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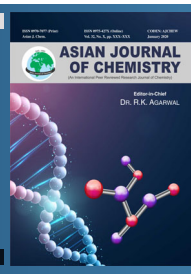

Solid Phase Synthesis and Antimicrobial Activity of Novel Triazolo[1,5-*a*]pyrimidine Derivatives

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A new series of triazolo[4,3-*a*]pyimidine derivatives *via* solid phase multicomponent reaction between 3-oxo-*N*-(4-(3-oxomorpholino)-phenyl)butanamide, aromatic aldehyde and aminoazole is reported. All the synthesized compounds have been characterized by elemental analysis and spectral analyses. Moreover, the synthesized compounds were also screened for their antibacterial activity against *Staphylococcus aureus* MTCC-96, *Escherichia coli* MTCC-443, *Bacillus subtilis* MTCC-441, *Pseudomonas aeruginosa* MTCC 1688, and antifungal activity against *Aspergillus niger* MTCC-282 and *Penicillium* sp. at different concentration and compared with standards drugs. The minimum inhibition concentration (MIC) of the compounds was studied by micro-broth dilution method.

Keywords: Aminoazole, Antimicrobial assay, Triazolo[4,3-*a*]pyimidine, Solid phase multicomponent reaction.

INTRODUCTION

Pyrimidines moieties are a pharmacophoric scaffold and represent a class of heterocyclic compounds with a wide range of biological applications. Other than their pharmacological importance, pyrimidine derivatives are valuable for the synthesis of fused ring compounds. It has been noticed that introduction of an additional ring to the pyrimidines core tends to exert profound influence in conferring novel biological activities in these molecules. Although many methods for synthesizing triazolopyrimidines ring systems have been reported, they continue to receive a great deal attentions [1-3]. Fused pyrimidines like triazolopyrimidines, pyrazolopyrimidines, pyrimidoazepines, pteridines, pyridopyrimidines, purines, quinazolines, furopyrimidines and pyrrolopyrimidines were studied in the past decade and found to demonstrated remarkable pharmacological properties. Triazolopyrimidines are new class of hybrid heterocycles of pyrimidine ring fused with triazole and showed improved activity. The condensation of pyrimidine with triazole ring gives bicyclic heterocycles known as 1,2,4-triazolopyrimidines, which exist in four isomeric structure [4-7]. Bicyclic heterocycles consisting fused pyrimidine rings have been synthesized and investigated for various biological properties because of its presence in number of biological and pharmacological active species [8-16]. Pyrimidine cores united with five membered heterocycles have been studied for variety of therapeutic actions for many years. Among them, triazole fused pyrimidine moieties, exhibits diverse pharmaceutical activities, such as antitumor potency [17-20], antimalarial [21], antimicrobial [22-25], anti-inflammatory [26] inhibition of KDR kinase [27], antifungal [28] and macrophage activation [29]. They have proved to be promising anticancer [30] agents with dual mechanisms of tubulin polymerization promotion [17,18] as well as cyclin depen-dent kinases 2 inhibition [31].

Due to promising biological profile of triazolopyrimidines holding carboxamide, amino and alkyl/aryl functionalities has attracted many organics chemists to develop novel route of synthesis for this class of compounds. So far, further modification is still under consideration to afford distinctly functionalized triazolo[4,3-*a*]pyrimidine nucleus. The traditional approach to construct triazolopyrimidines involves cyclocondensation of 1,3-dicarbonyl compounds with aldehyde and urea derivatives in appropriate organic solvent which is then followed by chlorination, hydrazination and finally cyclization leads to targeted building blocks [32-34].

Herein, novel 1,2,4-triazolo[4,3-*a*]pyrimidine derivatives have been synthesized by solid phase synthesis of 3-oxo-*N*-(4-(3-oxomorpholino)phenyl)butanamide, 5-amino-1,2,4-triazole

and various substituted aldehyde *via* solid phase synthetic methodology. The newly synthesized compounds were characterized by IR, mass, ^{1}H & ^{13}C NMR spectroscopy and elemental analysis. All the synthesized compounds were also evaluated for their antimicrobial activity.

EXPERIMENTAL

All chemicals were purchased from Sigma-Aldrich Chemicals and used as received. Reactions were monitored by thin layer chromatography (TLC) on pre-coated silica gel GF_{254} plates (E-Merck Co.) by using appropriate solvent systems. Melting points were determined in open capillaries and are uncorrected. Infrared (IR) spectra (KBr pellets) were recorded on a Shimadzu-FTIR-8400 spectrophotometer over frequencies ranging from 4000-400 cm^{-1}. The NMR spectra (^{1}H & ^{13}C NMR) were recorded on a Bruker Avance Spectrospin 400 MHz spectrometer using $CDCl_3$ as solvents and TMS as an internal standard. Mass spectra were recorded on a Shimadzu GC-MS-QP-2010 spectrometer by using Electron Impact (EI) (0.7 kV) ionization source. The ion source temperature was 220 ºC while the interface temperature was 240 ºC.

Synthesis of 3-oxo-*N*-(4-(3-oxomorpholino)phenyl)-butanamide (3): A mixture of 4-(4-aminophenyl)morpholin-3-one (**1**) (10 mmol), 4-methyl-3-oxopentanoate (**2**) (10 mmol) and catalytic amount of KOH (10 %) in 1,4-dioxane (50 mL) was refluxed at 110 ºC for 12-15 h. The reaction was monitored by TLC. After completion of reaction, cool the reaction mass and poured into chilled water to precipitate out the product filtered the solid product and washed with methanol to obtained analytical pure product (**Scheme-I**).

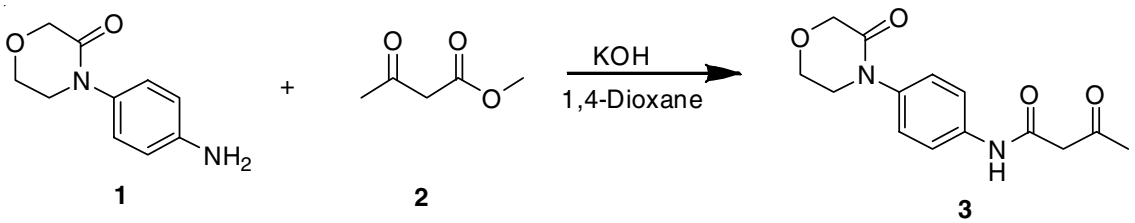
Synthesis of triazolopyrimidines (6a-j): A mixture of aminoazole (**5**) (0.01 mol), 3-oxo-*N*-(4-(3-oxomorpholino)-phenyl)butanamide (**3**) (0.01 mol) and an appropriate aromatic aldehyde **4a-j** (0.01 mol) was refluxed in 0.4 mL of DMF for 12-15 min. After cooling, methanol (~10 mL) was added. The reaction mixture was allowed to stand overnight and then filtered, washed with methanol and died at room temperature to furnish analytical pure product (70-80%) (**Scheme-II**). The physical characterization data are listed in Table-1.

TABLE-1
PHYSICAL DATA OF *N*-SUBSTITUTED PYRIMIDINE (**6a-j**)

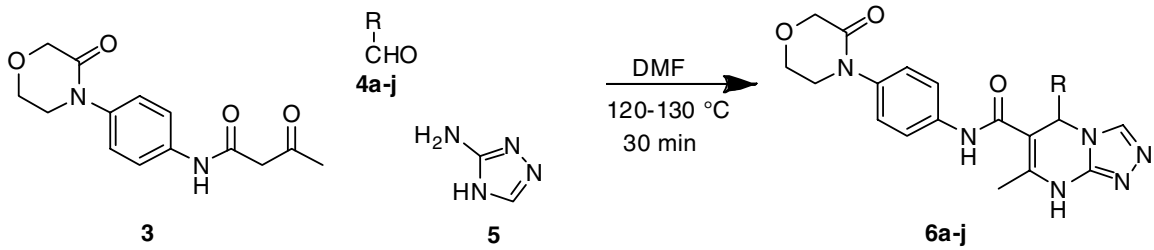
Compd.	R	Time (min)	Yield (%)	m.p. (°C)
6a	4-ClC_6H_4	17	75	268-270
6b	Benzaldehyde	14	78	270-272
6c	4-$OCH_3C_6H_4$	20	80	264-265
6d	2,5-di-OCH_3-C_6H_3	16	68	235-237
6e	4-FC_6H_4	24	80	238-240
6f	Vaniline	28	73	245-247
6g	Veratraldehyde	22	83	252-254
6h	Furfuraldehyde	26	88	227-229
6i	Propionaldehyde	17	84	247-249
6j	4-BrC_6H_4	18	76	245-247

5-(4-Chlorophenyl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidine-6-carboxamide (6a): IR (KBr, ν_{max}, cm^{-1}): 3643, 3375, 3061, 2922, 2858, 1919, 1790, 1635, 1552, 1504, 1458, 1294, 1192, 1076, 1026, 997, 856, 785, 696, 580; ^{1}H NMR (δ ppm): 2.20 (s, 3H, -CH_3), 3.65-3.67 (t, 2H, -CH_2- in morpholinone ring), 3.93-3.96 (t, 2H, -CH_2- in morpholinone ring), 4.18 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.58 (s, 1H, -CH pyrimidine ring), 7.24-7.28 (m, 4H, Ar-H), 7.38-7.40 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.53-7.55 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.68 (s, 1H, Ar-H), 9.85 (s, 1H, -NH pyrimidine ring), 10.32 (s, 1H, -NH amide), ^{13}C NMR (δ ppm): 17.33, 49.03, 59.57, 63.43, 67.68, 103.06, 119.80, 125.80, 128.55, 128.87, 132.74, 136.82, 136.99, 137.11, 139.63, 147.79, 150.08, 164.74, 165.89; MS (*m/z*): 464.14 (M^+); Anal. calcd. (found) % for $C_{23}H_{21}N_6O_3Cl$: C, 59.42 (59.47); H, 4.55 (4.59); N, 18.08 (18.04).

5-(4-Formylphenyl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazole[4,3-*a*]pyrimidine-6-carboxamide (6b): IR (KBr, ν_{max}, cm^{-1}): 3250, 3189, 3072, 2939, 2879, 1730, 1667, 1550, 1470, 1350, 1310, 1290, 1160, 1073, 884, 778, 677, 592; ^{1}H NMR (δ ppm): 2.17 (s, 3H, CH_3), 3.64-3.66 (t, 2H, -CH_2- in morpholinone ring), 3.92-3.94 (t, 2H, -CH_2- in morpholinone ring), 4.23 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.75 (s, 1H, -CH pyrimidine ring), 7.29 (d, 2H, Ar-H, *J* = 8.4 Hz), 7.34-7.49 (m, 5H, Ar-H), 7.72 (d, 2H,



Scheme-I: Synthesis 3-oxo-*N*-(4-(3-oxomorpholino) phenyl) butanamide [3]



Scheme-II: Synthesis of triazolopyimidine (**6a-j**)

Ar-H, *J*=8.0 Hz), 8.21 (s, 1H, Ar-H), 9.82 (s, 1H, -NH pyrimidine ring), 10.02 (s, 1H, -NH amide); ^{13}C NMR: 17.47, 49.65, 57.88, 62.24, 68.15, 103.48, 119.62, 125.24, 128.26, 129.31, 132.48, 135.24, 136.67, 137.37, 139.13, 147.92, 150.52, 163.86, 166.22; MS (*m/z*): 458.17 (M^+); Anal. calcd. (found) % for $C_{24}H_{22}N_6O_4$: C, 62.87 (62.91); H, 4.84 (4.88); N, 18.33 (18.37).

5-(4-Methoxyphenyl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidine-6-carboxamide (6c): IR (KBr, ν_{max}, cm^{-1}): 3610, 3244, 3113, 3055, 2933, 2868, 1791, 1622, 1593, 1321, 1271, 1205, 1166, 1028, 827, 794, 659, 565; ^{1}H NMR (δ ppm): 2.21 (s, 3H, -CH_3), 3.61-3.65 (t, 2H, -CH_2- in morpholinone ring), 3.88 (s, 3H, -OCH_3), 3.96-3.99 (t, 2H, -CH_2- in morpholinone ring), 4.37 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.34 (s, 1H, -CH pyrimidine ring), 7.24 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.31 (d, 2H, Ar-H, *J* = 7.6 Hz), 7.39 (d, 2H, Ar-H, *J* = 8.8 Hz), 7.78 (d, 2H, Ar-H, *J* = 7.6 Hz), 8.04 (s, 1H, Ar-H), 9.92 (s, 1H, -NH pyrimidine ring), 10.23 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 17.25, 49.64, 52.35, 58.38, 62.66, 66.87, 103.28, 115.41, 122.84, 129.78, 130.27, 132.87, 134.21, 140.87, 142.21, 149.64, 156.78, 163.75, 164.61; MS (*m/z*): 460.19 (M^+); Anal. calcd. (found) % for $C_{24}H_{24}N_6O_4$: C, 62.60 (62.64); H, 5.25 (5.28); N, 18.25 (18.29).

5-(2,5-dimethoxyphenyl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazole[4,3-*a*]pyrimidine-6-carboxamide (6d): IR (KBr, ν_{max}, cm^{-1}): 3379, 3305, 3284, 3099, 2978, 2870, 1705, 1658, 1610, 1597, 1432, 1408, 1348, 1238, 1192, 1126, 1081, 836, 786, 684, 648, 588, 511; ^{1}H NMR (δ ppm): 2.25 (s, 3H, -CH_3), 2.33 (s, 3H, -CH_3), 3.65-3.68 (t, 2H, -CH_2- in morpholinone ring), 3.88 (s, 3H, -OCH_3), 3.94-3.97 (t, 2H, -CH_2- in morpholinone ring), 4.17 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.48 (s, 1H, -CH pyrimidine ring), 7.10 (d, 2H, Ar-H, *J* = 8.68 Hz), 7.21 (d, 2H, Ar-H, *J* = 7.6 Hz), 7.38 (d, 2H, Ar-H, *J* = 8.8 Hz), 7.56 (d, 2H, Ar-H, *J* = 9.6 Hz), 7.89 (s, 1H, Ar-H), 9.87 (s, 1H, -NH pyrimidine ring), 10.15 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 17.55, 20.66, 49.10, 60.40, 63.47, 67.72, 102.61, 119.77, 125.61, 128.94, 129.14, 133.28, 136.42, 136.62, 137.30, 148.23, 149.62, 164.68, 165.82; MS (*m/z*): 490.20 (M^+); Anal. calcd. (found) % for $C_{25}H_{26}N_6O_5$: C, 61.22 (61.27); H, 5.34 (5.36); N, 17.13 (17.18).

5-(4-Fluorophenyl)-7-methyl-*N*-(4-(3-oxomorpholino)-phenyl)-5,8-dihydro[1,2,4]triazole[4,3-*a*]pyrimidine-6-carboxamide (6e): IR (KBr, ν_{max}, cm^{-1}):3634, 3527, 3280, 3228, 3099, 2958, 2872, 1778, 1708, 1664, 1583, 1531, 1473, 1378, 1317, 1253, 1132, 1078, 1020, 995, 827, 731, 684, 522; ^{1}H NMR (δ ppm): 2.19 (s, 3H, -CH_3), 3.59-3.63 (t, 2H, -CH_2- in morpholinone ring), 3.67-3.76 (t, 2H, -CH_2- in morpholinone ring), 4.38 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.21 (s, 1H, -CH pyrimidine ring), 7.31 (d, 2H, Ar-H, *J* = 8.4 Hz), 7.42 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.89 (d, 2H, Ar-H, *J* = 8.8 Hz), 8.12 (d, 2H, Ar-H, *J* = 8.4 Hz), 8.70 (s, 1H, Ar-H), 9.86 (s, 1H, -NH pyrimidine ring), 10.21 (s, 1H, -NH amide), ^{13}C NMR: 18.11, 32.6, 50.31, 52.2, 56.1, 58.94, 65.22, 69.42, 113, 121.08, 123.79, 128.54, 130.67, 133.34, 136.34, 141.16, 142.78, 144.10, 145.74, 150.58, 164.27, 165.76, 212; MS (*m/z*): 448.17 (M^+); Anal. calcd. (found) % for $C_{23}H_{21}N_6O_3F$: C, 61.60 (61.65); H, 4.72 (4.76); N, 18.74 (18.71).-

5-(5-Formyl-2-hydroxy-3-methoxyphenyl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazole-[4,3-*a*]pyrimidine-6-carboxamide (6f): IR (KBr, ν_{max}, cm^{-1}): 3258, 3108, 3068, 2950, 2860, 2638, 2758, 1712,1597, 1590, 1490, 1356, 1280, 1185, 1121, 1085, 1068, 831, 789, 680, 596; ^{1}H NMR (δ ppm): 2.32 (s, 3H, -CH_3), 3.27 (s, 3H, -OCH_3), 3.59-3.63 (t, 2H, -CH_2- in morpholinone ring), 3.87-3.92 (t, 2H, -CH_2- in morpholinone ring), 4.20 (s, 2H, -CH_2- in morpholinone ring near hydroxy), 6.28 (s, 1H, -CH pyrimidine ring), 7.07 (d, 2H, Ar-H, *J* = 7.6 Hz), 7.24-7.32 (m, 3H, Ar-H), 7.61-7.78 (m, 3H, Ar-H), 7.94 (s, 1H, Ar-H), 9.31 (s, 1H, -aldehyde ring), 10.15 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 18.09, 32.1, 42.9, 45.9, 50.21, 53.2, 68.47, 112.08, 120.74, 126.58, 127.24, 128.03, 129.87, 132.68, , 136.37, , 137.34, 141.75, 145.97, 148.58, 165.24, 166.37, 192, 213; MS (*m/z*): 504.18 (M^+); Anal. calcd. (found) % for $C_{25}H_{24}N_6O_6$: C, 59.52 (59.57); H, 4.80 (4.83); N, 16.66 (16.62).

5-(5-formyl-2,3-dimethoxyphenyl)-7-methyl-N-(4-(3-oxomorpholino)phenyl)-5,8-dihydro-[1,2,4]triazole[4,3-a]pyrimidine-6-carboxamide (6g): IR (KBr, ν_{max}, cm^{-1}): 3320, 3260, 3188, 3067, 2935, 2758, 2632, 1738,1718, , 1583, ,1487, 1338, 1282, 1124, 1093, 1062, 834, 796, 680, 595; ^{1}H NMR (δ ppm): 2.29 (s, 3H, -CH_3), 2.33 (s, 3H, -CH_3), 3.42 (d, 3H, -OCH_3), 3.63-3.65 (t, 2H, -CH_2- in morpholinone ring), 3.91-3.97 (t, 2H, -CH_2- in morpholinone ring), 4.22 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.31 (s, 1H, -CH pyrimidine ring), 7.17 (d, 2H, Ar-H, *J* = 8.68 Hz), 7.21 (d, 2H, Ar-H, *J* = 7.6 Hz), 7.38 (d, 2H, Ar-H, *J* = 8.8 Hz), 7.58 (d, 2H, Ar-H, *J* = 9.6 Hz), 7.92 (s, 1H, Ar-H), 9.34 (s, 1H, -aldehyde ring), 10.06 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 17.13,33.2, 43.1, 47.2, 49.1, 50.3, 103.24, 111.08, 119.02, 120.58, 122.4, 128.69, 129.67, 135.93, 136.81, 137.45, 148.51, 150.10, 163.89, 172, 194, 214; MS (*m/z*): 518.19 (M^+); Anal. calcd. (found) % for $C_{26}H_{26}N_6O_6$: C, 60.22 (60.26); H, 5.05 (5.09); N, 16.21 (16.19).

5-(5-Formylfuran-2-yl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazole[4,3-*a*]pyrimidine-6-carboxamide (6h): IR (KBr, ν_{max}, cm^{-1}): 3631, 3298, 3107, 3052, 2964, 2752, 2628, 1728, 1649, 1579, 1475, 1343, 1118, 1058, 828, 767, 657, 559; ^{1}H NMR (δ ppm): 2.24 (s, 3H, -CH_3), 3.66-3.69 (t, 2H, -CH_2- in morpholinone ring), 3.94-3.97 (t, 2H, -CH_2- in morpholinone ring), 4.16 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.52 (s, 1H, -CH pyrimidine ring), 7.18-7.28 (m, 4H, Ar-H), 7.30 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.43 (d, 2H, Ar-H, 7.96 Hz), 7.89 (s, 1H, Ar-H), 9.41 (s, 1H, -aldehyde ring), 9.96 (s, 1H, -NH pyrimidine ring), 10.03 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 17.41, 32.9, 46.3, 48.5, 51.1, 67.73, 111.2, 120.2, 123.8, 128.14, 128.72, 133.13, 136.69, 136.86, 137.14,149.95, 164.87, 170, 195, 216 ; MS (*m/z*): 448.15 (M^+); Anal. calcd. (found) % for $C_{22}H_{20}N_6O_5$: C, 58.92 (58.96); H, 4.50 (4.54); N, 18.74 (18.71).

7-Methyl-*N*-(4-(3-oxomorpholino)phenyl)-5-(3-oxopropyl)-5,8-dihydro[1,2,4]triazole[4,3-*a*]pyrimidine-6-carboxamide (6i): IR (KBr, ν_{max}, cm^{-1}): 3286, 3190, 3072, 2949, 2830, 2732, 2622, 1768, 1705, 1550, 1470, 1340, 1310, 1280, 1129, 1076, 821, 779, 678, 590; ^{1}H NMR (δ ppm): 2.31 (s, 3H, -CH_3), 3.61-3.65 (t, 2H, -CH_2- in morpholinone ring), 3.68-3.79 (t, 2H, -CH_2- in morpholinone ring), 4.26 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.34 (s, 1H, -CH pyrimidine

ring), 7.29 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.53-7.59 (m, 2H, Ar-H), 7.81 (m, 3H, Ar-H), 7.95 (d, 1H, Ar-H, *J* = 7.6 Hz), 8.84 (s, 1H, Ar-H), 9.2 (s, 1H, -aldehyde ring), 9.79 (s, 1H, -NH pyrimidine ring), 9.97 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 17.62, 38.3, 40.2, 45.3, 48.9, 50.1, 105, 108, 120.6, 122.8, 124.3, 133.61, 134.78, 135.62 141.67, 143.11, 147.82, 149.67, 162, 164.79, 192, 218; MS (*m/z*): 410.17 (M^+); Anal. calcd. (found) % for $C_{20}H_{22}N_6O_4$: C, 58.53 (58.57); H, 5.40 (5.44); N, 20.48 (20.43).

5-(4-bromophenyl)-7-methyl-*N*-(4-(3-oxomorpholino)phenyl)-5,8-dihydro[1,2,4]triazole[4,3-*a*]pyrimidine-6-carboxamide (6j): IR (KBr, ν_{max}, cm^{-1}): 3277, 3155, 3058, 2920, 2874, 1670, 1590, 1478, 1327, 1288, 1210, 1192, 1022, 976, 817, 747, 662, 556; ^{1}H NMR (δ ppm): 2.28 (s, 3H, -CH_3), 3.57-3.61 (t, 2H, -CH_2- in morpholinone ring), 3.72-3.81 (t, 2H, -CH_2- in morpholinone ring), 4.02 (s, 2H, -CH_2- in morpholinone ring near ketone), 6.42 (s, 1H, -CH pyrimidine ring), 7.15 (d, 2H, Ar-H, *J* = 7.6 Hz), 7.28 (d, 2H, Ar-H, *J* = 8.4 Hz), 7.71 (d, 2H, Ar-H, *J* = 8.0 Hz), 7.92 (d, 2H, Ar-H, *J* = 7.6 Hz), 8.12 (s, 1H, Ar-H), 9.79 (s, 1H, -NH pyrimidine ring), 10.18 (s, 1H, -NH amide); ^{13}C NMR (δ ppm): 17.41, 49.52, 59.78, 64.14, 68.41, 103.62, 120.62, 124.92, 129.15, 130.02, 133.11, 136.55, 136.87, 137.28, 139.47, 147.85, 150.31, 164.65, 165.97; MS (*m/z*): 508.09 (M^+); Anal. calcd. (found) % for $C_{23}H_{21}N_6O_3Br$: C, 54.23 (54.28); H, 4.16 (4.12); N, 16.50 (16.54).

Biological activities: Triazolopyrimidine derivatives were screened for their *in vitro* antibacterial and antifungal activities following micro broth dilution method [35-37]. Antibacterial activity was screened against Gram-positive (*Bacillus subtillis* (MTCC 441), *Staphylococcus aureus* (MTCC 96)) and Gram-negative (*Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 1688)) microorganisms. Antifungal activity was screened against *Aspergillus niger* (MTCC 282) and *Penicillium* sp. microorganisms. The standard drugs used for this study were penicillin and streptomycin for antibacterial screening whereas griseofulvin was used for antifungal screening. The standard strains used for screening of antibacterial and antifungal activities were procured from the Culture collection and gene bank (MTCC), Chandigarh, India. Mueller Hinton Broth was used as a nutrient medium for bacteria and sabouraud dextrose broth for fungal growth. Inoculums size for test strain was adjusted to 108 CFU/mL by comparing the turbidity. The results were recorded in the form of primary and secondary screening. The stock solution (2000 μg/mL) of the compounds under investigation and standard drugs were prepared by successive two-fold dilution. In primary screening, 1000, 500 and 250 μg/mL concentrations of the compounds were used. The compounds found to be active in this primary screening were further screened. In secondary screening, 200, 100, 50, 25, 12.5 and 6.25 μg/mL concentrations were used. The inoculated wells were incubated overnight at 37 ºC in a humid atmosphere. The highest dilution showing complete inhibition was considered as a minimum inhibition concentration (MIC).

RESULTS AND DISCUSSION

The present work reports solid phase synthesis approch for the synthesis of triazolo[1,5-*a*]pyrimidnes (**6a-j**). 3-Oxo-*N*-(4-(3-oxomorpholino)phenyl)butanamide (**3**) was obtained by reaction of 4-(4-aminophenyl)morpholin-3-one (**1**) with 4-methyl-3-oxopentanoate (**2**) and catalytic amount of KOH in 1,4-dioxane at reflux temperature. The reaction of **3** with various aldehyde **4a-j** and 4*H*-1,2,4-triazol-3-amine (**5**) in DMF at refluxed temperature for appropriate time to afford targeted compound **6a-j** in moderate to excellent yield (70-80%).

Biological activities: The MIC values revealed that the synthesized compounds showed moderate to good inhibition. Compounds **6b**, **6d**, **6e**, **6h** and **6i** exhibited good activities against bacterial strains. The MIC values of antifungal activity showed that compounds **6b** and **6h** exhibited good activity against all fungal strain. Antimicrobial activity data of the synthesized compounds (**6a-j**) are listed in Table-2.

Conclusion

In summary, synthesis of novel triazolopyrimidine derivatives **6a-j** using solid phase synthesis reaction was executed successfully. The entire synthesized compound characterized and confirmed by spectroscopic data and elemental analysis. Additionally, all the synthesized compounds were screened for their antimicrobial activity against the selected pathogens and compared with standard drugs. Compound **6b** containing benzaldehyde moiety and compound **6h** with furfuraldehyde

TABLE-2
ANTIMICROBIAL ACTIVITY OF COMPOUNDS (**6a-j**)

Compound	Antibacterial MIC (μg/mL)				Antifungal MIC (μg/mL)	
	Bacillus subtilis	*Staphyaloccocus aureus*	*P. aeruginosa*	*E. coli*	*Penicillium sp.*	*Aspergillus niger*
Penicillin	50	50	–	–	–	–
Streptomycin	–	–	100	100	–	–
Griseofulvin	–	–	–	–	100	100
6a	500	500	500	1000	500	1000
6b	125	250	250	500	500	250
6c	500	1000	1000	1000	1000	1000
6d	250	500	500	250	500	1000
6e	250	500	500	250	1000	500
6f	500	1000	1000	500	1000	1000
6g	1000	500	500	500	500	1000
6h	250	500	125	250	500	250
6i	500	250	250	500	1000	500
6j	500	1000	1000	1000	1000	500

substituent were observed as most active against tested antibacterial and antifungal strains.

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CONFLICT OF INTEREST

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

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