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Synthesis, *in vitro* Antimicrobial Evaluation, Molecular Docking Studies and ADME Prediction of Furan-2-yl-Morpholinophenylpyrimidine Derivatives

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A new series of novel 4-(furan-2-yl)-6-(4-morpholinophenyl)pyrimidine-amines (**4a-c**) were synthesized and characterized by elemental analysis and spectral analysis like IR, 1D ^{1}H & ^{13}C NMR. The synthesized compounds **4a-c** were evaluated for their biological studies. The zone of inhibitions were examined for synthesized compounds **4a-c** besides the identical set of microbial strains, especially that compound **4a** against *S. aureus, S. pyogenes*, *E. coli*, compound **4b** against *P. aeruginosa* has excellent antibacterial activity. Compound **4c** shows good inhibition against *C. albicans*. Also *in silico* molecular docking and ADME predictions were carried for all the compounds. The docking studies were examined by two different proteins like 1UAG protein and 1OQA protein. *in silico* docking provides of the compounds have good docking score compared with the standard. In the ADME predictions all the compounds were met criteria. The synthesized compounds all of them obeyed the drug-likeness properties.

Keywords: 4′-Morpholino acetophenone, Antimicrobial activity, Molecular docking.

INTRODUCTION

In modern days, a vast range of microorganisms are the attractive opposition to drugs that were utilize to treat various communicable diseases. In worldwide this resistance is a major hurdle to treatment of communicable diseases [1]. One of the cause of problems is infections, particularly microbial infections are a fill out problem in present-time medicine and the use of antibiotics is common across the world. Accordingly, an urgent need to wide number of antimicrobial agents, which is have a broad spectrum of activity against the resistant microorganism [2]. Therefore, it is requisite posses' microbial agents with improved capability. There has been fill out pertaining to development of bioactive compounds in the field of organic chemistry. Heterocyclic compounds containing 'N' in six membered rings; especially pyrimidines seemingly obtained appreciable importance owing to their varied biological activities and medicinal importance. Pyrimidine compounds have large variety of biological properties like adenosine receptor antagonists [3], kinase inhibitors [4], analgesic, anti-inflammatory [5], inhibitors of cyclin-dependent kinase 1 and 2 [6], calcium channel antagonist [7], anti-histaminic [8] and antitubercular [9] activities. Encouraging manifold pharmacological properties were manifest beyond diverse *N*-functionalized morpholines. Morpholine compounds were reported to exert a number of physiological properties such as antidiabetic [10], antiemetic [11], platelet aggregation inhibitors, anti-hyperlipoproteinemics [10] bronchodilators, growth stimulants [12], antidepressants [13], inflammatory diseases, pain, migraine and asthma [14]. Morpholine derivatives were used as antifungal agent in the trade name of Tridemorph [15].

4-Phenyl morpholine derivatives were reported to possess anti-inflammatory [16] and central nervous system [17] activities. With the expectation of, some of the clinically important drugs contain morpholine moiety in addition to *N*-heterocycles are separated one or more carbon atoms. The drugs are acquired from morpholine assimilated compounds encompass dextromoramide, a narcotic analgesic and doxapram HCl, a respiratory stimulant. Doxapram used in the treatment of respiratory depression following anaesthesia [18]. Minoxidil is a good antihypertensive vasodilator and used for the treatment of hair growth for men and women.

The drug designing's are of two important categories *e.g.* structural and ligand based drug designing which are engaged as important tools in rational drug development process [19]. *in silico* Study is facilitating computational used tech-niques in SBDD to obtain optimized conformation of ligand-receptor reciprocity and to study their relative intention through the minimized energy free system [20]. Computer aided drug designing (CADD) is fast, economical modernized technique that gives valuable, precise and deep understandings of experimental findings and new suggestions for molecular structures to be prepared [21].

Drug molecules force fail during development because of several reasons of failures is related with poor pharmacokinetics and ADME properties predictions [22]. Unpredicted drug toxicity is the one of the main factors to pull out drug from the market. Therefore, ADME properties are the crucial determinants for the clinical success of the drug [23]. ADME modeling has attracted the considerable attention of the pharmaceutical researchers for the drug discovery as they are high throughput in nature and cost effective [24,25]. In continuation of our interest in synthesizing the structurally diverse biologically active heterocycles [26-31], we report now the synthesis of 4-(furan-2-yl)-6-(4-morpholinophenyl)pyrimidine-2-amines, a novel series of furfuryl amino pyrimidine derivatives.

EXPERIMENTAL

4′-Morpholino acetophenone, furfuraldehyde, 2-bromofurfuraldehyde, 2-methyl furfuraldehyde, sodium hydroxide, guanidine nitrate and absolute ethanol were obtained from Sigma-Aldrich, USA. All products purity was checked by TLC. The melting points were determined by MELT Temp melting pointing apparatus using open capillary technique of the target compounds and the results are uncorrected. The FT-IR spectrum was recorded on an FT-IR Shimadzu 8400s spectrometer in the range of 4000-400 cm^{-1}. ^1H & ^{13}C NMR spectra were recorded by Brucker 400 MHz spectrometer (in δ ppm) using internal standard trimethyl silyl iodide. CHN were carried out by Perkin-Elmer CHN analyzer.

The literature survey method followed to synthesize the starting chalcones (**3a-c**) [31].

Synthesis of 4-(furan-2-yl)-6-(4-morpholino phenyl)-pyrimidine-2-amines (4a-c): Ethyl alcohol (30 mL) was taken in a round bottom flask and 0.01 mol of morpholine chalcone **3a-c** and 0.01 mol of guanidine nitrate were added. The reaction mixture was fixed with a reflux condenser and then 20 mL solution of 20% NaOH were added portion wise for 2 h and then the reflux was continued till the products formed. TLC was used to check the conversion of the product. The product was transferred into 400 mL beaker containing ice cubes and aside overnight. The formed solid product was separated by filtration, washed excess amount of water to remove strong base, dried and purified by recrystallization using rectified spirit to obtain the target compounds **4a-c** in good to moderate yield. The synthetic compounds procedure was adopted using literature survey method [32].

4-(Furan-2-yl)-6-(4-morpholinophenyl) pyrimidine-2-amine (4a): Yield: 55%, colour: pale yellow, *m.w.*: 332.36, m.p.: 160 ºC. IR (KBr, cm^{-1}): 3511, 3038, 2958, 2921, 2852, 1667, 1598, 1566, 1519, 1450, 1352, 752, 645. ^1H NMR (δ ppm): 6.85 (H-3 & H-4 of furan ring), 6.96 (H-5 of furan ring), 6.16 (H-5 of pyrimidine ring), 5.13 (NH_2 of pyrimidine ring), 3.87 (O-$(CH_2)_2$ of morpholine moiety, J = 4.8 Hz), 3.27 (N$(CH_2)_2$ of morpholine moiety, J = 4.4 Hz), 7.08-8.02 (Ar-H's); ^{13}C NMR (δ ppm): 165.30, 163.22 (C=N of pyrimidine moiety), 66.58, 66.73 (O$(CH_2)_2$ of morpholine moiety), 47.57, 48.35 (N$(CH_2)_2$ of morpholine moiety), 152.90 (C-N of pyrimidine ring), 100.60 (C_5 of pyrimidine ring), 156.61 (C_2 carbon of furan ring), 108.69 (C_3 of furan moiety), 112.80 (C_4 of furan moiety), 144.44 (C_5 of furan ring), 113.32-130.87 (arom. carbons). Elemental analysis of $C_{18}H_{18}N_4O_2$ calcd. (found) %: C, 67.08 (67.56); H, 5.59 (5.92); N, 17.39 (17.50).

4-(5-Bromofuran-2-yl)-6-(4-morpholinopnenyl)pyrimidine-2-amine (4b): Yield: 60%, colour: yellow, *m.w.*: 401.26, m.p.: 185 ºC. IR (KBr, cm^{-1}): 3498, 3084, 3047, 2954, 2934, 1662, 1592, 1566,1522, 1452, 1354, 756, 648, ^1H NMR: δ ppm, 6.95(H 3& H 4 proton of furan ring), 6.16 (H-5 of pyrimine ring), 3.86 (O$(CH_2)_2$ of morpholine ring) J = 4.8 Hz, 3.28 (N$(CH_2)_2$ of morpholine ring) J = 4.4 Hz, 7.51-8.04 (Ar H's); ^{13}C NMR: δ ppm, 167.85, 166.58 (C=N carbon of pyrimidine ring), 66.71 (O$(CH_2)_2$ carbon of morpholine moiety), 47.65, 48.21 (N$(CH_2)_2$ carbon of morpholine moiety), 152.49 (C-N carbon of pyrimidine ring), 100.98 (C-5 carbon of pyrimidine ring), 156.86 (C_2 of furan ring), 109.77 (C_3 of furan ring), 112.48 (C_4 of furan moiety), 142.23 (C_5 carbon of furan ring), 114.57-132.49 (arom. carbons). Elemental analysis of $C_{18}H_{17}N_4O_2Br$ calcd. (found) %: C, 53.88 (54.24); H, 4.27 (4.52); Br, 19.91 (19.45); N, 13.96 (13.65).

4-(5-Methylfuran-2-yl)-6-(4-morpholinophenyl)-pyrimidine-2-amine (4c): Yield: 59%, Colour: yellow, *m.w.*: 336.39, m.p.: 185 ºC. IR (KBr, cm^{-1}): 3498, 3078, 3064, 2988, 2924, 1660, 1594, 1542, 1454, 1352, 768, 642. ^1H NMR (δ ppm): 6.85 (H-3 & H-4 of furan ring), 6.55 (H-5 of pyrimine ring), 5.08 (NH_2 of pyrimidine ring), 3.87 (O-$(CH_2)_2$ of morpholine ring) J = 4.8 Hz, 3.27 (N-$(CH_2)_2$ of morpholine ring) J = 4.4 Hz, 7.16-8.04 (aromatic protons), 2.17 (methyl substituent at H-5 of furan ring), ^{13}C NMR (δ ppm): 167.35, 165.92 (C=N of pyrimidine ring), 66.58, 66.73 (O$(CH_2)_2$ of morpholine moiety), 47.55, 48.32 (N$(CH_2)_2$ of morpholine moiety), 153.41 (C-N of pyrimidine ring), 101.19 (C_5 of pyrimidine ring), 154.72 (C_2 of furan ring), 111.25 (C_3 of furan ring), 112.22 (C_4 of furan moiety), 144.48 (C_5 of furan ring), 66.00 (methyl carbon), 113.33-130.26 (arom. carbons). Elemental analysis of $C_{19}H_{20}N_4O_2$ calcd. (found) %: C, 67.86 (67.40); H, 5.95 (6.35); N, 16.66 (16.42).

Biology activity

Antimicrobial screening: Synthesized compounds were used to under the investigation microbial screening process carried for the individually tested using agar well disc diffusion method [33-35]. By adopting the literature precedent the antimicrobial activity procedure was followed [36].

Computational study

Molecular docking study: Auto dock version 4.2.5.1 docking software was used to predict the hydrogen bond inter-

action and binding score of the synthesized compounds **4a-c**. *in silico* docking predictions were accomplished by literature survey method [37].

ADME study: *in silico* ADME predictions were implementing for synthesized 4-(furan-2-yl)-6-(4-morpholinophenyl)-pyrimidine-2-amine derivatives **4a-c** were predicted using free online software's like Swiss ADME and Molinspiration software.

RESULTS AND DISCUSSION

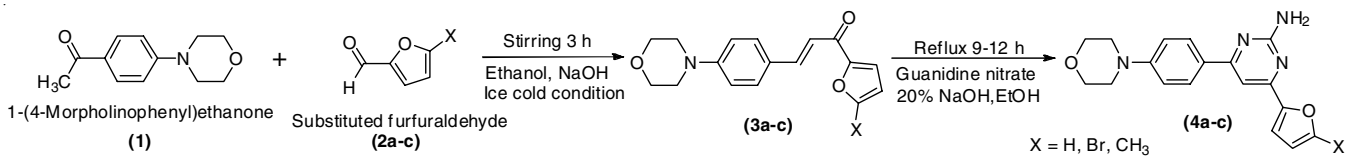
Reactions of morpholine chalcones (**3a-c**) with an appropriate amount of guanidine nitrate, ethanol, 20% of NaOH yielded 4-(furan-2-yl)-6-(morpholinophenyl)pyrimidine-2-amines are shown in **Scheme-I**. The synthesized compounds **4a-c** were elucidated in accordance with CHN and spectral analysis. The FT-IR spectrum explains that the synthesized compound **4a** shows that the characteristics absorption frequency at 3511 cm^{-1} due to the presence of NH_2 absorption of pyrimidine ring. The sharp absorption band appeared at 1598 cm^{-1} is due to the presence of C=N stretching frequency. A strong absorption at 1450 cm^{-1} is attributed to C-N stretching frequency. The absorption at in the range of 3038-2921 cm^{-1} is attributed to aromatic CH stretching vibration of morpholine ring. Similarly, a sharp peak with strong intensity around 1228 cm^{-1} found in all the compounds is ascribed to the C-O-C asymmetric vibrations of morpholine ring. The peaks due to C=C of the furan ring is observed as a sharp peak around 1450 cm^{-1}. A sharp peak appeared at 1118 cm^{-1} is assigned to the characteristic absorption of C-O stretching of furan ring. Other peaks appeared at in the finger print region of 819-645 cm^{-1} are due the stretching of aromatic ring stretching frequency.

In ^{1}H NMR, compound **4a** showed that the doublet at 3.87 ppm, which is assigned to $-O-(CH_2)_2$ proton of morpholine moiety. Similarly, the doublet signal appeared in the upfield chemical shift region at 3.27 ppm is assigned to $-N-(CH_2)_2$ of morpholine moiety. The singlet signal appeared in the downfield region of 6.16 ppm is unambiguously assigned to H-5 proton of pyrimidine moiety. A broad singlet appeared at 5.13 ppm is due to NH_2 proton of pyrimidine ring. Furthermore, the protons observed at 6.85and 6.96 ppm are due to the presence of H-3, H-4 &H-5. The multiplet present in the region of 7.08-8.02 ppm is assigned to aromatic protons. The ^{13}C NMR spectrum of compound **4a** showed that the ^{13}C resonance at 165.30 and 163.22 ppm are assigned to C=N of pyrimidine moiety. The ^{13}C resonance at 66.58 and 66.73 ppm is which assigned to $-O(CH_2)_2$ of morpholine moiety. The ^{13}C resonance at 47.57 and 48.35 ppm is apparently assigned to $-N(CH_2)_2$ of morpholine moiety. The ^{13}C resonance at in the down field region of 152.90 ppm is assigned to C-N of pyrimidine moiety. The ^{13}C resonance at 100.60 ppm is assigned to C-5 carbon of pyrimidine moiety. The ^{13}C resonance at in the most down field region of 156.61 ppm is assigned to C-2 carbon of furan ring. The signal at 108.69, 112.80 and 144.44 ppm is unambiguously assigned to C-3, C-4 and C-5 carbon of furan ring, respectively. The aromatic carbons appeared in the range of 113.32-130.87 ppm. From the above spectral characterization, the skeleton structure of the target compounds were confirmed.

Antimicrobial study: Novel 4-(furan-2-yl)-6-(morpholinophenyl)pyrimidine-2-amines (**4a-c**) were evaluated for their antibacterial activity by disc diffusion method against tested microbial strains. Compound **4a** shows excellent zone of inhibition against *S. pyogenes* and *E. coli* and also the good zone of inhibition against *S. aureus* and *P. aeruginosa* (Table-1). Compound **4b** shows excellent zone of inhibition against *E. coli* and *P. aeruginosa* and also good zone of inhibition against *S. aureus* and *S. pyogenes*, whereas compound **4c** exhibits good zone of inhibition against *S. aureus*, *S. pyogenes*, *E. coli* and *P. aeruginosa*. Among the synthesized compounds **4a-c**, compound **4a** exhibits best zone of inhibition when compared with ciprofloxacin as a standard (Table-1). In the antifungal studies, compound **4c** exhibits excellent zone of inhibition against *C. albicans* and also compounds **4a** and **4b** shows good zone of inhibition when compared with the clotrimazole as a standard (Table-1).

Computational study

Molecular docking study: Novel synthesized compounds (**4a-c**) have been subjected to *in silico* docking studies with 1UAG bacterial protein to ascertain the bacterial activity of the compounds and 1OQA breast cancer protein to carry the anticancer properties of the synthesized compounds. The docking results were compared with the standard drug ciprofloxacin for bacterial protein. All the compounds **4a-c** showed excellent binding score (-8.4 to -8.8 kcal) with bacterial protein,



Scheme-I: Prompted synthetic route for the compound **4a-c**

TABLE-1
ANTIMICROBIAL ACTIVITY SCREENING OF THE SYNTHESIZED COMPOUNDS **4a-c** AT 10 mg/mL

Entry	Bacterial strain				Fungal strain
	S. aureus	*S. pyogenes*	*E. coli*	*P. aeruginosa*	*C. albicans*
4a	23	21	22	19	15
4b	18	17	19	24	17
4c	19	15	13	16	21
Ciprofloxin/Clotrimazole	26	19	17	22	24

while the same standard was -7.7 kcal. Similarly, compounds **4a-c** were docked with the breast cancer protein gave the good docking score of -6.9 to -7.1 kcal. Compound **4a** has no H-bond relationship with the bacterial protein but have a hydrophobic interaction with amino residue ALA A: 329, which have the bond length of 3.78 Å. Compound **4b** have two hydrogen bond interactions with amino acid residue like LEU A: 299 and ASN A: 269, respectively and has the hydrogen bond interaction bond length of 3.07 Å and 2.95 Å. Similarly, compound **4c** docked with the same protein 1UAG have two hydrogen bond relationships with the same amino acid residues, respectively. Compounds **4b** and **4c** have no hydrophobic attraction with the bacterial proteins. All the synthesized compounds were also docked with the breast cancer protein 1OQA. Compound **4a** has two hydrogen bond interactions with the breast cancer protein with the amino acid residue ASP A: 98 and ILE A: 102, which have the bond length of 2.09 Å, 2.42 Å and 2.44 Å. Compounds **4b** and **4c** docked with the breast cancer protein have three hydrogen bond contracts with the amino acid residues of GLN A: 32, SER A: 32 and GLY A:1 and has the bond length of 2.41 Å,2.43 Å and 3.00 Å, respectively. Due to presence of the electronegativity groups at the 5th position of furan ring in compounds **4a** and **4b** give more binding affinity score when they have docked with proteins 1UAG and 1OQA. The docking predictions values of the synthesized compounds (**4a-c**) are given in Table-2, while the docking results of 2D and 3D images are represented in Table-3.

ADME study: The evaluation of the ADME properties of the synthesized 4-(furan-2-yl)-6-(morpholinophenyl)pyrimidine-2-amine derivatives (**4a-c**) were fulfilled by swissADME and Molinspiration online tools. The favourable outcome of the drug is set on not only by good effectiveness but also by an bearable ADME profile. In this investigation, the log $P_{o/w,}$ log S, MW, TPSA, drug-likeness, HBA, HBD, MRty, drug score and pharmacokinetics study of GI absorption, BBB, Glycoprotein subrate, cytochrome P450 family and sub family members and log K_p, Lipinski's violation, Ghose filter, Veber, Egan, Muegge and Bioavailability score, Pains, Breaks, Lead-likeness and synthetic accessability were evaluated. In addition, we also predicted the ADME predictions by Molinspiration software [38,39]. The percentage of absorption (% ABS) values were carried by the literature survey method [40].

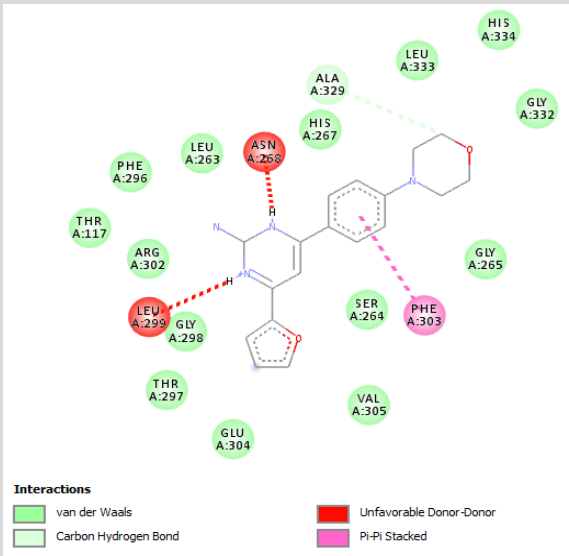
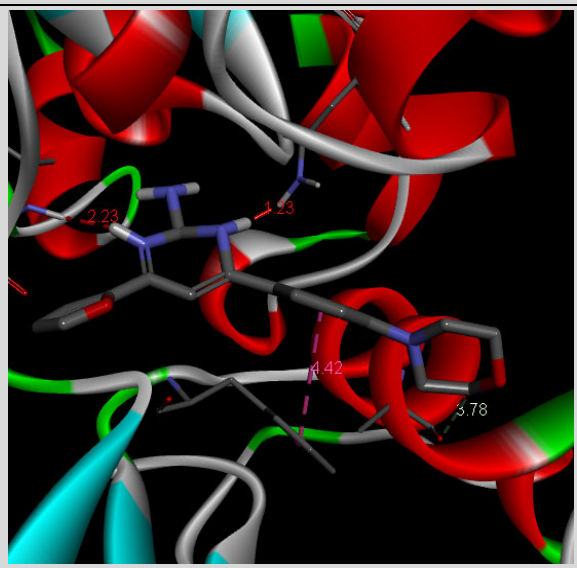
$$\text{ABS (\%)} = 109 - (0.345 \times \text{Topological polar surface area})$$

Compounds **4a-c** obeyed the Lipinski's rule of five and also these compounds excellent solubility (-2.94 to -4.02) and absorption values of 82.29. All the compounds having log P values were ranged from 2.15 to 2.66.The ADME prediction values of the synthesized compounds **4a-c** are given in Tables 4 and 5.

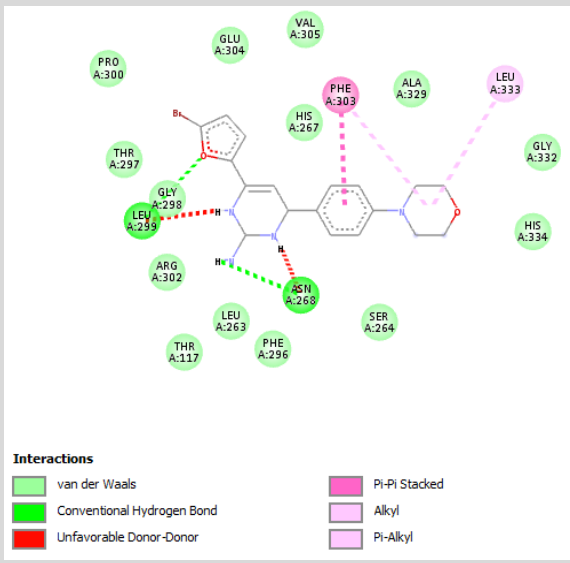
TABLE-2
DOCKING PREDICTIONS OF THE COMPOUNDS **4a-c** USING 1UAG AND 1OQA PROTEINS

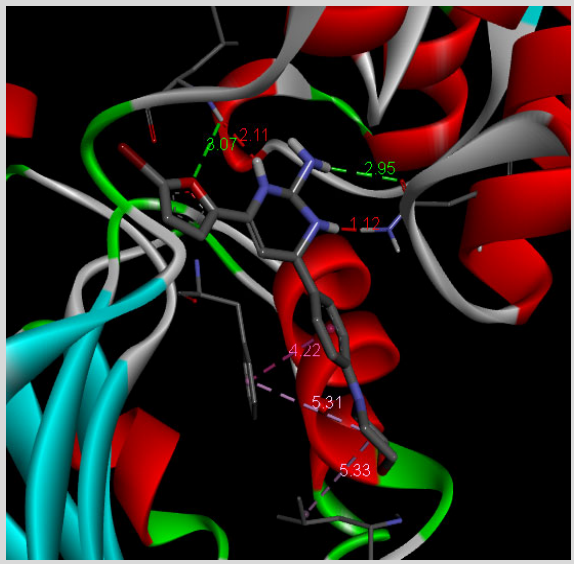
Compd.	Protein	Binding affinity (score/kcal)	Conventional hydrogen bond	Length of hydrogen bond (Å)	Hydrophobic interactions	Length of hydrophobic interaction bond (Å)
4a	1UAG	-8.4	–	–	ALA A: 329	3.78
4b	1UAG	-8.8	LEU A: 299, ASN A: 269	3.07, 2.95	–	–
4c	1UAG	-8.8	LEU A: 299, ASN A: 269	3.04,2.91	–	–
4a	1OQA	-6.9	ASP A: 98, ILE A: 102	2.09,2.42,2.44	–	–
4b	1OQA	-7.1	GLN A: 32, SER A: 37, GLY A: 1	2.41,2.43,3.00	–	–
4c	1OQA	-7.1	GLN A: 32, SER A: 37, GLY A: 1	2.41,2.43,3.00	–	–

TABLE-3
2D AND 3D IMAGES OF THE SYNTHESIZED COMPOUNDS **4a-c** USING 1UAG AND 1OQA PROTEINS

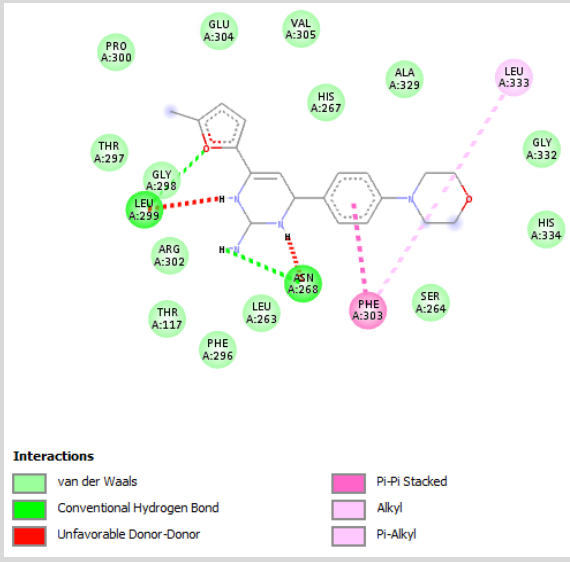
Compound	2D	3D
4a 1UAG protein		

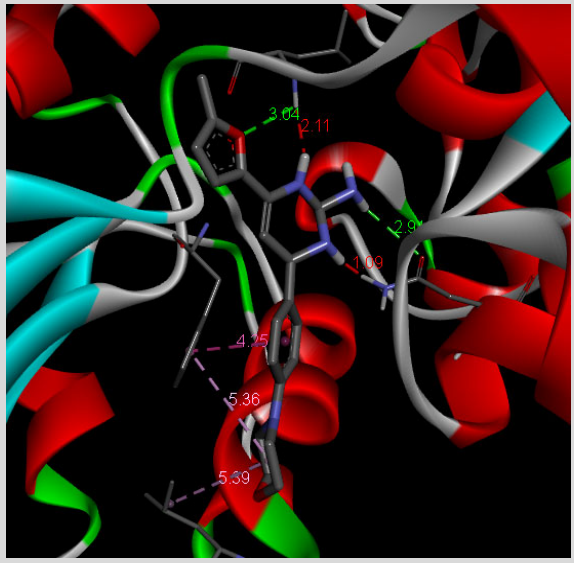
4b
1UAG
protein



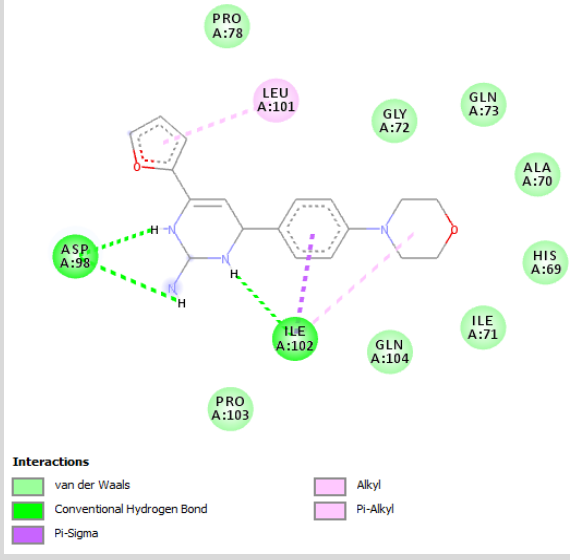


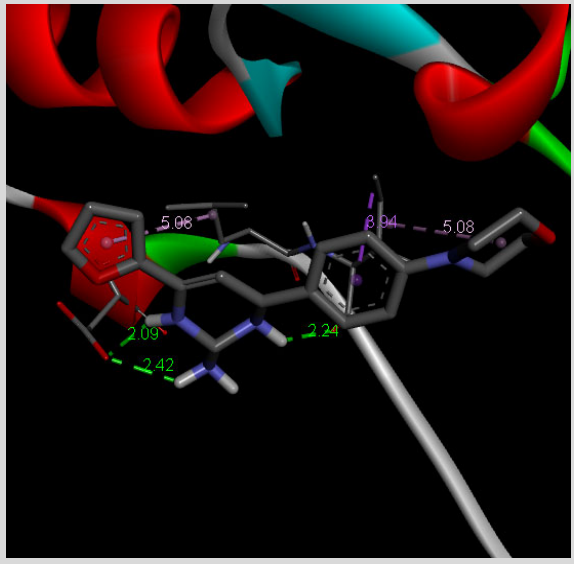
4c
1UAG
protein



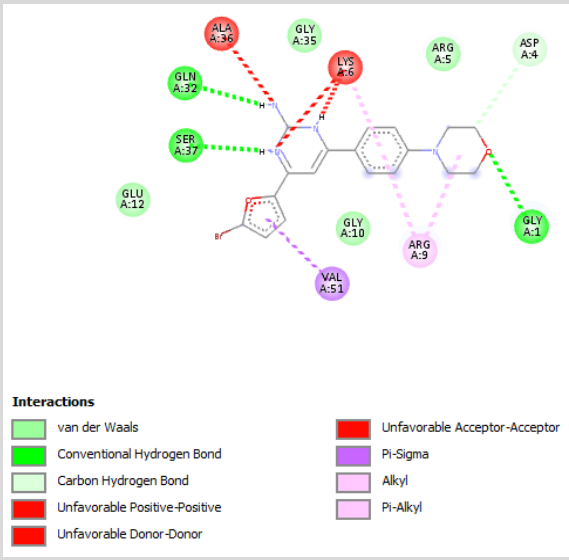


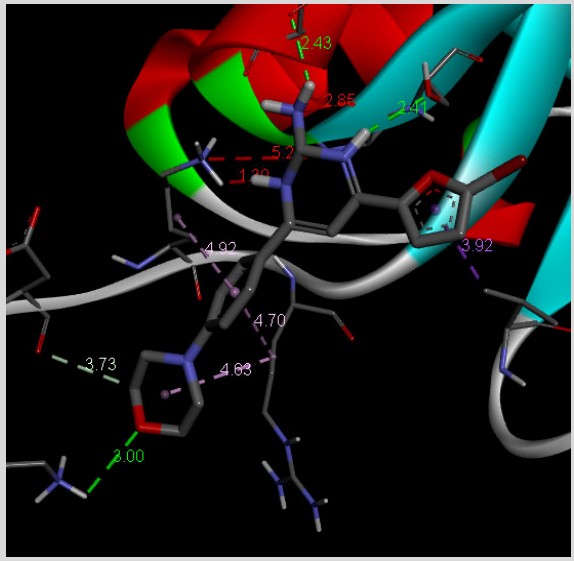
4a
1OQA
protein



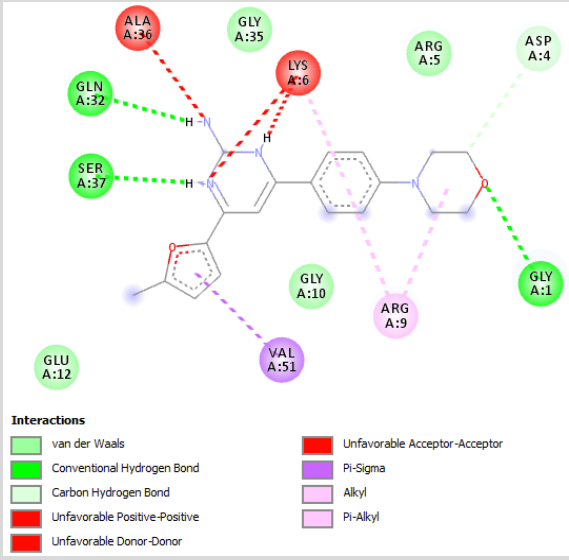


4b
1OQA
protein





4c
1OQA
protein



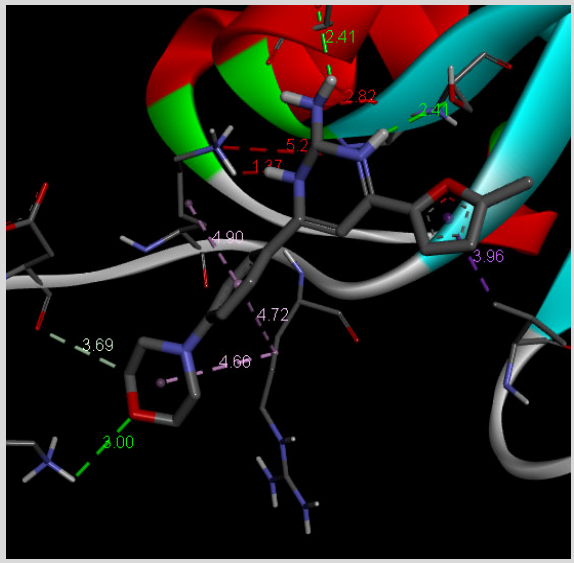


TABLE-4
ADME PROPERTIES OF THE SYNTHESIZED COMPOUNDS **4a-c** USING SWISS ADME

Compound	MW	log P o/w	*n*-OH	*n*-NHOH	MR	No, of violation	log S	TPSA (Å)	log K_p
4a	322.36	2.15	4	1	95.30	0	-2.94	77.41	-7.06
4b	405.26	2.66	4	1	103.83	0	-4.02	73.50	-7.07
4c	340.42	2.16	4	1	100.76	0	-3.31	73.50	-7.02

TABLE-5
ADME PROPERTIES OF THE SYNTHESIZED COMPOUNDS **4a-c** BY MOLINSPIRATION ONLINETOOL

Compound	% ABS	Milog P	TPSA	n-atoms	MW	N-OH	N-OHNH	n-violation	n-rotb	Volume
4a	82.29	2.47	77.42	24	322.37	6	2	0	3	289.54
4b	82.29	3.40	77.42	25	401.26	6	2	0	3	307.42
4c	82.29	2.69	77.42	25	336.39	6	2	0	3	306.10

Pharmacodynamics property: All the synthesized compounds **4a-c** have blood brain barrier permeability. Similarly, all compounds **4a-c** also exhibited the inhibition to cytochrome P450 isomers. The synthesized compounds **4a-c** have the skin permeability values in the acceptable range of -6.83 to -7.07 cm/s (Table-6). The drug-likeness carried depend on the important rules like Lipinski's, Ghose, veber, Egan, Muegge and bioavalability score. The Lipinski's rule of five states indicated that the absorption or permeation of a molecule is more probable when the molecular weight is below 500 g/mol, the values of log P is below five and the molecule has utmost five hyrogen donor and ten hydrogen acceptor. Ghose filter rule defines

drug-likeness restriction as follows: calculated log P values is present in the range from 2.15 to 2.66 and its molecular weight is also occur in the range of 322 and 401, the molar refractivity value appeared in the range 95 and 103 and also the total number of atoms present between 24 and 25. Veber rule states the drug-likeness limitations as rotatable bond count ≤ 10 and total polar surface area (TPSA) ≤ 140. All the compounds have the similar bioavailability score of 0.55. Screening of Lipinki's rule of five explained that all the synthesized compounds **4a-c** met the drug-likeness assesment. Nonetheless, the drug likeness screen with Ghose rule, Veber rule, Egan, Muegge rules, all the compounds **4a-c** met the creteria of this assesment.

Medicinal properties were also carried by Molinspiration online software. In this property, they have zero alert in PAINS and Brenk. In lead-likeness property, the compound **4b** and **4c** have one violation *i.e.*, MW > 350. The synthesized compounds **4a-c** have the synthetic accessibilty value which occured in the range of 3.00 to 3.97. Fig. 1 shows the scattering activity score of the most important drug categories compared with those of average drug-like molecules. The larger values of the score, the higher is also probability. So that the particular molecule will be active. The best drug-likenes score was found to be 0.14 (GCPR ligand), -0.28 (ion channel modular), -0.15 (kinase inhibitors), -0.22 (nuclear receptor ligand), -0.34 (protease

TABLE-6
PHARMACOKINETICS, DRUG LIKENESS AND MEDICINAL PROPERTIES CARRIED BY SWISS ADME ONLINE TOOL

Compound	**4a**	**4b**	**4c**
Pharmacokinetics properties			
GI absorption	High	High	High
BBB permeant	Yes	Yes	Yes
P-gp substrate	Yes	Yes	Yes
CYP1A2 inhibitor	Yes	No	No
CYP2C19 inhibitor	No	Yes	No
CYP2C9 inhibitor	Yes	No	No
CYP2D6 inhibitor	Yes	Yes	Yes
CYP3A4 inhibitor	Yes	Yes	Yes
Log kp (skin permiation) cm/s	-6.83	-7.07	-7.02
Drug likeness			
Lipinski	Yes, 0 violation	Yes, 0 violation	Yes, 0 violation
Ghose	Yes	Yes	Yes
Veber	Yes	Yes	Yes
Egan	Yes	Yes	Yes
Muegge	Yes	Yes	Yes
Bioavailability score	0.55	0.55	0.55
Medicinal properties			
PAINS	0 alert	0 alert	0 alert
Brenk	0 alert	0 alert	0 alert
Leadlikeness	Yes	No: 1 violation, MW > 350	No-1 violation, MW> 350
Synthetic accessibility	3.00	3.97	3.85

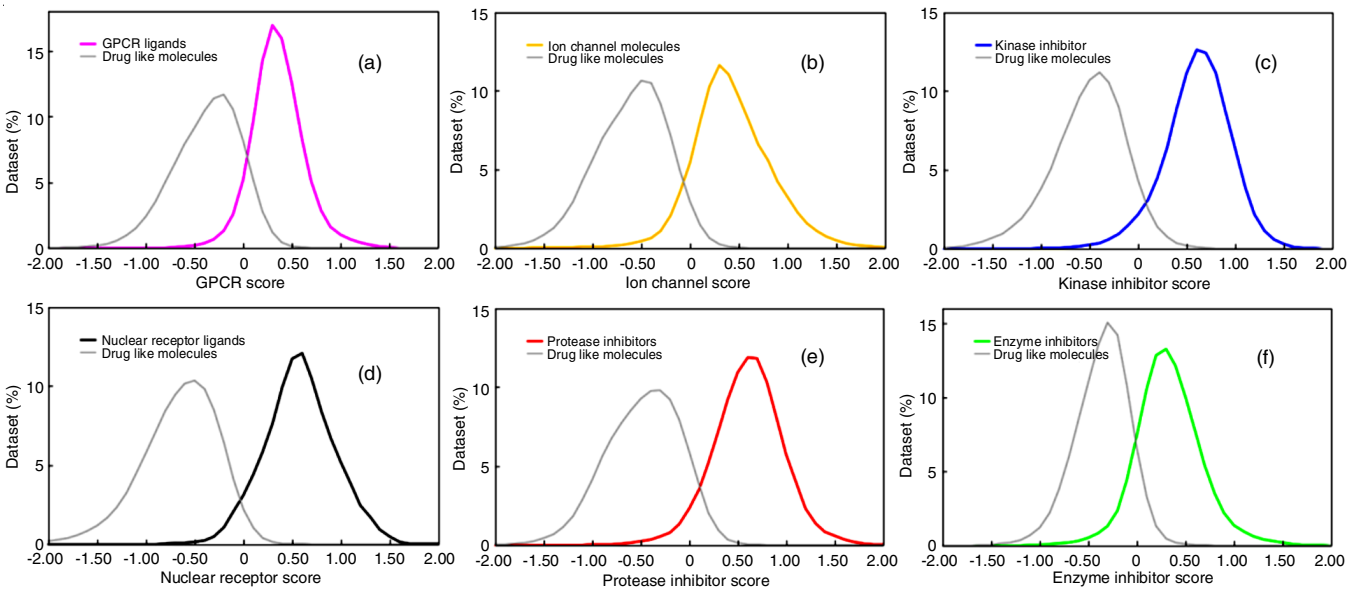


Fig. 1. Drug-likeness model score of synthesized compoud **4a**

TABLE-7
BIOACTIVITY SCORE OF THE SYNTHESIZED COMPOUNDS **4a-c** BY MOLINSPIRATION ONLINE TOOL

Compound	Glcoprotein coupled receptor ligand	Ion channel modulators	Kinase inhibitors	Nuclear receptor ligand	Protease inhibitors	Enzyme inhibitors
4a	0.14	-0.28	0.32	-0.22	-0.34	0.05
4b	0.11	-0.33	0.15	-0.65	-0.45	-0.13
4b	0.02	-0.37	0.26	-0.22	-0.33	-0.04
Ciprofloxacin	0.12	-0.04	-0.07	-0.19	-2.0	-0.28
Clotrimazole	0.17	0.30	0.14	-0.21	-0.13	0.42

inhibitors), 0.05 (enzyme inhibitors). These graphs proved that molinsipration virtual screening methodology was effectively seperates the molecules with good drug-likeness studies were carried out from inactive structures.

Bioavalability score: The ADME prediction results explained that all the synthesized compounds **4a-c** possess the physical and chemical properties present within the bearable creteria. The 'online test' of the bioactivity scores of the synthesized compounds were determined by Molinspiration software and the values are shown in Table-7. The bioactivity scores of the GCPR ligand appeared in the acceptable range between 0.02 and 0.14, the ion channel moduators present in the values between -0.28 and -0.37, while the kinase inhibitors appears between 0.15 and 0.32. Nuclear receptor ligand present between -0.22 and -0.65, whereas the protease inhibitors appears in the range between -0.33 and -0.45 and also the other enzyme inhibitors where present at between -0.04 and 0.05. From the values the synthesized compounds **4a-c** represented that the likelihood of excellent to good activity towards GCPR ligand, ion channel modulator, kinase inhibitors, nuclear receptor ligand, protease inhibitors and enzymes inhibitors and there values are contrast with ciprofloxacin and clotrimazole standard drug [41].

Conclusion

A new and efficient synthetic route for the some amino pyrimidine derivatives were accomplished. The structures of the newly synthesized compounds were elucidated on the basis of elemental analysis and spectral analysis data. The newly synthesized compounds were studied for their antimicrobial evaluation against bacterial strains as well as fungal stains. Compound **4a** showed excellent zone of inhibition against *S. aureus* and *S. pyogenes*, when contrast with the standard drug. Similarly, compound **4c** exhibited good zone of inhibition against the fungal stain *C. albicans* due to the presence of the substituted methyl group in the fifth position of the furan ring. The molecular docking studies were carried by proteins 1UAG and 1OQA and all the compounds showed good binding affinity scores. All the compounds exhibited good % ABS value of 82.29 and also have the better TPSA values.

CONFLICT OF INTEREST

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

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