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# Synthesis and characterization of pyrimidine bearing 1,2,4-triazole derivatives and their potential antibacterial action

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**ABSTRACT**

*A series of pyrimidine bearing 1,2,4-triazole derivatives have been synthesized and evaluated for antibacterial activity. All the structures of the newly synthesized compounds have been supported by IR, $^{1}$H-NMR, $^{13}$C-NMR, GC-MS and CHN analysis. Most of the compounds have shown promising antibacterial activity when compared with the standard drug ciprofloxacin.*

**Key words**: Pyrimidine, triazole, carbothioamide, thiosemicarbazide, antibacterial activity.

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## INTRODUCTION

Literature survey has revealed the importance of pyrimidine derivatives and antimicrobial agent[1], which are found to be associated with variety of biological activities such as insecticidal, antimicrobial, antiviral etc, pyrimidine derivatives[2-8] are powerful C-C bond formation process has wide applications for the preparation of diverse aminoalkyl derivatives. It involves the condensation of a compound capable of supplying one or more active hydrogen atom with aldehyde and primary or secondary amine. Mannich bases are physiologically reactive because of the basic function rendering the molecule soluble in aqueous solvent when it is transformed into ammonium salt. Several medicinally useful mannich bases have been reviewed by Tromontini and Angiolini [9]. Besides this, considerable work has been reported on synthesis and pharmacological activities of various mannich bases for analogies, antispasmodic, anesthetic and antimalarial as well as intermediates in drug synthesis. Antiviral properties of certain thiourea and urea derivatives have been reported in which the antiviral effect is attributed to the presence of an intact NH-(C=S)-NH and NH-(C=O)-NH grouping[10]. In this direction the synthesis and pharmacological study of mannich bases of 3-and 5-mercapto derivatives of 1,2,4-triazole have been reported in literature[11-16]. Further, pyrimidine, fused heterocyclic pyrimidine derivatives and dihydropyrimidones are well known for their potential biological activity such as antiviral, antitumor, antimicrobial fungicide, algaecide and as antibiotics[17-22]. Moreover the presences of different interacted functional groups determine their great synthetic potential.

In continuation of this work, herein is reported that the synthesis and *in vitro* study of antibacterial activity of heterocyclic N-mannich bases of 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-phenylpyrimidin-2(1H)-one**(3)** against *Pseudomonas aeruginosa (Gram –ve), Staphylococcus aureus(Gram +ve) and Escherichia coli (Gram –ve).* Ciprofloxacin was used as standard drug. For this purpose, heterocyclic precursors DHPMs (1a-j) were synthesized by Biginelli reaction of aromatic aldehydes, ethylacetoacetate and thiourea according to the

literature procedure. Subsequently, these DHPMs were used to synthesis compounds (2a-j). All the synthesised compounds were characterized by using elemental analysis, mass spectras, $H^1$& $C^{13}$-NMR spectral studies.

## MATERIALS AND METHODS

Melting points were determined using open capillary method and are uncorrected. The compounds were checked for homogeneity by TLC on silicagel-G. The IR spectra were recorded on FT-IR Thermo Nicolet Avatar 370 spectrophotometer using KBr disc method. The $^1$H-NMR and $^{13}$C-NMR were recorded on Bruker Avance III 400 MHz – FTNMR spectrophotometer using DMSO-$d_6$. Elemental analyses were recorded on Elemental Vario EL III. The mass spectrums were recorded on Joel GC-mate spectrometer. All compounds gave satisfactory micro analytical results. Pyrimidine (**1)** was prepared by reported method.

**General Procedure**

**Synthesis of 5-(Carbothioamide)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H)-one2a.**

General procedure for the synthesis of compounds (2a-j), an equimolar mixture of compound **1** (0.01 mole) and thiosemicarbazide (0.01 mole) in acetone was refluxed for 10-12hrs and allowed to cool and yellow solid was recrystallized from alcohol. Melting point of the compound is $140^0$C yield 85%.

$H^1$-NMR (DMSO-$d_6$) – **δ** 2.251( s, 3H, $CH_3$), 5.152(J= 3.2Hz, d,1H, CH), 6.501 (s, 2H, $NH_2$), 7.213 – 7.336 (m,5H, Ar-H), 7.702 (J= 2.8Hz, d, 1H, NH), 8.175 (J= 6.4Hz, d, 2H, NHx2), 9.149 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) - **δ** 17.72, 59.17, 99.33, 126.21, 127.23, 128.34, 148.25, 151.71, 152.16, 165.33, 178.40. FT-IR($cm^{-1}$) -3365, 3241(NH), 3079 (Ar-H), 2978(CH),1724 (C=O),1598 (C=N),1385(C-N),1219(C=S),1089(N-N). GCMS: (m/z)[305 $M^+$].

**Synthesis of 5-(Carbothioamide)-4-(4-chlorophenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-one 2b.**

$H^1$-NMR (DMSO-$d_6$) **δ** -2.251 ( s, 3H, $CH_3$), 5.146 (J= 3.6Hz, d, 1H, CH), 6.530 (s, 2H, $NH_2$), 7.239 – 7.260 (dd, 2H, Ar-H), 7.377-7.399 (dd, 2H,Ar-H), 7.733 (J= 1.2Hz, d, 1H, NH), 8.096 (J= 2Hz, d, 2H, NHx2), 9.204 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** -17.75, 59.22, 98.87, 128.15, 128.34, 131.74, 143.74, 148.64, 151.92, 165.18, 178.43. FT-IR($cm^{-1}$)-3376, 3240 (NH), 3029 (Ar-H), 2978 (CH), 1724 (C=O), 1597 (C=N), 1340 (C-N), 1220 (C=S), 1090 (N-N). GCMS: (m/z)[339 $M^+$].

**Synthesis of 5-(Carbothioamide)-4-(4-(dimethylamino)phenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-one 2c.**

$H^1$-NMR (DMSO-$d_6$) – **δ** 2.226 ( s, 3H, $CH_3$), 2.846 (s, 6H, $N(CH_3)_2$), 5.5036(J= 3.2Hz, d, 1H, CH), 6.130 (s, 2H, $NH_2$), 6.650 (J= 8.8Hz, d, 2H, Ar-H), 7.036 (J= 8.8Hz, d, 2H, Ar-H) 7.534 (J= 2.8Hz, d, 2H, NHx2), 9.036 (J= 1.2Hz, d, 1H, NH), 9.866 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) –**δ** 17.67, 53.29, 59.06, 99.93, 112.20, 126.85, 132.61, 149.73, 151.27, 165.46, 178.43. FT-IR($cm^{-1}$)- 3365, 3241(NH), 3053 (Ar-H), 2978 (CH), 1724 (C=O), 1598 (C=N), 1340 (C-N), 1219 (C=S), 1089 (N-N). GCMS: (m/z)[349 $M^+$].

**Synthesis of 5-(Carbothioamide)-4-(3-nitrophenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-one 2d.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.276( s, 3H, $CH_3$), 5.309 (J= 4Hz, d, 1H, CH), 6.970 (s, 2H, $NH_2$), 7.656-7.760 (m, 4H, Ar-H), 7.826 (J= 3.7Hz, d, 2H, NHx2), 9.345 (J= 2.4Hz, d, 1H, NH), 9.872 (s,1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.81, 58.61, 98.35, 129.61, 130.19, 132.95, 147.65, 147.73, 149.36, 151.62, 151.73, 165.04, 178.44. FT-IR($cm^{-1}$)- 3377, 3239 (NH), 3029 (Ar-H), 2977 (CH), 1719 (C=O), 1561 (C=N), 1365 (C-N), 1219 (C=S), 1091 (N-N). GCMS: (m/z)[350 $M^+$].

**Synthesis of 5-(Carbothioamide)-4-(4-hydroxyphenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-one 2e.**

$H^1$-NMR (DMSO-$d_6$) –**δ** 2.233 ( s, 3H, $CH_3$), 5.049(J= 3.2Hz, d, 1H, CH), 6.176 (s, 2H, $NH_2$), 6.676-6.698 (dd, 2H, Ar-H), 7.019-7.040 (dd, 2H,Ar-H), 7.572 (J= 2.4Hz, d, 2H, NHx2), 7.956 (s, 1H, OH), 9.065 (J= 1.2Hz, d, 1H, NH), 9.868 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) –**δ** 17.69, 59.07, 99.80, 114.96, 127.37, 135.40, 151.66, 152.19, 156.50, 165.39, 178.43. FT-IR($cm^{-1}$)- 3515 (OH), 3377, 3234(NH), 2997 (Ar-H), 2904 (CH), 1684 (C=O), 1596 (C=N), 1367 (C-N), 1268 (C=S), 1098 (N-N). GCMS: (m/z)[321 $M^+$].

**Synthesis of 5-(Carbothioamide)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-thione 2f.**
$H^1$-NMR (DMSO-$d_6$) – **δ** 2.292( s, 3H, $CH_3$), 5.176 (J= 3.6Hz, d, 1H, CH), 6.681 (s, 2H,$NH_2$), 7.211-7.366 (m, 5H, Ar-H), 7.981 (J= 4Hz, d, 2H, NHx2), 9.887 (J=1.2Hz, d, 1H, NH), 10.308 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **-δ** 17.47, 59.54, 100.75, 126.35, 127.62, 128.50, 143.47, 144.95, 165.10, 178.47, 183.94. FT-IR($cm^{-1}$) -3328, 3172(NH), 2979 (Ar-H), 2936 (CH), 1669(C=O), 1573 (C=N), 1327 (C-N), 1283 (C=S), 1117 (N-N).GCMS: (m/z)[321$M^+$].

**Synthesis of 5-(Carbothioamide)-4-(4-chlorophenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-thione 2g.**
$H^1$-NMR (DMSO-$d_6$) **-δ** 2.296 ( s, 3H, $CH_3$), 5.174 (J= 2Hz, d, 1H, CH), 7.023 (s, 2H, $NH_2$), 7.209-7.243 (dd,2H, Ar-H), 7.413-7.503 (dd, 2H, Ar-H), 8.295 (J=0.8Hz, d, 2H, NHx2), 9.648 (J= 2.8Hz, d, 1H, NH), 10.363 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **-δ** 17.48, 59.63, 100.34, 128.27, 128.52, 142.33, 145.28, 164.96, 178.43, 183.89. FT-IR($cm^{-1}$)- 3377, 3327(NH), 3158 (Ar-H), 2996 (CH), 1731 (C=O), 1596 (C=N), 1335 (C-N), 1281 (C=S),1041(N-N). GCMS: (m/z)[355$M^+$].

**Synthesis of 5-(Carbothioamide)-4-(4-(dimethylamino)phenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-thione 2h.**
$H^1$-NMR (DMSO-$d_6$)-**δ** 2.277 (s, 3H, $CH_3$), 2.855 (s, 6H, $N(CH_3)_2$), 5.048 (J=4Hz, d, 1H, CH), 6.305 (s, 2H, $NH_2$), 6.663 (J=8.8Hz, d, 2H, Ar-H), 7.016 (J=8.8Hz, d, 2H, Ar-H), 9.509 (J=1.6Hz, d, 2H, NHx2), 9.887 (s, 1H, NH), 10.197 (J=0.8Hz, d, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **-δ** 17.48, 53.53, 59.43, 101.27, 112.16, 127.08, 131.19, 149.93, 151.56, 165.25, 178.47, 183.93. FT-IR($cm^{-1}$)- 3377, 3356(NH), 3105 (Ar-H), 2981 (CH), 1669 (C=O), 1577 (C=N), 1366 (C-N), 1285 (C=S), 1117 (N-N). GCMS: (m/z)[364 $M^+$].

**Synthesis of 5-(Carbothioamide)-4-(3-nitrophenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-thione 2i.**
$H^1$-NMR (DMSO-$d_6$) **-δ** 2.498( s, 3H, $CH_3$), 4.931 (J= 1.2Hz, d, 1H, CH), 6.557(s, 2H, $NH_2$), 7.540-7.817 (m, 4H, Ar-H), 8.178 (J=0.8Hz, d, 2H, NHx2), 8.566 (J=2.4Hz, d, 1H, NH), 9.855 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **-δ** 17.49, 60.26, 98.35, 122.96, 123.05, 129.73, 135.27, 141.64, 149.51, 151.64, 168.09, 175.39, 183.85. FT-IR($cm^{-1}$)-3379, 3273(NH), 3088 (Ar-H), 2982 (CH), 1727 )C=O), 1530 (C=N), 1315 (C-N), 1233 (C=S), 1117 (N-N). GCMS: (m/z)[366 $M^+$].

**Synthesis of 5-(Carbothioamide)-4-(4-hydroxyphenyl)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H )-thione 2j.**
$H^1$-NMR (DMSO-$d_6$) **-δ** 2.277 ( s, 3H, $CH_3$), 5.063 (J= 3.6Hz, d, 1H, CH), 6.120 (s, 2H, $NH_2$), 6.699-6.720 (t, 2H, Ar-H), 6.999-7.070(q, 2H, Ar-H), 7.500 (s, 1H, Ar-H), 7.965(J=3.5Hz, d, 2H, NHx2), 9.528(J=1.6Hz, d, 1H, NH), 9.883 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **-δ** 17.50, 59.47, 101.12, 115.17, 127.61, 134.08, 144.42, 151.68, 165.18, 178.38, 183.83. FT-IR($cm^{-1}$) - 3429(OH), 3245, 3179(NH), 3036 (Ar-H), 2988 (CH), 1715 (C=O), 1597 (C=N), 1314 (C-N), 1259 (C=S), 1082 (N-N). GCMS: (m/z)[337 $M^+$].

**General procedure for Synthesis of 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-phenylpyrimidin-2(1H)-one 3a.**
General procedure for the synthesis of compounds (3a-j), carbothioamide**2** (0.01 mole) was added into 8% NaOH it was heated, under refluxed for 4hrs. The reaction mixture was cooled to room temperature and acidified with dilute acetic acid then filtered and washed well with water and purified by recrystallization from alcohol as shiny crystals. Melting point $120^0$C, yield 85%.
$H^1$-NMR (DMSO-$d_6$) **δ** -2.304 ( s, 3H, $CH_3$), 3.217 (s, 1H, SH), 5.507 (J= 3.6Hz, d, 1H, CH), 6.975 (s, 1H, NH), 7.268 – 7.338 (m,5H, Ar-H), 7.766 (J= 2.4Hz, d, 1H, NH), 9.217 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.74, 59.14, 99.24, 126.22, 127.21, 128.33, 144.84, 148.29, 152.15, 155.11, 165.32. FT-IR($cm^{-1}$)- 3423(NH), 3027 (Ar-H), 2968 (CH), 2235 (SH), 1654 (C=O),1590 (C=N), 1373 (C-N), 1057 (N-N). GCMS: (m/z)[287 $M^+$].

**Synthesis of 4-(4-chlorophenyl)-3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methylpyrimidin-2(1H)-one 3b.**
$H^1$-NMR (DMSO-$d_6$) **δ** - 2.259 ( s, 3H, $CH_3$), 3.153 (s, 1H, SH), 5.156 (J= 2.4Hz, d, 1H, CH), 7.004 (s, 1H, NH), 7.365 – 8.214 (m, 4H, Ar-H), 9.286 (J=3.1Hz, d, 1H, NH), 9.973 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.76,

59.25, 98.85, 128.15, 128.33, 128.65, 128.88, 131.76, 133.17, 134.21, 140.89, 165.18, 178.12. FT-IR($cm^{-1}$) - 3436(NH), 3036 (Ar-H), 2978 (CH), 2265 (S-H), 1682 (C=O), 1526 (C=N), 1322 (C-N), 1090 (N-N).GCMS: (m/z)[321 $M^+$].

**Synthesis of 4-(4-(dimethylamino)phenyl)-3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl pyrimidin-2(1H)-one 3c.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.226 ( s, 3H, $CH_3$), 2.846 (s, 6H, $N(CH_3)_2$), 2.992 (s, 1H,SH), 5.035 (J= 3.2Hz, d, 1H, CH), 6.353 (s, 1H, NH), 6.650 (J=8.4Hz, d, 1H, Ar-H), 6.765 (J=8.8Hz,d,1H, Ar-H), 7.026-7.062 (dd, 2H, Ar-H), 8.475 (J= 15.2Hz, d, 1H, NH), 9.051(s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.68, 53.29, 59.05, 99.91, 111.67, 126.85, 129.46, 149.73, 152.26, 159.76, 165.46. FT-IR (cm-1) - 3244(NH), 3010 (Ar-H), 2976 (CH), 2376 (SH), 1709 (C=O), 1524 (C=N), 1365 (C-N), 1089 (N-N). GCMS: (m/z) [330 $M^+$].

**Synthesis of 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-(3-nitrophenyl)pyrimidin-2(1H)-one 3d.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.285 (s, 3H, $CH_3$), 2.973 (s, 1H, SH), 5.319 (J= 2.4Hz, d, 1H, CH), 7.182 (s, 1H, NH), 7.643-7.721 (m, 4H, Ar-H), 7.940 (J= 2.4Hz, d, 1H, Ar-H), 8.110 (J=15.6Hz, d, 1H, Ar-H), 8.178 (J= 2.3Hz, d, 1H, NH), 9.408 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.80, 59.38, 98.36, 120.96, 122.31, 130.19, 132.98, 139.08, 146.96, 147.72, 149.41, 151.85, 165.07. FT-IR ($cm^{-1}$)- 3440(NH), 3090 (Ar-H), 2966 (CH), 2385 (SH), 1687 (C=O), 1560 (C=N), 1346 (C-N), 1088 (N-N).GCMS: (m/z)[332 $M^+$].

**Synthesis of 3,4-dihydro-4-(4-hydroxyphenyl)-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methylpyrimidin-2(1H)-one 3e.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.340 (s, 3H, $CH_3$), 3.226 (s, 1H,SH), 5.738 (J= 8.8Hz, d, 1H, CH), 7.282 (s, 1H, NH), 7.664 (J= 8.8Hz, d, 2H, Ar-H), 7.853-7.857 (dd, 1H, Ar-H), 8.031 (J=8Hz, d, 1H, Ar-H), 8.080 (J= 1.2Hz, d, 1H, NH), 9.918 (s, 1H, NH), 11.276 (s, 1H, OH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.76, 59.22, 98.85, 115.53, 125.10, 129.01, 140.89, 142.77, 151.22, 159.22, 177.44. FT-IR($cm^{-1}$)- 3468(NH), 3128 (OH), 3015 (Ar-H), 2925 (CH), 2335 (SH), 1609 (C=O), 1547 (C=N), 1388 (C-N), 1097 (N-N).GCMS-(m/z)[303 $M^+$].

**Synthesis of 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-phenylpyrimidine-2(1H)-thione 3f.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.289 ( s, 3H, $CH_3$), 3.112 (s, 1H, SH), 5.376 (J= 2.4Hz, d, 1H, CH), 7.498(s, 1H, NH), 7.594(dd, 2H, Ar-H), 7.778-7.962 (dd, 2H, Ar-H), 8.112(J= 4Hz, d, 1H, NH), 9.694 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.76, 59.22, 98.85, 127.24, 128.62, 129.81, 134.13, 142.38, 165.18, 177.99. FT-IR($cm^{-1}$) - 3421(NH), 3054 (Ar-H), 2982 (CH),2336 (SH), 1590 (C=N), 1372 (C-N), 1293 (C=S), 1067 (N-N). GCMS: (m/z)[303 $M^+$].

**Synthesis of 4-(4-chlorophenyl)-3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methylpyrimidine-2(1H)-thione 3g.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.310 ( s, 3H, $CH_3$), 3.065 (s, 1H, SH), 5.356 (J= 2.4Hz, d, 1H, CH), 7.199 (s, 1H, NH), 7.460 (J= 8.4Hz, d,1H, Ar-H), 7.590 (J=8.4Hz, d, 1H, Ar-H), 7.840 (J= 8.4Hz,d, 1H, Ar-H), 7.904 (J= 11.6Hz, d, 1H, Ar-H), 8.177 (J= 2.4Hz, d, 1H, NH), 8.715 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.76, 59.21, 98.85, 128.66, 128.89, 129.05, 129.99, 133.18, 134.19, 140.89, 178.12. FT-IR($cm^{-1}$)- 3437(NH), 3065 (Ar-H),2994 (CH), 2372 (SH), 1525 (C=N), 1367 (C-N), 1283 (C=S), 1016 (N-N).GCMS: (m/z)[337 $M^+$].

**Synthesis of 4-(4-(dimethylamino)phenyl)-3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl pyrimidine-2(1H)-thione 3h.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.283 ( s, 3H, $CH_3$), 2.864 (s, 6H, $N(CH_3)_2$), 3.098 (s, 1H, SH), 5.058 (J= 3.6Hz, d, 1H, CH), 6.881 (s, 1H, NH), 7.522 (J= 8.8Hz, d,2H, Ar-H), 7.766 (J=9.2Hz, d, 1H, Ar-H), 7.641-7.734 (t, 1H, Ar-H), 7.951 (J= 9.2Hz, d, 1H, Ar-H), 9.506 (J= 3.6Hz, d, 1H, Ar-H), 10.195 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ**- 17.07, 53.49, 59.44, 101.27, 121.39, 127.08, 128.57, 129.46, 131.18, 149.94, 151.39, 165.26. FT-IR($cm^{-1}$)- 3415(NH), 3056 (Ar-H), 2981 (CH), 2386 (SH), 1521 (C=N), 1365 (C-N), 1229 (C=S), 1030 (N-N). GCMS: (m/z)[346 $M^+$].

**Synthesis of 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-(3-nitrophenyl)pyrimidine-2(1H)-thione 3i.**$H^1$-NMR (DMSO-$d_6$) **δ** - 2.093 (s, 3H, $CH_3$), 3.088 (s, 1H, SH), 5.113 (J=4Hz, d, 1H, CH),6.624 (s, 1H,

NH), 7.064 (J= 7.6Hz, d, 1H, Ar-H), 7.451-7.831 (m, 1H, Ar-H), 8.333 (J= 16Hz, d, 1H, NH), 11.317 (s, 1H, NH). $C^{13}$-NMR (DMSO-$d_6$) **δ** - 17.81, 59.35, 98.35, 115.79, 128.80, 129.13, 133.11, 134.25, 134.48, 140.96, 143.52, 162.02, 177.82. FT-IR($cm^{-1}$)- 3326(NH), 3010 (Ar-H), 2986 (CH), 2386 (SH), 1585 (C=N), 1320 (C-N), 1279 (C=S), 1089 (N-N). GCMS: (m/z)[348 $M^+$].

**Synthesis of 3,4-dihydro-4-(4-hydroxyphenyl)-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methylpyrimidine-2(1H)-thione 3j.**

$H^1$-NMR (DMSO-$d_6$) **δ** - 2.526 ( s, 3H, $CH_3$), 3.120 (s, 1H, SH), 5.295 (J= 3.2Hz, d, 1H, CH), 6.764-6.798 (m, 2H, Ar-H), 7.590-7.625 (m, 2H, Ar-H), 7.802 (s, 1H, NH), 7.991 (J=2.7Hz, d, 1H,NH), 9.858 (s, 1H, NH), 11.221 (s, 1H, OH). $C^{13}$-NMR (DMSO-$d_6$) - 17.81, 59.35, 98.35, 115.52, 125.11, 129.00, 132.94, 133.57, 142.77, 159.22, 177.46. FT-IR($cm^{-1}$) - 3468(NH), 3191 (OH), 3015 (Ar-H), 2810 (CH), 2471 (SH), 1586 (C=N), 1384 (C-N), 1265 (C=S), 1097 (N-N). GCMS: (m/z)[319 $M^+$].

**Antibacterial studies**

Among the newly synthesized pyrimidine derivatives were screened for their antibacterial activity *in vitro* against the species of *Pseudomonas aeruginosa (Gram –ve), Staphylococcus aureus(Gram +ve) and Escherichia coli (Gram –ve)*, using agar well disk diffusion method. The test compounds were dissolved in DMSO to get a solution of 10µg/ml concentration.

The inhibition zones were measured in millimeters at the end of an incubation period of 18hrs at $37^0$C. Ciprofloxacin was used as a reference and the results were shown in Table-III. Most of the tested compounds showed antibacterial activity comparable with that of the standard drug ciprofloxacin.

**Table-III-Antibacterial activities of compounds (3a-j)**
**Antibacterial activity in (mm) Std. Ciprofloxacin (25mm)**

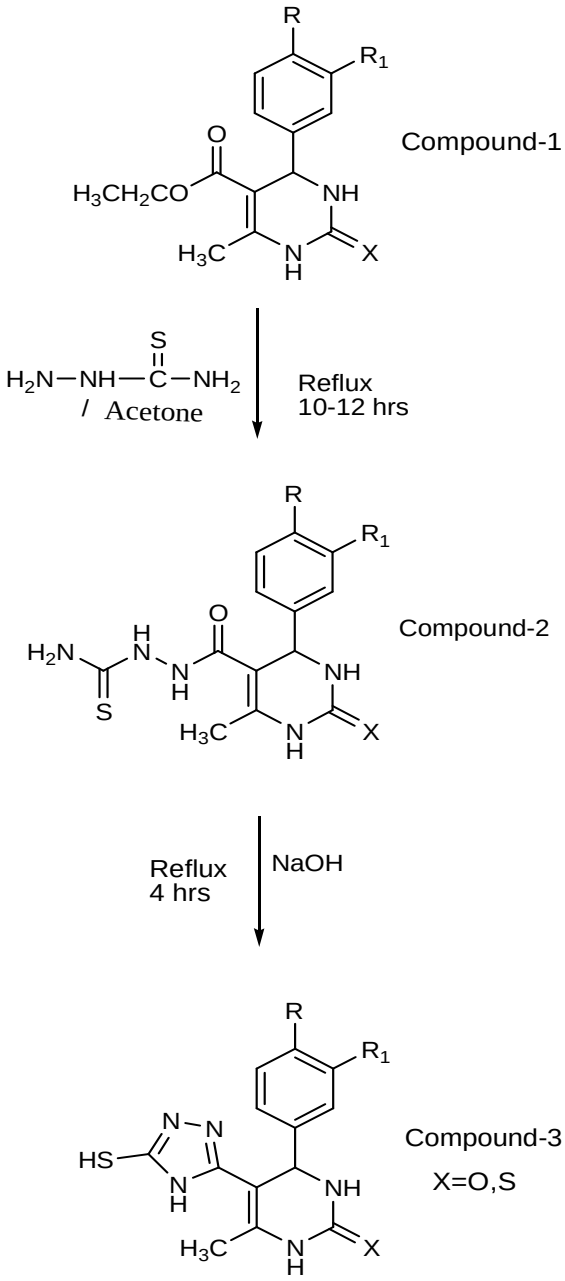
| Compound | *Pseudomonas aeruginosa* | *Staphylococcus aureus* | *Escherichia coli* |
|---|---|---|---|
| **Control(DMSO)** | 0 | 0 | 0 |
| **3a** | 7 mm | 8mm | 8mm |
| **3b** | 9mm | 12mm | 11mm |
| **3c** | 5mm | 7mm | 7mm |
| **3d** | 5mm | 7mm | 5mm |
| **3e** | 20mm | 14mm | 10mm |
| **3f** | 7mm | 12mm | 12mm |
| **3g** | 23mm | 8mm | 14mm |
| **3h** | 8mm | 6mm | 15mm |
| **3i** | 10mm | 10mm | 12mm |
| **3j** | 8mm | 10mm | 9mm |

**Concentration was 10µg/ml @ 10% DMSO; "-" and"0" no inhibition zone.**

## RESULTS AND DISCUSSION

Compounds were synthesized as per the scheme-I, where final compound (**3)** prepared by reacting carbothioamide compound (**2)** with NaOH. 5-(Carbothioamide)-3,4-dihydro-6-methyl-4-phenylpyrimidin-2(1H)-one (compound **2)** were synthesized by reacting pyrimidine ethyl ester (**1)** with thiosemicarbazide in acetone followed by condensation reaction[23-26]. The pyrimidine ethyl ester compound (**1)** was prepared by reacting benzaldehyde, ethylacetoacetate and urea or thiourea in the presence of mineral acid followed by Biginelli reaction. The structures of the synthesized compounds were confirmed by IR, $^1$H-NMR, $^{13}$C-NMR, GC-MS and CHN analysis (Table-I). Formation of compound (**2)** was confirmed by the presence of N-H stretching peaks at 3365, 3241 $cm^{-1}$ and 3116 $cm^{-1}$ and C=O stretching peaks at 1724 $cm^{-1}$ in IR and singlet at $\delta$ 6.50 for $NH_2$ group in $^1$H-NMR spectra. Treatment of compound (2) with NaOH, furnished 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-phenylpyrimidin-2(1H)-one **(3).**

**Scheme-I**




**3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-phenylpyrimidin-2(1H)-one3a**

The structure of (**3)** was elucidated on the basis of C-N linkage in the triazole ring, which caused a sharp absorption band at 1373 $cm^{-1}$ in its IR spectrum. $^1$H-NMR spectrum showed a singlet at δ 3.21 due to SH functionality confirmations of their structure were obtained through spectral and analytical data. (Physical and analytical data are given in Table-II) IR and $^1$H-NMR spectral data revealed carbonyl absorption band at 1654 $cm^{-1}$ of NH-CO-NH group, N-N stretching band at1053 $cm^{-1}$ aliphatic C-H and aromatic C-H stretching at 2968 $cm^{-1}$and 3027$cm^{-1}$ group of pyrimidine moiety **(3)**. Mass spectrum also supported the proposed structure by viewing molecular ion peak at m/z = 287 $M^{+\cdot}$

All these compounds were screened for antibacterial activity by against *Pseudomonas aeruginosa (Gram –ve), Staphylococcus aureus(Gram +ve) and Escherichia coli (Gram –ve).* Ciprofloxacin was used as standard drug. Most of the synthesized compounds showed moderate to good inhibition at 10µg/ml concentration. However the activity was less compared to the standard drugs.

**Table – I- Physical and analytical data of compounds- (2a-j)**

| S. No. | M. Formula | R | $R_1$ | X | M.Wt | Yield(%) | M.p ($^0$C) | Calculated./Found (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | C | N | H | S |
| **2a** | $C_{13}H_{15}N_5O_2S$ | H | H | O | 305 | 85 | 140 | 51.17 (51.94 | 22.50 22.24 | 4.94 4.85 | 10.47 10.94) |
| **2b** | $C_{13}H_{14}N_5O_2SCl$ | Cl | H | O | 339 | 70 | 145 | 46.05 (46.30 | 20.65 20.94 | 4.15 4.60 | 9.42 9.49) |
| **2c** | $C_{15}H_{20}N_6O_2S$ | $N(CH_3)_2$ | H | O | 348 | 78 | 170 | 52.35 (52.79 | 24.42 24.77 | 5.84 5.83 | 9.28 9.85) |
| **2d** | $C_{13}H_{14}N_6O_4S$ | H | $NO_2$ | O | 350 | 81 | 132 | 44.60 (44.06 | 24.00 24.07 | 4.02 4.43 | 9.13 9.22) |
| **2e** | $C_{13}H_{15}N_5O_3S$ | OH | H | O | 321 | 83 | 160 | 48.62 (48.75 | 21.18 21.19 | 4.70 4.32 | 9.95 9.36) |
| **2f** | $C_{13}H_{15}N_5OS_2$ | H | H | S | 321 | 65 | 143 | 48.63 (48.46 | 21.80 21.97 | 4.70 4.55 | 19.91 20.10) |
| **2g** | $C_{13}H_{14}N_5OS_2Cl$ | $N(CH_3)_2$ | H | S | 355 | 72 | 110 | 43.90 (43.41 | 19.72 19.42 | 3.97 4.09 | 18.00 18.06) |
| **2h** | $C_{15}H_{20}N_6OS_2$ | Cl | H | S | 364 | 75 | 148 | 49.47 (49.00 | 23.08 23.26 | 5.49 5.22 | 17.56 17.69) |
| **2i** | $C_{13}H_{14}N_6O_3S_2$ | H | $NO_2$ | S | 366 | 70 | 125 | 42.65 (42.59 | 22.95 23.00 | 3.85 3.54 | 17.46 17.72) |
| **2j** | $C_{13}H_{15}N_5O_2S_2$ | OH | H | S | 337 | 78 | 118 | 46.32 (46.53 | 20.77 21.03 | 4.47 4.70 | 18.96 19.06) |

**Table – II- Physical and analytical data of compounds- (3a-j)**

| S. No. | M. Formula | R | $R_1$ | X | M.Wt | Yield (%) | M.p ($^0$C) | Calculated./Found (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | C | N | H | S |
| **3a** | $C_{13}H_{13}N_5OS$ | H | H | O | 287 | 85 | 120 | 54.41 (54.38 | 24.35 24.39 | 4.22 4.56 | 11.53 11.13) |
| **3b** | $C_{13}H_{12}N_5OSCl$ | Cl | H | O | 321 | 88 | 115 | 48.92 (48.62 | 21.44 21.80 | 3.39 3.76 | 9.54 9.95) |
| **3c** | $C_{15}H_{18}N_6OS$ | $N(CH_3)_2$ | H | O | 330 | 90 | 220 | 54.74 (54.57 | 25.65 25.45 | 5.47 5.49 | 9.55 9.68) |
| **3d** | $C_{13}H_{12}N_6O_3S$ | H | $NO_2$ | O | 332 | 84 | 118 | 47.18 (47.02 | 25.58 25.30 | 3.30 3.64 | 9.43 9.62) |
| **3e** | $C_{13}H_{13}N_5O_2S$ | OH | H | O | 303 | 82 | 198 | 51.86 (51.52 | 23.22 23.16 | 4.00 4.32 | 10.42 10.54) |
| **3f** | $C_{13}H_{13}N_5S_2$ | H | H | S | 303 | 84 | 123 | 51.98 (51.52 | 23.03 23.10 | 4.02 4.32 | 21.12 21.09) |
| **3g** | $C_{13}H_{12}N_5S_2Cl$ | $N(CH_3)_2$ | H | S | 337 | 78 | 175 | 46.41 (46.32 | 20.31 20.77 | 3.78 3.59 | 18.83 18.97) |
| **3h** | $C_{15}H_{18}N_6S_2$ | Cl | H | S | 346 | 82 | 155 | 52.38 (52.05 | 24.42 24.28 | 5.63 5.24 | 18.89 18.47) |
| **3i** | $C_{13}H_{12}N_6O_2S_2$ | H | $NO_2$ | S | 348 | 76 | 115 | 45.00 (44.86 | 24.04 24.14 | 3.26 3.47 | 18.69 18.37) |
| **3j** | $C_{13}H_{13}N_5OS_2$ | OH | H | S | 319 | 85 | 202 | 48.01 (48.93 | 21.97 21.94 | 4.17 4.10 | 20.32 20.04) |

## CONCLUSION

The investigation of antibacterial screening data for synthesised compounds revealed that all the tested compounds showed moderate to good inhibition at 10µg/ml concentration. Especially the compounds 3b, 3e, 3g and 3i showed very good activity than the others. However the activity was less compared to the standard drug.

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