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Research Article

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NOVEL PYRIMIDINE LINKED INDOLES WITH B-LACTAMS AND [1,2,4]TRIAZOLO[4,3-C]MOIETIES

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ABSTRACT

Objectives: To synthesize a variety of Pyrimidine analogs 3, 5, 6, 8(a-e), 9(a-e) and their anti fungal activity was determined. **Methods:** Using 2,4 di chloro Pyrimidine and hydrazine hydrate ,new compounds are established on the basis of FT-IR,^{1}H NMR, and mass spectral data. Anti fungal activity was done by disc diffusion method. **Results:** All the compounds were synthesized in good yield. Among the new compounds 9a,9b are found to most potent anti fungal activity. **Conclusions:** The results obtained justify the usage of these compounds from their promising antibacterial activity. Therefore, the nature of group is very important for antibacterial activity in disc diffusion model.

Keywords: 2,4 di chloro Pyrimidine, triazole, Indole, anti bacterial and anti fungal activity.

INTRODUCTION

Heterocyclic structures, in particular azoles and azines, form the basis of many pharmaceutical and agrochemical products. Publications devoted to the chemistry of azoles in recent decade refer to the synthesis of 1,2,4-triazoles, 1,3,4-oxa(thia)diazoles and thiazolidines. Different approaches have been reported for the preparation of such heterocycles[1,2]. Their significance deals with a broad spectrum of biological activity and technological interest. The efficacy of clinical use of antiviral, anticancer and antifungal drugs (*Ribavirin*, *Anastrozole*, *Fluconazole*, *Voriconazole* etc.) led to intense investigation of 1,2,4-triazole derivatives. 1,2,4-Triazole containing molecules have increasing interest as anticancer[3],fungicidal, antimicrobial[4], antitubercular[5] or anti-inflammatory[6] agents. They also are significant in agrochemical industry as plant protecting materials[7].

Literature survey has revealed the importance of pyrimidine derivatives and antimicrobial agent[8], which are found to be associated with variety of biological activities such as insecticidal, antimicrobial, antiviral etc.

pyrimidine derivatives[9-15]

Heterocyclic compounds are those cyclic compounds in which one or more of the ring carbons are replaced by another atom. The non-carbon atoms in such rings are referred to as ‘‘heteroatoms.’’ Such bicyclic heterocyclic compounds containing pyrrole ring with benzene ring fused to α,β-position are known as Indoles. Indole has a benzene ring and pyrrole ring sharing one double bond. It is a heterocyclic system with 10 electrons from four double bonds and the lone pair from the nitrogen atom. Indole is an important heterocyclic system because it is built into proteins in the form of amino acid tryptophan,

because it is the basis of drugs like indomethacin and because it provides the skeleton of indole alkaloids—biologicallyactive compounds from plants including strychnine and LSD.

The incorporation of indole nucleus, a biologically accepted pharmacophore in medicinal compounds.

Importance of INDOLE derivatives in medicinal chemistry		
S.No.	**Indole derivative**	**Biological activity**
1.	Indomethacin	Anti-inflammatory & analgesic
2.	Fendosal	Analgesic
3.	Etodolac	Antiarthritis
4.	umatriptan	Antimigraine
5.	Besipirdine	Nootropic
6.	Adrenochrome	Hemostatic

Along with the varied biological activities of pyrimidine, other heterocycles fused with pyrimidines play an essential rolein several biological processes and have a considerable chemical and pharmacological importance. Triazole in association with the pyrimidine has shown good antifungal (Singh et al., 2004) and hypoglycemic action (Agarwal, 1991). [1,2,4]Triazole fused pyrimidine exhibit good antimicrobial activity(Fathy et al., 2004), antitumour activity (Swelam, 1998), analgesic,anti-inflammatory and ulcerogenic activities (Hendet al., 2008).

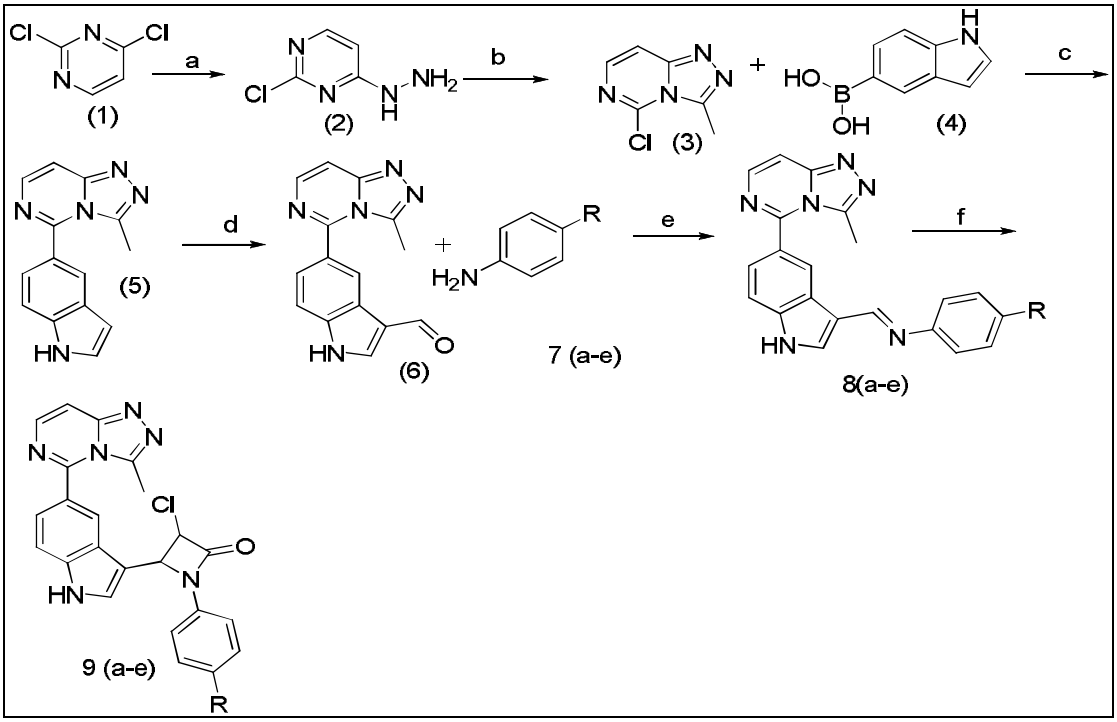
In the view of the facts mentioned above and as part of ourinitial efforts to discover potentially active new agents. Hence, we have synthesized some new Pyrimidine its triazole fused derivatives. The novel derivatives were characterized by spectral data and elemental analysis and thesecompounds were used for their Antimicrobial evaluation screening.

2. MATERIALS AND METHODS

2.1 Materials and physical measurements

Melting points were measured by a Stuart Scientific melting point apparatus in open capillaries and are uncorrected. Infrared spectra (KBr discs) were recorded on a Bruker Alpha (FTIR) Spectrometer. 1H-NMR spectra were recorded on a Bruker spectrometer operating at 400 MHz using DMSO-d6 and CDCl3 as a solvent with TMS as an internal standard. Mass spectra was recorded on an agilent-1100 periods LC-MSD. Elemental analysis was performed using a (EURO EA 3000 instrument). Acme silica gel-G and Merck silica gel (100 to 200, 60 to 120 meshes) were used for analytical TLC and Column chromatography respectively. All other analytical grade chemicals and solvents were obtained from commercial sources and used as received standard procedure.

Scheme:



Reagents & Reaction conditions: (a) Hydrazinehydrate,methanol,TEA,RT, 1hr**(b)**Aceticanhydride,reflux,4hrs(**c)**Pd(pph_3)$_4$,Cs_2CO_3,1,4Dioxane,water, reflux,2 hrs **(d)**DMF,$POCl_3$,80^{0}c,2hrs**(e)**Ethanol,acetic acid,reflux,3 hrs **(f)**Chloro acetylchloride,TEA,RT,2 hrs

The title compounds were synthesised in six sequential steps using different reagents and reaction conditions the 9(a-c) were obtained in moderate yields. The structure were established by spectral (IR, ^{1}H-NMR, ^{13}C-NMR and mass) and analytical data.

Compound	9(a)	9(b)	9(c)	9(d)	9(e)
R	-CF_3	-F	-OCH_3	-CN	-NO_2

EXPERIMENTAL Section

Synthesis of 2-chloro-4-0hydrazinylpyrimidine (2)

A mixture of 2,4 di chloro Pyrimidine(1) (0.01mol) in methanol was taken and cooled to 0-5^0 c in an ice bath,tri ethyl amine(0.01 mol)was added to the cold reaction mixture and then hydrazine hydrate (0.012 mol) was added slowly at 5-10^0 c. The reaction mass was allowed to stir at room temperature for 1 hr.The solid thus obtained was filtered ,washed with chilled water and dried to afford compound(2),pale yellow solid. Melting point 140^{0}c-142^{0}c.

^{1}H NMR(DMSO-d6,ppm)

δ 7.5(1H,d,j=8HZ),6(1H,d,J=8HZ),2(2H,S,broad),3.9(1H,S,broad).

IR (KBr, cm-1)

700(C-Cl),3450(-NH),3350 and 3400(Two peaks indicates-NH_2), 1080(C-N),1600(N-H bending),3100(aromatic C-H),1500(aromatic C=C).

^{13}C NMR(DMSO-d6,ppm)

155,160,105,170(4 Aromatic carbons)

Synthesis of 5-chloro-3-methyl-[1,2,4]triazolo[4,3-c]Pyrimidine(3)

A mixture of compound2 (0.01 mol) and acetic anhydride(10 ml) was heated under reflux for 4 hrs.The reaction mixture was concentrated under reduced pressure. The solid obtained was filtered off,washed with water,dried and crystallized from methanol to give the compound 3 (white solid).
Yield:70%,M.p.:180-182 ^{0}c
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),722(C-Cl).

^{1}H NMR(DMSO-d6,ppm)

δ 8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S).

^{13}C NMR(DMSO-d6,ppm)

110,160,150,162,140,24

Synthesis of 5-(1H-indol-5-yl)-3-methyl-[1,2,4]triazolo[4,3-c]Pyrimidine(5)

To a solution of the compound(4) in anhydrous 1,4-dioxane (30 volumes)in a sealed tube was introduced Indole 5- boronic acid (1.5 equiv) and finely ground potassium carbonate(2.0 equiv). The solution was degassed (N_2 bubbling) for 5 min, $Pd(OAc)_2$ (5 mol percent) and di-tert-butylphosphinoferrocene (5 mol percent) introduced and degassing continued for a further 5 min. The tube was sealed under nitrogen and heated with rapid stirring at 100 °C for 5 h. After cooling, the reaction mixture was filtered in vacuum through a celite pad and the precipitated material washed with 1,4-dioxane. The combined filtrates were evaporated and purified by flash column chromatography (neat hexane to 1:1 hexane/EtOAc gradient containing 2.5percent by volume Et_3N) to furnish the title compound(5).
Yield:70%,M.p.:160-162 ^{0}c.

IR(KBr,cm^{-1})

2937(C-H),1635(C=N),1463(C=C),1372(C-N).

^{1}H NMR(DMSO-d6,ppm)

δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(5H,m),10(1H,s,-N**H** Proton), 2.4(3H,s).

^{13}C NMR(DMSO-d6,ppm)
110-165(13 Aromatic carbons),24(methyl carbon).

Synthesis of 5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indole-3-carbaldehyde(6)
Introduce 8.5 mL (110 mmol) of dry Dimethylformamide,Cool the dimethylformamide and add over 30 minutes 2.61 mL (28 mmol) of phosphoryl chloride($POCl_3$),Then add, over 40 minutes, the solution of 3 g (25.5 mmol) of compound(5) in 5 mL of anhydrous dimethylformamide, making sure that the temperature does not rise above 10° C.Stir the mixture for 45 minutes at 10° C. then for 40 minutes at 35° C.Add 10 g of crushed ice, stir the compact mixture vigorously and add a further 10 g of crushed ice. Continue the stirring and add progressively, by a dropping funnel, a solution of 11.3 g (282 mmol) of sodium hydroxide in 30 mL of water, slowly at first, then more rapidly, maintaining a good level of stirring.
Then bring the solution to the boil for 15 minutes, recover by filtration and wash the isolated solid several times with water.
Yield: 98 percent Melting point: 124-125° C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),1690(C=O).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(5H,m),10(1H,s,-N**H** Proton),9.6(1H,s,aldehyde proton –**H**C=O),2.4(3H,s).

^{13}C NMR(DMSO-d6,ppm)
110-165(13 Aromatic carbons),24(methyl carbon),190(Carbonyl carbon in aldehyde gp).

Synthesis of -N-((5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)methylene)-4-(trifluoromethyl/Fluoro/Methoxy/cyno/Nitro)aniline(8 a-e)
Equimolar mixture of various substituted aniline (0.01 mol) and substituted Indole 3-carboldehyde(0.01 mol), was refluxed in ethanol with few drops of glacial acetic acid up to 10 hrs,The solvent was removed and the crude product thus obtained was crystallized in ethanol.

N-((5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)methylene)-4-(trifluoromethyl)aniline(8a)
Yield: 80% Melting point: 144-146^{0} C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),1200(C-F).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
8.6(1H,S),7.3(1H,d,j=8HZ),7.7(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons),24(methyl carbon),160(imine carbon), 123(-**C**F_3).

4-fluoro-N-((5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl) methylene) aniline(8b)
Yield: 70% Melting point: 134-136^{0} C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),1200(C-F).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
8.6(1H,S),7.3(1H,d,j=8HZ),7.2(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons),24(methyl carbon),160(imine carbon).

4-methoxy-N-((5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)methylene) aniline(8c)
Yield: 78% Melting point: 184-186^{0} C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),11009C-O).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
8.6(1H,S),7.3(1H,d,j=8HZ),7.0(1H,d,j=8HZ),3.8(3H,S).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon), 160(imine carbon),55(methoxy carbon).

4-((5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)methyleneamino) benzonitrile(8d)
Yield: 68% Melting point: 204-206^0 C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),2200(-CN Group).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
2.4(3H,s),8.6(1H,S),7.3(1H,d,j=8HZ),7.7(1H,d,j=8HZ)
7.4 (1H,S),7.3(1H,d,j=8HZ),7.6(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm):
110-165(19 Aromatic carbons), 24(methyl carbon), 160(imine carbon),118(Nitrie gp carbon).

N-((5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)methylene)-4-nitro aniline(8e)
^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton), 2.4(3H,s),8.6(1H,S),
7.0(1H,d,j=8HZ),8.1(1H,d,j=8HZ),

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon), 160(imine carbon).

Synthesis of 3-chloro-4-(5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)-1-(4-(trifluoromethyl/Fluoro/methoxy/Cyno/Nitro)phenyl)azetidin-2-one (9a-e)
Monochloroacetyl chloride (0.01mol) was added drop wise to schiff's base 8(a-c)(0.01mol) and triethyl amine (0.02mol) in dioxane (25ml) at room temperature. The mixture was stirred for 8h and left at room temperature for 3 days. The contents were poured on crushed ice. The product thus formed was filtered and washed with sodium bicarbonate solution. The dried product was recrystalised with absolute alcohol.

3-chloro-4-(5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)-1-(4-(trifluoromethyl)phenyl)azetidin-2-one (9a)
Yield: 80% Melting point: 144-146^0 C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),1200(C-F),1740(C=O).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
7.0(1H,d,j=8HZ),7.7(1H,d,j=8HZ), 5.1(1H,d,j=8HZ),5.4(1H,d,j=8HZ)

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon),124(-**C**F$_3$),175(Carbonyl carbon in 4 membered ring), 63, 65(4 membered ring carbons).

Chemical Formula
$C_{24}H_{16}ClF_3N_6O$

Molecular Weight
496.87.

MS
m/z: 496.10 (100.0%), 498.10 (32.6%).

Elemental Analysis
Calculated
C, 58.01; H, 3.25N, 16.91.

Found
C, 58.00; H, 3.20 N, 16.89.

3-chloro-1-(4-fluorophenyl)-4-(5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)azetidin-2-one (9b)
Yield: 78% Melting point: 149-151^0 C.
IR(KBr,cm^{-1}):2937(C-H),1635(C=N),1463(C=C),1372(C-N),1200(C-F),1740(C=O).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
7.3(1H,d,j=8HZ),7.2(1H,d,j=8HZ), 5.1(1H,d,j=8HZ),5.4(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon),175(Carbonyl carbon in 4 membered ring), 63,65(4 membered ring carbons).

Chemical Formula
$C_{23}H_{16}ClFN_6O$.

Molecular Weight
446.86.

MS
m/z: 446.11 (100.0%), 448.10 (32.0%).

Elemental Analysis
Calculated: C, 61.82; H, 3.61; N, 18.81.
Found: C, 61.80; H, 3.60; N, 18.80.

3-chloro-1-(4-methoxyphenyl)-4-(5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)azetidin-2-one(9c)
Yield: 68% Melting point: 189-191^0 C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
7.5(1H,d,j=8HZ),7.7(1H,d,j=8HZ), 5.1(1H,d,j=8HZ),5.4(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon),175(Carbonyl carbon in 4 membered ring),63,65(4 membered ring carbons),55(methoxy carbon).

Chemical Formula
$C_{24}H_{19}ClN_6O_2$.

Molecular Weight
458.90.

MS
m/z: 458.13 (100.0%), 460.12 (32.0%).

Elemental Analysis
Calculated: C, 62.81; H, 4.17N, 18.31 .
Found: C, 62.80; H, 4.15 N, 18.30.

4-(3-chloro-2-(5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)-4-oxoazetidin-1-yl)benzonitrile(9d)
Yield: 48% Melting point: 129-131^0 C.
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N), 1740(C=O),1150(C-O),2200(-CN).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10(1H,s,-N**H** Proton),
7.5(1H,d,j=8HZ),7.7(1H,d,j=8HZ), 5.1(1H,d,j=8HZ),5.4(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon175 (Carbonyl carbon in 4 membered ring), 63, 65(4 membered ring carbons), 118(Nitrile carbon).

Chemical Formula
$C_{24}H_{16}ClN_7O$.

Molecular Weight
453.88.

MS
m/z: 453.11 (100.0%), 455.11 (32.8%).

Elemental Analysis
Calculated: C, 63.51; H, 3.55; N, 21.60
Found: C, 63.50; H, 3.53; N, 21.59.

3-chloro-4-(5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indol-3-yl)-1-(4-nitro phenyl)azetidin-2-one(9e)
Yield: 57% Melting point: 109-111^0 C
IR(KBr,cm^{-1}): 2937(C-H),1635(C=N),1463(C=C),1372(C-N),
1740(C=O),1150(C-O),1550,1360(N-O Stretch).

^{1}H NMR(DMSO-d6,ppm)
δ8.4(1H,d,J=8HZ),7(1H,d,J=HZ),2.5(3H,S),6.5-7.8(4H,m),10 (1H,s,-N**H** Proton), 6.8(1H,d,j=8HZ),8.3 (1H,d,j=8HZ), 5.1(1H,d,j=8HZ),5.4(1H,d,j=8HZ).

^{13}C NMR(DMSO-d6,ppm)
110-165(19 Aromatic carbons), 24(methyl carbon175 (Carbonyl carbon in 4 membered ring), 63, 65(4 membered ring carbons).

Chemical Formula
$C_{23}H_{16}ClN_7O_3$.

MS
m/z: 473.10 (100.0%), 475.10 (33.2%).

Elemental Analysis
Calculated: C, 58.30; H, 3.40; N, 20.69
Found: C, 58.28; H, 3.38,N, 20.67.

Antimicrobial evaluation
Representative samples were screened for their antimicrobial and antifungal activity against gramnegative bacteria, E coli and P aeruginosa and gram-positive bacteria, S aureus, and C diphtheriae using disc diffusion method[16,17] The zone of inhibition was measured in mm and the activity was compared with standard drug. The results of antibacterial screening studies are reported in Table 2.

Table 2: Antibacterial and Antifungal data for the newly synthesized compounds 9(a-e)

compound	Antibacterial data in MIC(µg/ml)				Antifungal data in MIC (µg/ml)	
	Gram +ve Bacteria		Gram -ve Bacteria		A.niger	A.fumigatus
	S. aureus	B. cereus	P. aeruginosa	E.coli	-	-
9a	14	18	18	18	15	14
9b	13	16	18	14	13	13
9c	8	11	11	10	12	14
9d	11	8	12	12	12	13
9e	12	10	14	12	11	12
Ampicillin trihydrate	26	28	24	21	27	25
DMSO	00	00	00	00	00	00

* Diameter of the disc was 6 mm, concentration of the compounds taken was about 100 µg/mL.

RESULTS AND DISCUSSION

2-chloro-4-0hydrazinylpyrimidine(2) was synthesised according to the reported procedure[18].The reaction of 2-chloro-4-hydrazinylpyrimidine(2) which was reacted with acetic anhydride at reflux condition as per the reported procedure[19] to afford 5-chloro-3-methyl-[1,2,4]triazolo[4,3-c]Pyrimidine(3) .Compound (3) which was reacted with Indole 5- boronic acid in presence of Pd catalyst as per the reported procedure[20] to afford5-(1H-indol-5-yl)-3-methyl-[1,2,4]triazolo[4,3-c]Pyrimidine(5) which was reacted with $POCl_3$ and DMF to give 5-(3-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-5-yl)-1H-indole-3-carbaldehyde(6) as per the reported procedure[21], which was reacted with para substituted benzaldehydes to afford Schiff bases 8(a-e) as per the reported procedure[22],which was reacted with chloro acetyl chloride to give Title compounds 9(a-e) as per the reported procedure[23] with good yields.
Further, the representative compounds were screened for their antimicrobial activity against gram negative as well as gram positive bacteria, which shows convincing activity.

CONCLUSION

IN conclusion, a series of new Pyrimidine analogs 3, 5,6,8(a-e),9(a-e) were synthesized in good yield, characterized by different spectral studies and their biological activity evaluated.various derivatives of Pyrimidine showed potent antifungal activity,like compounds with electron withdrawing groups. Among the synthesized compounds 9a ,9b,9e showed excellent antifungal activity.

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