min)
1a	$-C_6H_5$	94	5
1b	$-4-Cl-C_6H_5$	92	5
1c	$-4-OH-C_6H_5$	86	10
1d	$-3-NO_2-C_6H_5$	90	8
1e	$-2-OH-C_6H_5$	91	6
1f	$-3,4,5-(OCH_3)_3-C_6H_5$	84	5

ppm for NH proton, a singlet at δ 5.10-5.20 ppm for -CH- proton and singlet at δ 1.60-1.67 ppm for $-CH_2$ proton. The ^{13}C NMR spectra of compounds (**1a-f**) revealed characteristic peaks at δ 197.20-198.90, 45.50-52.3 and δ 21.30-30.40 ppm corresponding to C=O, -CH and $-CH_2$ carbons, respectively.

Antibacterial activity: The synthesized pyrimidine derivatives (**1a-f**) were assessed for antibacterial activity towards several bacterial strains. When comparing to the standard, compound **1a** showed considerable activity. When associated to ciprofloxacin (MIC 4 µg/mL), compound **1a** exhibited strong activity towards *S. aureus* (MIC 2 µg/mL) and compound **1e** possess equally active (MIC 4 µg/mL). While compound **1c** was tremendously active towards *K. pneumoniae* (MIC 8 µg/mL). Compound **1e** showed considerable action towards *E. coli* (MIC 2 µg/mL) but lesser activity towards *P. aeruginosa* (MIC 20 µg/mL) than ciprofloxacin. In terms of antibacterial activity, synthesized compounds (**1a-f**) were much more effective than conventional ciprofloxacin (Table-3).

Antifungal activity: The synthesized pyrimidine derivatives (**1a-f**) were assessed for antifungal activity towards the studied fungal strains. When compared to the standard, compound **1b** showed significant antifungal action (MIC 0.5 µg/mL) towards *A. niger*. Compound **1a** was shown to be equally active towards *C. albicans* (MIC 0.5 µg/mL) and *A. niger* (MIC 1 µg/mL) fungi. While relative to clotrimazole, compound **1f** (MIC 2 µg/mL) was tremendously antifungal action towards *M. audouinii*. Compound **1d** was shown to be significant activity towards *C. albicans* (MIC 0.25 µg/mL) than clotrimazole (MIC 0.5 µg/mL). When associated to clotrimazole (MIC 2 µg/mL), compound **1e** (MIC 1 µg/mL) having significant action towards C.neoformans. When compared to standard clotrimazole, the synthesized compounds (**1a-f**) had a better antifungal activity (Table-3).

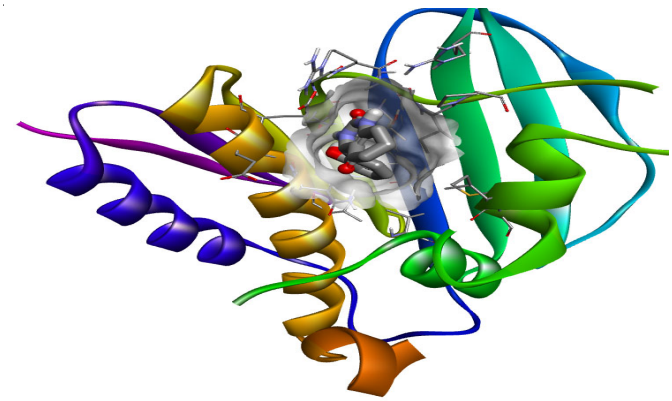
Docking studies: Docking simulations have been carried out in order to achieve an improved understanding of the probable mechanism of biological activity. Antibacterial protein *E. coli* topoisomerase II DNA gyrase B (PDB ID: 1KZN) [39] and antifungal protein mevalonate-5-diphosphatede carboxylase (PDB ID: 1FI4) answerable for sterol/isoprenoid biosynthesis [40] was described as a virtuous target for studying inhibitory action towards these microbes. The docking behaviour of compound **1a**, ciprofloxacin and clotrimazole with proteins 1KZN and 1FI4 was investigated using the Autodock Vina software. In 1KZN protein, compound **1e** has a strong binding affinity (-9.8 kcal/mol) than ciprofloxacin, which has a binding affinity of (-7.2 kcal/mol). With the receptor 1KZN, compound **1e** creates three hydrogen bonds with the receptor 1KZN. The residues of aminoacids Asn46, Asp73 and Gly77 with the bond lengths of 2.09, 2.17, 2.20 and 2.40 Å, respectively. Hydrophobic interactions were found between the amino acid residues Ile78 and Val120. Ciprofloxacin does not create a hydrogen bond with the receptor 1KZN when used as a control. Hydrophobic interactions were found between the amino acid residues Asn46, Ala47, Glu50, Asp73, Ile78, and Ile90.

Figs. 1 and 2 illustrated the hydrophobic interactions and hydrogen bonding of residues of amino acids in 1KZN protein with compound **1e** and ciprofloxacin. Compound **1d** has significant binding affinity (-9.2 kcal/mol) in 1FI4 protein than clotrimazole, which has a binding affinity of (-6.8 kcal/mol). Compound **1d** makes five hydrogen bond with the protein 1FI4. Hydrogen bonding was observed between the amino acid residues Leu118 (bond length: 2.73, 2.71 Å), Ala119 (bond length: 2.37 Å), Arg158 (bond length: 2.23 Å), Ser208 (bond length: 2.15 Å). Hydrophobic interactions were found in the amino acid residue Ala119. Clotrimazole, which is used as a control, establishes one hydrogen bond with the receptor 1FI4. In hydrogen bonding interaction, the amino acid residue Arg158 (bond length: 5.83 Å) was involved. Hydrophobic interactions were found in the amino acid residues Ala15, Lys18, Tyr19, Trp20, Ala119, Phe260, Asp302 and Ala303.

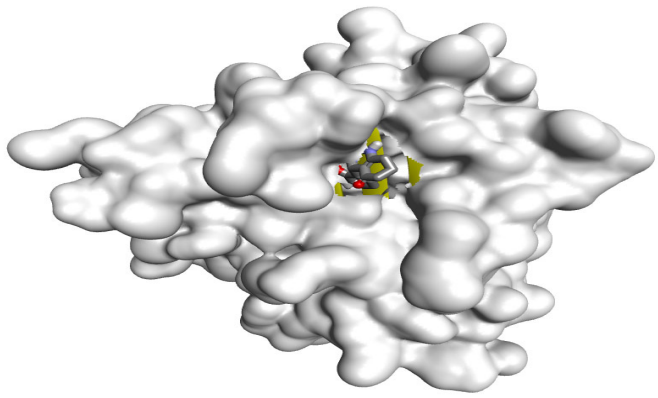
Figs. 3 and 4 illustrated the hydrophobic connections and hydrogen bonding of residues of amino acids in 1FI4 protein

TABLE-3
ANTIMICROBIAL ACTIVITY: MIC (µg/mL)

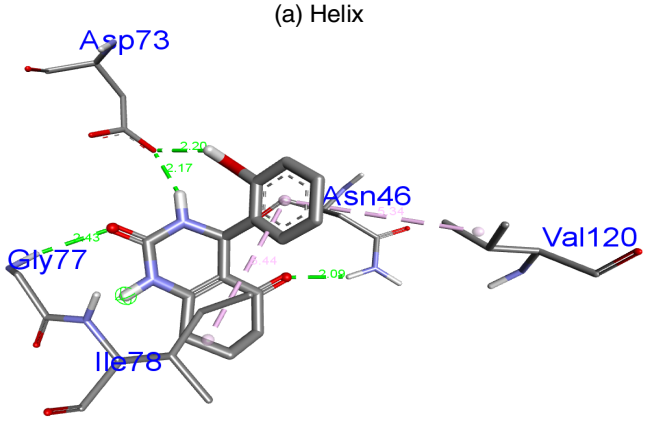
Compounds	Antibacterial activity				Antifungal activity			
	S. aureus	*K. neumoniae*	*E. coli*	*P. saeruginosa*	*A. niger*	*C. albicans*	*M. audouinii*	*C. neoformans*
1a	02	12	06	32	01	0.5	18	08
1b	06	18	12	24	0.5	06	10	12
1c	10	08	04	18	04	02	06	06
1d	08	16	08	20	03	0.25	12	10
1e	04	20	02	16	06	03	08	01
1f	06	18	10	12	10	08	02	05
Ciprofloxacin	04	16	04	02	–	–	–	–
Clotrimazole	–	–	–	–	01	0.5	04	02



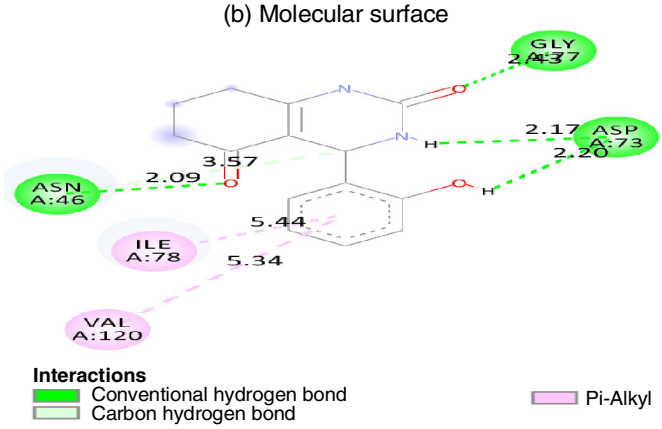
(a) Helix



(b) Molecular surface

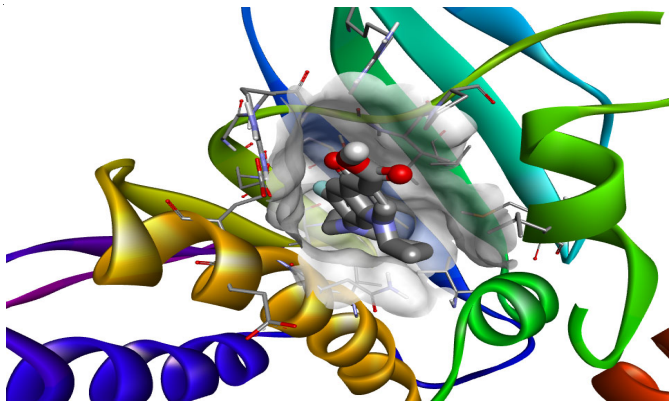


(c) 3D

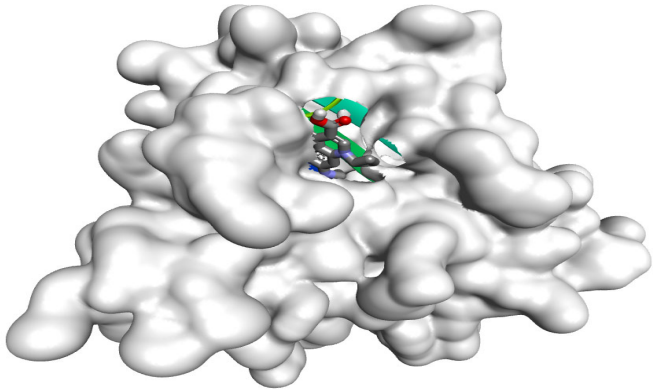


(d) 2D

Fig. 1. Interaction modes of compound **1e** within the binding pocket of 1KZN protein



(a) Helix



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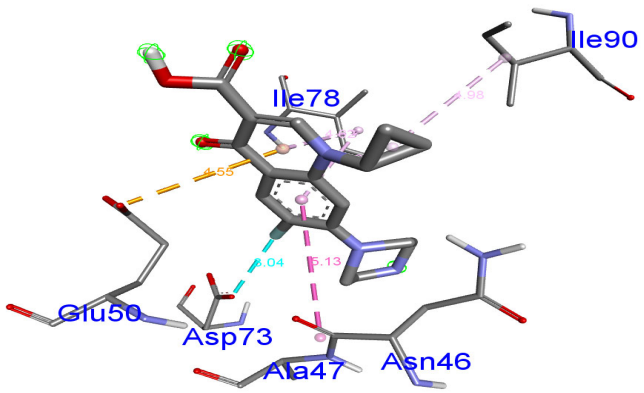
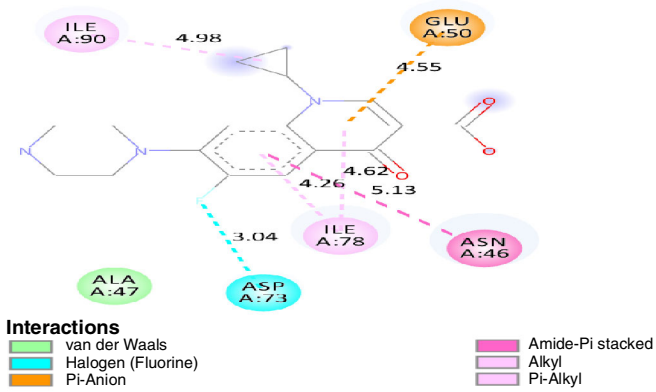


(c) 3D



(d) 2D

Fig. 2. Interaction modes of control ciprofloxacin within the binding pocket of 1KZN protein

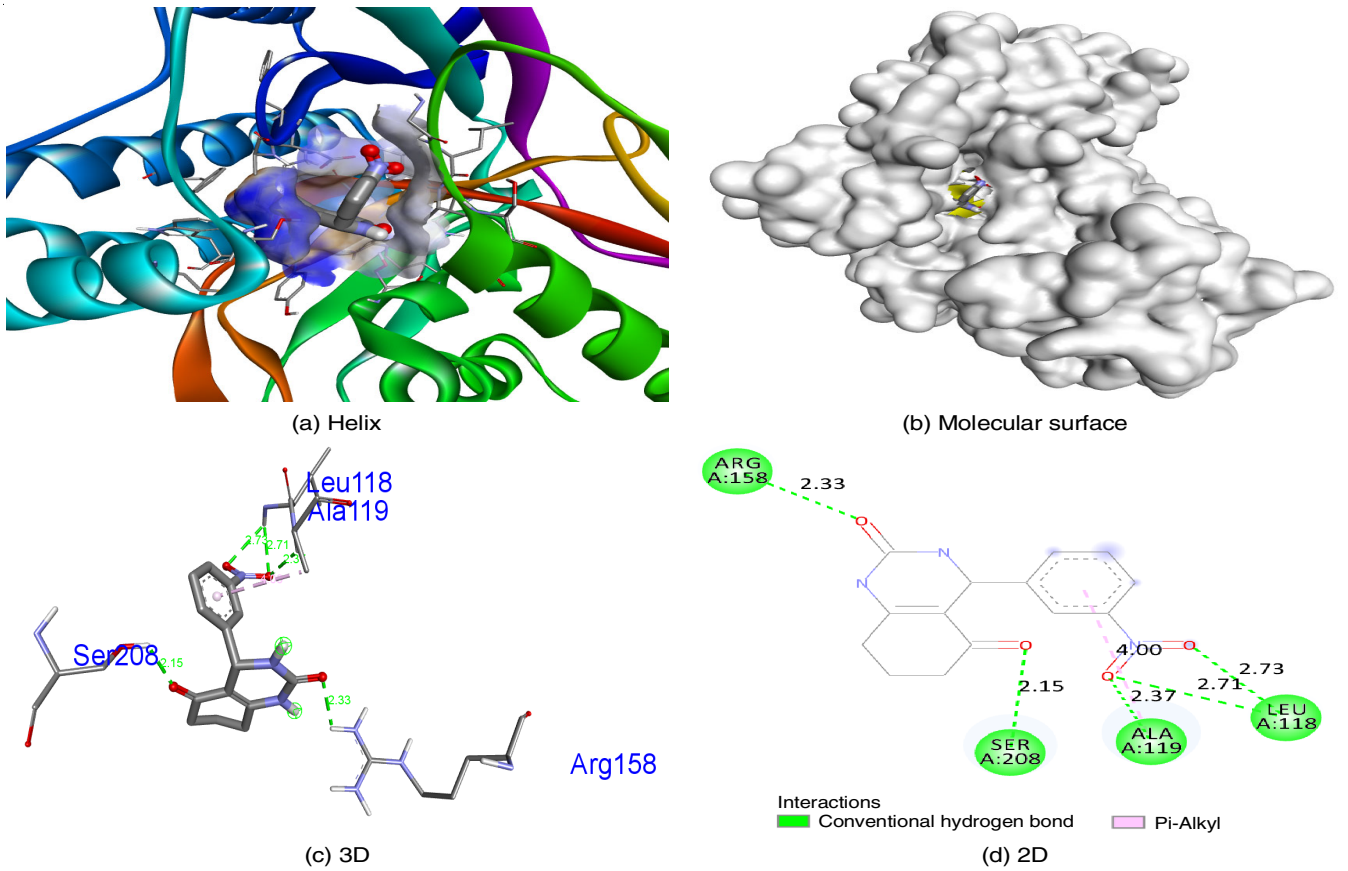


Fig. 3. Interaction modes of compound **1d** within the binding pocket of 1FI4 protein

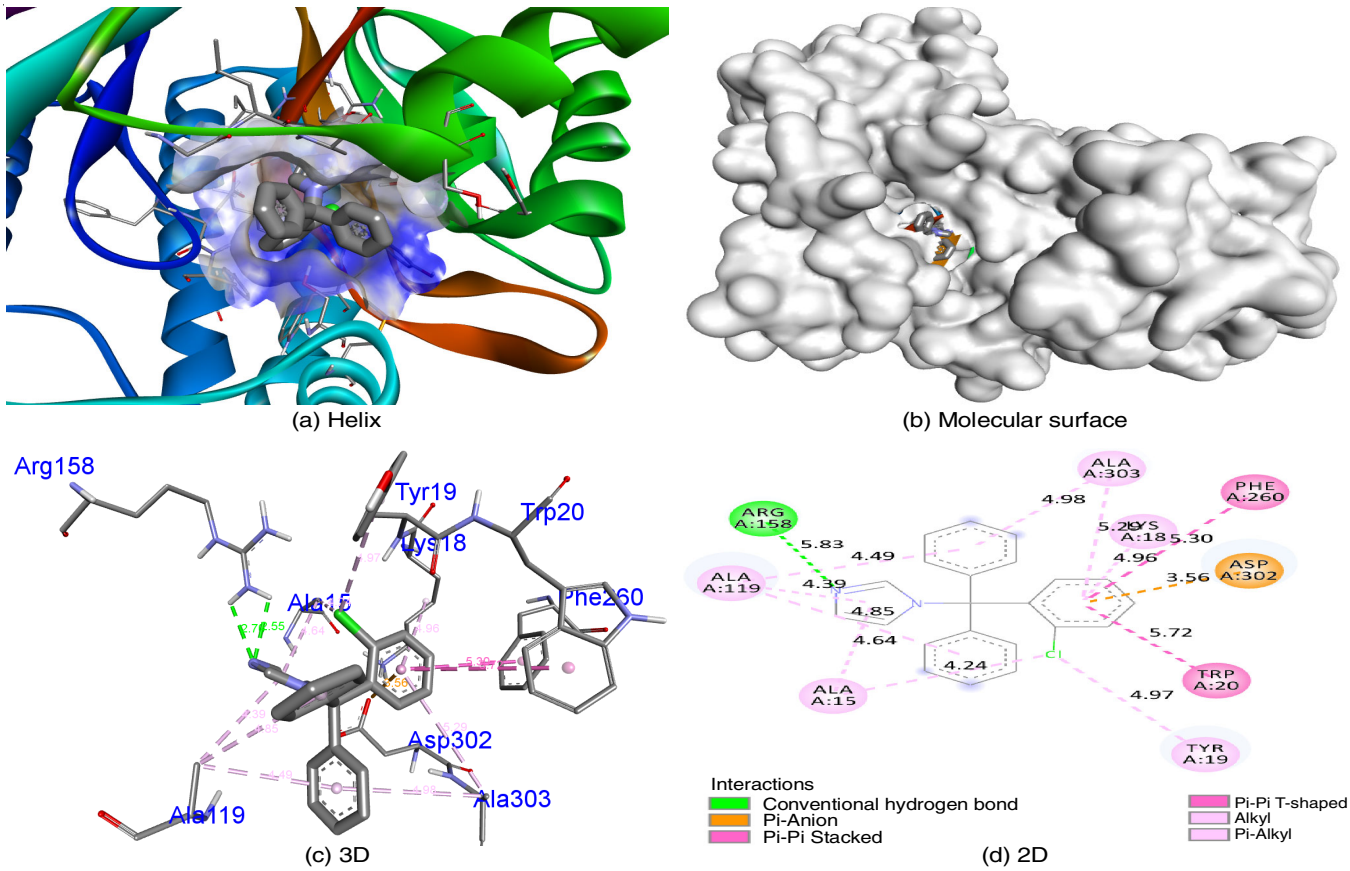


Fig. 4. Interaction modes of control clotrimazole within the binding pocket of 1FI4 protein

TABLE-4
MOLECULAR DOCKING RELATIONS

Compd.	1KZN			1FI4		
	Binding affinity (kcal/mol)	No. of H-bonds	H-bonding residues	Binding affinity (kcal/mol)	No. of H-bonds	H-bonding residues
1a	-8.8	3	Asn46, Asp73, Gly77	-7.7	0	–
1b	-8.5	3	Asn46, Asp73, Gly77	-8.8	2	Arg158, Ser208
1c	-8.4	3	Asn46, Asp73, Gly77	-7.4	4	Ser155, Arg158, Ser208, Ala303
1d	-8.8	4	Asn46, Asp73, Gly77, Val167	9.2	5	Leu118, Ala119, Arg158, Ser208
1e	-9.8	3	Asn46, Asp73, Gly77	-8.1	3	Ser155, Arg158, Ser208
1f	-6.5	1	Asn46	-7.7	2	Ser155, Ala303
Ciprofloxacin	-7.2	0	–	–	–	–
Clotimazole	–	–	–	-6.8	1	Arg158

with compound **1d** and clotrimazole, respectively. The findings indicate that compound **1e** has a greater capacity to inhibit antibacterial and compound **1d** has a greater capacity to inhibit antifungal proteins than the control compounds ciprofloxacin and clotrimazole. Table-4 shows a summary of the findings.

Conclusion

In conclusion, pyrimidine derivatives (**1a-f**) were synthesized by using novel green chemistry technique with laccase as a enzyme catalyst. FT-IR, ^{1}H NMR, and elemental analyses were used to characterize the synthesized compounds (**1a-f**). Antibacterial, antifungal and molecular docking investigations were conducted on the synthesized pyrimidine derivatives. In antibacterial testing, compound **1e**, showed considerable action towards *E. coli* as associated to ciprofloxacin. When related to clotrimazole in antifungal assessment, compound **1d** was shown to be significant activity towards *C. albicans* than clotrimazole. Molecular docking experiments further indicate that compound **1e** inhibited antibacterial and compound **1d** inhibited antifungal proteins more effectively than the control compounds ciprofloxacin and clotrimazole. As a result, compounds **1e** and **1d** may be a future source of antimicrobial drugs.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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