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Synthesis of pyrimidine analogues linked with 1,2,3-triazole and morpholine as potential antibacterial agents

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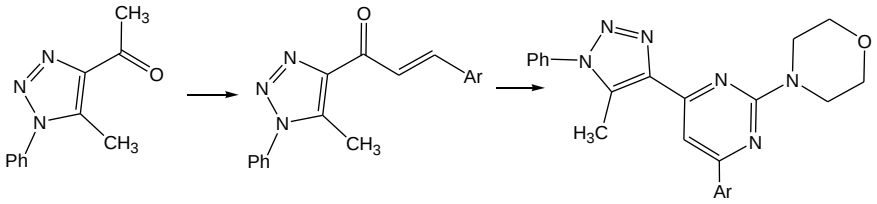
Abstract:
*A series of new 4-[4-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-6-aryl-2-pyrimidinyl] morpholine **4(a-j)** were synthesized and evaluated for their antibacterial activity against human pathogenic Gram-positive and Gram-negative bacterial strains. The structure activity relation (SAR) of compounds revealed that, which contain 4-methoxyphenyl **(4b)** 2,6-difluorophenyl **(4d)** and 4-chlorophenyl **(4f)** moiety on pyrimidine ring, displayed considerable antibacterial activity to that of standard drug against Gram-positive bacteria. Compounds, containing 4-methylphenyl **(4c)** and 4-hydroxy-3-methoxyphenyl **(4i)** were significant activity against B. subtilis, and M. luteus. The other compounds also exhibited considerable antibacterial activities.*



Keywords: Morpholine, Pyrimidine, Triazole, Antibacterial Activity.

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I. INTRODUCTION

The morpholine is an important pharmacophore played a vital role in medicinal chemistry and it is a core part of many important and clinically used drug structures, which possesses the desired biological and pharmacological activities such as Linezolid (antibiotic) contains a morpholine moiety is a commercially available antimicrobial drug. Aprepitant is a neurokinin 1 (NK1) receptor antagonist and is the first drug approved by Food and Drug Administration (FDA) for the treatment of chemotherapy induced nausea and vomiting. Gefitinib is a selective inhibitor of epidermal growth factor and clinically used for the treatment of chemoresistant non-small cell lung cancer patients. On the other hand, Timolol is a non-selective β-adrenergic receptor antagonist, used for the treatment of glaucoma. Emorfazone is an effective analgesic, antiinflammatory and antipyretic drug in animal models as well as in humans. The other activities of morpholine nucleus are, anti-inflammatory [1], analgesic [2], local anesthetic [3], anti-HIV [4], anticancer [5], appetite suppressant [6], antidepressant [7], antiplatelet [8], selective inhibitor of protein kinase C [9], neuroprotective [10], antitumor [11], antituberculosis [12], antimalarial [13], antiparasitic [14], hypocholesterolemic and hypolipidemic activities [15].

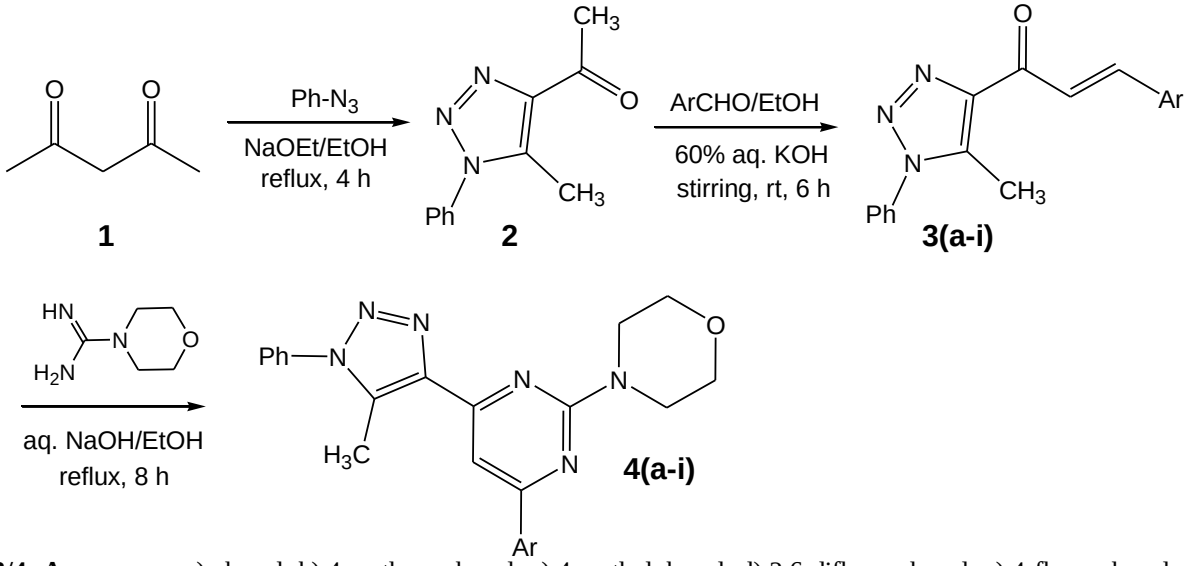
Similarly, the medicinal values of pyrimidine derivatives are significant and are found to possess antineoplastic [16], antiviral [17], antibiotic [18] and anti-inflammatory [19]. Further, the substituted pyrimidines with six membered rings exhibit a broad spectrum of biological effectiveness such as antitubercular [20], calcium channel blockers [21], anticancer and herbicidal activities [22]. Buspirone is a well known drug with pyrimidine moiety, indicated in the management of anxiety disorder encompassed with or without depression [23,24]. Terry *et al*, have evaluated the pyrimidine derivatives linked to morpholine group for its VEGF-R2 inhibitor activity and showed to the effective in a mouse model of cornealneo vascularisation [25]. Further, the applications of triazoles are increasingly found in all aspects of drug discovery, derivatives of triazole have been found to have antitubercular [26], anti-HIV [27], anti-allergenic [28], cytostatic [29], virostatic [30], anti-cancer [31], anticonvulsant [32], analgesic [33] and anti-inflammatory [34] activities. Triazoles are also being studied for the treatment of obesity [35] and osteoarthritis [36]. There are number of drugs, which are containing triazole nucleus, viz. Fluconazole [37], Isavuconazole [38], Itraconazole [39], Voriconazole [40], Pramiconazole [41] and Posaconazole, which have been used for the treatment of fungal infections.

Owing to the immense importance and varied biological activities exhibited by derivatives of morpholine, pyrimidine and triazoles, it was considered to combine these three active pharmacophores to get hybrid molecule for further investigation of their varied/enhancing biological and pharmacological activities. In the present study, a series of 4-[4-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-6-aryl-2-pyrimidinyl]morpholine **4(a-i)** were designed and synthesized. All the synthesized compounds were also screened for their antibacterial activity.

II. RESULTS AND DISCUSSION

The condensation and cyclization reaction of phenylazide with acetylacetone **1** in the presence of anhydrous potassium carbonate in DMF under reflux with stirring at 70 ^{o}C for 6-12 h, afforded 1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-1-ethanone **2**. The condensation of compound **2** with corresponding aromatic aldehydes in ethanol in the presence of 60% aq. potassium hydroxide at 5-10 ^{o}C under stirring at room temperature for 6 h, furnished the (*E*)-1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-3-aryl-2-propen-1-one **3(a-i)** in good yields. Further, the corresponding compound **3** was refluxed with 4-morpholinecarboximidamide in the presence of sodium hydroxide in ethanol for 8 h, at the end of the reaction, the ethanolic solution was concentrated to half of its volume under reduced pressure and poured into cold 10% HCl solution. The solid that separated was filtered and on purification by recrystallization from benzene-ethanol gave 4-[4-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-6-aryl-2-pyrimidinyl]morpholine **4(a-i)** in 60-70% yields (**Scheme 1**). The structures of the synthesized compounds were elucidated by IR, ^{1}H, ^{13}C NMR and MS spectral analysis.

The IR spectrum of compound **2**, the absorption bands due to C=O and C=N are appeared at 1713, 1619 cm^{-1}. Its ^{1}H NMR spectra, the aromatic protons of phenyl groups were appeared as a multiple at δ 7.40-7.50 and protons of CH_3 groups appeared as singlet at δ 2.32 and 2.50 ppm. Its ^{13}C NMR spectrum, the signals of triazole ring appeared at δ 128.8 and 139.4 ppm. The IR spectra of compounds **3a**, the absorption for C=O and C=C appeared at 1702 and 1612 cm^{-1}. N=N of triazole ring absorption bands appeared at 1532 cm^{-1}. Its proton NMR spectrum showed, aromatic protons and α-CH, β-CH proton signal at δ 7.30-7.40 and 7.60-7.70 ppm as multiplets for eight and four protons in each and a signal at δ 2.78 as singlet, integrating three protons assigned for methyl group. Its ^{13}C NMR spectrum exhibit the signal at δ 134.5 and 133.9 for (C-5) and (C-4) carbons of triazole ring, the carbonyl carbon and ene carbons appeared at 172.9 (C=O) 130.6 (α-C) and (β-C) 145.6 ppm.



3/4: Ar = a) phenyl; b) 4-methoxyphenyl; c) 4-methylphenyl; d) 2,6-difluorophenyl; e) 4-fluorophenyl; f) 4-chlorophenyl; g) 4-bromophenyl; h) 4-nitrophenyl; i) 4-hydroxy-3-methoxyphenyl.

Scheme 1

The IR spectrum of **4a** showed absorption bands at 1532 and 1612 cm^{-1} due to N=N and C=N of triazole and pyrimidine ring. Its proton NMR spectra, the signal for methyl protons attached to triazole ring appeared at δ 2.62 as singlet. The morpholine protons signals appeared at δ 3.45-3.50 and 3.65-3.70 ppm as multiplets integrating four protons in each. The signal for aromatic protons of phenyl ring on triazole and on pyrimidine ring appeared as a multiplet in the region of δ 7.35-7.40, 7.60-7.70 respectively. The aromatic proton of pyrimidine ring on 4th position appeared as a singlet at δ 8.88 ppm. Its ^{13}C NMR spectra the signals of triazole ring carbons appeared at δ 135.7 (C-4), 127.9 (C-5) and the pyrimidine ring carbons appeared at δ 159.0

(C-2), 172.4 (C-4), 118.5 (C-5), 162.8 (C-6) ppm, the morpholine ring carbons appeared as a multiplet in the range of δ 47.5 and 69.0 ppm.

III. ANTIBACTERIAL ACTIVITY

All the newly sythesized compounds **4(a-i)** were evaluated for their *in vitro* antibacterial activity against three representative Gram-positive bacteria *viz. Bacillus subtilis* (ATCC 6633), *Staphylococcus aureus* (ATCC 6538p) and *Micrococcus luteus* (IFC 12708) and three Gram-negative bacteria *viz. Proteus vulgaris* (ATCC 3851), *Salmonella typhimurium* (ATCC 14028) and *Escherichia coli* (ATCC 25922) by the broth dilution method[42]. For the determination of minimum inhibitory concentration (MIC, μg/mL), the bacteria were grown over night in Luria Bertani (LB) broth at 37 °C, harvested by centrifugation, and then washed twice with sterile distilled water. Stock solutions of the series of compounds were prepared in dimethyl sulfoxide (DMSO). Each stock solution was diluted with standard method broth (Difco) to prepare serial two-fold dilutions in the range of 50 to 0.8 µg/mL. Ten microliters of the broth containing about 10^5 colony forming units (cfu)/mL of test bacteria were added to each well of 96-well microtiter plate. Culture plates were incubated for 24 h at 37 °C, and the growth was monitored visually and spectrophotometrically. The lowest concentration required to arrest the growth of bacteria was regarded as MIC (µg/mL), was determined for all the compounds and compared Amphicillin.

The structure activity relation (SAR) for compounds **4(a-i)** with different substituents on the benzene ring attached to pyrimidine ring, revealed that these compounds were more active only towards Gram-positive bacteria. Compounds, which contain 4-methoxyphenyl (**4b**) 2,6-difluorophenyl (**4d**) and 4-chlorophenyl (**4f**) moiety on pyrimidine ring, displayed considerable antibacterial activity to that of standard drug against Gram-positive bacteria. Compounds, containing 4-methylphenyl (**4c**) and 4-hydroxy-3-methoxyphenyl (**4i**) were significant activity against *B. subtilis*, and *M. luteus* (**Table 1**). The other compounds also exhibited considerable antibacterial activities. In general, most of the newly synthesized compounds displayed good to excellent antibacterial activity.

Table 1. Antibacterial activity of compounds 4(a-i)

Compound	Minimum Inhibitory Concentration (MIC) in μg/mL					
	B. subtilis	***S. aureus***	***M. luteus***	***P. vulgaris***	***S. typhimurium***	***E. coli***
4a	6.25	12.5	6.25	25.0	6.25	50.0
4b	3.12	1.56	1.56	6.25	12.5	25.0
4c	3.12	3.12	3.12	12.5	12.5	25.0
4d	1.56	1.56	1.56	2.25	12.5	25.0
4e	6.25	6.25	12.5	25.0	25.0	50.0
4f	1.56	3.12	1.56	12.5	25.0	50.0
4g	12.5	6.25	6.25	50.0	12.5	12.5
4h	6.25	3.12	3.12	25.0	12.5	25.0
4i	1.56	12.5	1.56	12.5	6.25	12.5
Ampicillin	1.56	1.56	1.56	3.12	3.12	12.50

IV. MATARIALS AND METHODS

All reagents are commercial grade and were used as supplied. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized by exposure to UV light. Chromatographic columns 70–230 mesh silica gel for separations were used. IR spectra were recorded using KBr disk on a Perkin–Elmer FTIR spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C). Chemical shifts are reported in δ ppm units with respect to TMS as internal standard and coupling constants (*J*) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer.

Preparation of 1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-1-ethanone (2): To a mixture of phenylazide **1** (0.01 mol), acetylacetone (0.04 mol) in DMF (30 mL), anhydrous K_2CO_3 (0.06 mol) was added and refluxed with stirring at 70 ^{0}C for 6-12 h, the progress of the reaction was checked by TLC. After the completion of reaction, the solvent was removed and solid mass was quenched in ice water and then neutralized with 5%

hydrochloric acid. Extracted the product with DCM and the crude product was purified by chromatography using petroleum ether/ethyl acetate (8:1-6:1) as eluent to get compound **2**. IR (KBr) ν_{max}: 3057, 2978, 1714, 1619, 1548, 1467 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 7.40-7.50 (m, 5H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 14.9, 29.6, 114.7, 128.8, 129.1, 134.3, 139.0, 139.9, 193.1; MS: *m/z* 199 (M^+).

General procedure for synthesis of (*E*)-1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-3-aryl-2-propen-1-one 3(a-j): A solution of compound **2** (0.01 mol) and corresponding aldehyde (0.01 mol) in ethanol (20 mL) was treated with 60% aq. KOH solution (20 mL) at 5-10 ^oC. The reaction mixture was stirred at room temperature for 6 h. It was then diluted with water (20 mL) and extracted with diethyl ether (3 x 20 mL). The aqueous solution was acidified with dilute HCl. The solid obtained was filtered washed thoroughly with water and dried. The crude product was purified by crystallization from benzene: methanol (3: 2) to get the pure compound **3(a-i)**.

(*E*)-1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-3-aryl-2-propen-1-one (3a): IR (KBr) ν_{max}: 3078 (CH-Ar), 2968 (CH-Ali), 1702 (C=O), 1612 (C=C), 1532 (N=N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.78 (s, 3H, CH_3), 7.30-7.40 (m, 8H, ArH), 7.60-7.70 (m, 4H, ArH, CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 24.3, 125.3, 128.7, 129.4, 130.1, 130.6, 131.2, 131.9, 133.9, 134.5, 137.9, 139.0, 145.6, 172.9; MS: *m/z* 290 (M^++1).

General procedure for the synthesis of 4-[4-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-6-aryl-2-pyrimidinyl]morpholine 4(a-i): A solution of **3(a-i)** (0.01 mol) and 4-morpholine- carboximidamide (0.03 mol) in 20 mL ethanol was added 5 mL of aqueous NaOH (0.02 mol). The reaction mixture was refluxed. TLC (EtOAc: Petroleum-ether, 2:1) showed that the reaction was complete in 8 h. The reaction mixture was poured in 50 mL of 10% cold HCl solution and the precipitate was filtered, washed with water, until free from acid and on recrystallized from benzene-ethanol gave **4(a-i)**.

4-[4-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-6-phenyl-2-pyrimidinyl]morpholine (4a): IR (KBr) ν_{max}: 3064, 2967, 1612, 1595, 1532, 1484, 1394, 1210 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.62 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.35-7.40 (m, 5H, ArH), 7.60-7.70 (m, 5H, ArH), 8.88 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.7, 47.5, 69.0, 116.8, 118.6, 125.1, 125.9, 127.9, 128.6, 128.9, 129.0, 129.9, 135.7, 138.7, 139.0, 159.0, 162.8, 171.2; MS: *m/z* 399 (M^++1).

4-[4-(4-methoxyphenyl)-6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-pyrimidinyl] morpholine (4b): IR (KBr) ν_{max}: 3067, 2969, 1614, 1594, 1532, 1487, 1395, 1210, 1072 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.65 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.70-7.75 (m, 7H, morpholine-CH_2 and CH_3), 7.05 (d, *J* = 8.6 Hz, 2H, ArH), 7.35-7.40 (m, 5H, ArH), 7.75 (d, *J* = 8.6 Hz, 2H, ArH), 8.86 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.6, 48.1, 56.0, 69.2, 113.7, 115.7, 118.4, 125.4, 127.5, 127.9, 128.0, 128.2, 135.1, 137.9, 141.6, 157.8, 158.9, 162.2, 171.2; MS: *m/z* 428 (M^+).

4-[4-(4-methylphenyl)-6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-pyrimidinyl] morpholine (4c): IR (KBr) ν_{max}: 3072, 2968, 1617, 1597, 1533, 1487, 1391, 1212 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.41 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.12 (d, *J* = 8.4 Hz, 2H, ArH), 7.35-7.40 (m, 5H, ArH), 7.71 (d, *J* = 8.4 Hz, 2H, ArH), 8.82 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 21.9, 23.7, 47.7, 68.9, 116.2, 118.4, 124.9, 125.4, 127.3, 127.9, 128.5, 129.0, 135.5, 136.8, 137.5, 137.9, 158.8, 161.4, 171.2; MS: *m/z* 413 (M^++1).

4-[4-(2,6-difluorophenyl)-6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-pyrimidinyl] morpholine (4d): IR (KBr) ν_{max}: 3087, 2991, 1616, 1592, 1536, 1486, 1395, 1213 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.60 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.05 (d, *J* = 8.4 Hz, 2H, ArH), 7.35-7.40 (m, 6H, ArH), 8.89 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.3, 47.1, 69.5, 111.9, 115.9, 118.9, 119.1, 125.8, 126.8, 128.1, 128.8, 134.6, 135.0, 137.2, 158.5, 160.1, 161.5, 171.2; MS: *m/z* 434 (M^+).

4-[4-(4-fluorophenyl)-6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-pyrimidinyl] morpholine (4e): IR (KBr) ν_{max}: 3087, 2993, 1615, 1594, 1530, 1482, 1393, 1214 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.68 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.07 (d, *J* = 8.2 Hz, 2H, ArH), 7.35-7.40 (m, 5H, ArH), 7.72 (d, *J* = 8.4 Hz, 2H, ArH), 8.87 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-

d_6): δ 22.5, 47.1, 69.1, 115.8, 116.7, 118.2, 125.4, 126.9, 127.7, 128.8, 129.0, 134.9, 137.5, 138.5, 158.8, 161.5, 164.7, 171.2; MS: *m/z* 416 (M^+).

4-[4-(4-chlorophenyl)-6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-pyrimidinyl] morpholine (4f): IR (KBr) ν_{max}: 3069, 2987, 1614, 1597, 1535, 1481, 1399, 1211, 686 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.61 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.09 (d, *J* = 8.7 Hz, 2H, ArH), 7.35-7.40 (m, 5H, ArH), 7.81 (d, *J* = 8.7 Hz, 2H, ArH), 8.83 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 21.5, 46.9, 68.9, 115.8, 118.1, 125.5, 127.8, 128.0, 128.8, 129.0, 129.9, 132.8, 134.8, 137.9, 138.5, 158.7, 160.1, 171.2; MS: *m/z* 432 (M^+).

4-[4-(4-bromophenyl)-6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-pyrimidinyl] morpholine (4g): IR (KBr) ν_{max}: 3072, 2989, 1618, 1593, 1537, 1480, 1395, 1213, 587 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.66 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.35-7.40 (m, 5H, ArH), 7.55-7.60 (m, 5H, ArH), 8.87 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.5, 46.9, 68.8, 115.2, 117.9, 123.0, 124.5, 126.8, 128.1, 129.2, 129.7, 132.0, 134.8, 137.5, 138.5, 158.3, 161.2, 171.2; MS: *m/z* 477 (M^+).

4-[4-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-6-(4-nitrophenyl)-2-pyrimidinyl] morpholine (4h): IR (KBr) ν_{max}: 3089, 2982, 1618, 1591, 1578, 1536, 1481, 1393, 1212 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.71 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 7.35-7.40 (m, 5H, ArH), 8.10-8.20 (m, 4H, ArH), 8.85 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.4, 47.8, 68.7, 115.9, 119.1, 124.1, 125.5, 126.8, 127.8, 128.4, 129.0, 135.2, 138.1, 139.8, 145.8, 159.2, 162.5, 171.2; MS: *m/z* 443 (M^+).

2-methoxy-4-[6-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-morpholino-4-pyrimidinyl] phenol (4i): IR (KBr) ν_{max}: 3437, 3091, 2989, 1617, 1599, 1537, 1485, 1397, 1214, 1078 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.69 (s, 3H, CH_3), 3.45-3.50 (m, 4H, morpholine-CH_2), 3.65-3.70 (m, 4H, morpholine-CH_2), 3.91 (s, 3H, OCH_3), 5.27 (s, 1H, OH), 7.10 (d, *J* = 8.2 Hz, 1H, ArH), 7.35-7.40 (m, 6H, ArH), 7.75 (d, *J* = 8.2 Hz, 1H, ArH), 8.83 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.7, 47.5, 56.7, 69.0, 111.3, 116.8, 117.8, 118.6, 124.0, 125.1, 127.9, 128.6, 128.9, 135.7, 136.2, 138.7, 146.8, 149.8, 159.0, 162.8, 172.1; MS: *m/z* 445 ($M^+ + 1$).

V. CONCLUSION

A series of new 4-[4-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-6-aryl-2-pyrimidinyl] morpholine **4(a-j)** were synthesized and evaluated for their antibacterial activity against human pathogenic bacterial strains *viz. Bacillus subtilis*, *Staphylococcus aureus* and *Micrococcus luteus*, *Proteusvulgaris*, *Salmonella typhimurium* and *Escherichia coli*. The structure activity relation (SAR) of compounds, which contain 4-methoxyphenyl (**4b**) 2,6-difluorophenyl (**4d**) and 4-chlorophenyl (**4f**) moiety on pyrimidine ring, displayed considerable antibacterial activity to that of standard drug against Gram-positive bacteria. Compounds, containing 4-methylphenyl (**4c**) and 4-hydroxy-3-methoxyphenyl (**4i**) were significant activity against *B. subtilis*, and *M. luteus.* The other compounds also exhibited considerable antibacterial activities.

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