ARTICLE

Study of Antimicrobial Activity of Some Synthesized Pyrimidine-Triazole Derivatives

J.J. Majithiya✉ and B.M. Bheshdadia

www.asianpubs.org

Asian Journal of Organic & Medicinal Chemistry

Volume: 7 Year: 2022
Issue: 2 Month: April–June
pp: 205–210
DOI: https://doi.org/10.14233/ajomc.2022.AJOMC-P385

Received: 4 April 2022
Accepted: 14 June 2022
Published: 29 June 2022

ABSTRACT

Some novel derivatives of 2,2′-(4,4′-(((4-(3-oxomorpholino)phenyl)-azanediyl)-*bis*(methylene))*bis*(1*H*-1,2,3-triazole-4,1-diyl))*bis*(N-(4-phenyl-pyrimidin-2-yl)acetamide) have been synthesized from 4-(4-aminophenyl)morpholin-3-one molecule by multistep process. The structures of all the synthesized compounds were established by different spectroscopic techniques such as ^{1}H NMR, infrared and mass. The antimicrobial activity of these pyrimidine-triazole derivatives were also investigated against selected bacterial and fungal strains in two different organic solvents (*N,N*-dimethyl formamide and dimethyl sulphoxide).

KEYWORDS

Pyrimidine-triazole derivatives, Antimicrobial activity, *N,N*-Dimethyl formamide, Dimethyl sulphoxide.

INTRODUCTION

In chemistry, heterocyclic compounds containing nitrogen as heteroatom plays important role in agrochemical and pharmaceuticals [1,2]. Nitrogen containing five- and six-membered heterocyclic compounds are found in many naturally occurring compounds as well as synthesized in the laboratories [3]. Triazole is one of the five member heterocyclic compounds possess different biological and pharmaceutical activities such as antibacterial [4,5], antifungal [6,7], antimalarial [8,9], antitubercular [10-12], anticancer [13,14] and antioxidant [15]. As a core structure, triazole scaffolds was found in many drugs present in the market [16,17].

Further, six membered heterocyclic compounds having nitrogen as a heteroatom; pyrimidine also shows excellent activity in medicinal field. Pyrimidine display a broad range of biological activities and are found in many biological and pharmaceutical active molecules occurring naturally as well as synthesized in laboratory [18-21]. Literature survey show that the biological activity enhanced when two different heterocycles present in the same molecule [22]. It is observed that the when molecule have two or more than two heterocyclic scaffolds than molecule show vast biological and pharmaceutical activities.

In present work, some new heterocyclic compounds having triazole-pyrimidine scaffold were synthesized by multi step process from 4-(4-aminophenyl)morpholin-3-one. For the structure conformation, different spectroscopic techniques such as ^{1}H NMR, IR and mass spectrometry were used. Further,

Author affiliations:

Department of Chemistry, Shree M.M. Science College, Morbi-363642, India

✉To whom correspondence to be addressed:

E-mail: majithia.j@gmail.com

Available online at: http://ajomc.asianpubs.org

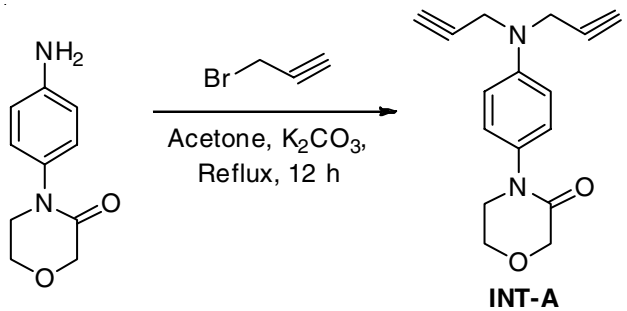
antimicrobial activity of the synthesized compounds was also tested against some selected bacterial as well as fungal strains in two different solvents such as *N,N*-dimethyl formamide and dimethyl sulphoxide solvents.

EXPERIMENTAL

For structure conformation of all the synthesized compounds, some analytical spectroscopic techniques such as infrared (IR), proton magnetic resonance (^{1}H NMR) and mass analysis were used. For the infrared spectrum, Fourier Transform infrared spectrophotometer (IRaffinity-1S Shimadzu) was used. The IR spectrum was done in moisture free atmosphere. The proton spectrum of all the synthesized compounds was recorded on a Bruker AVANCE III (400 MHz frequencies). For ^{1}H NMR analysis, solution of compounds was prepared in Deuterated dimethyl sulphoxide (DMSO-d_6) solvent and tetra methylsilane was used as reference material. Mass spectra were determined using direct inlet probe on a Shimadzu GC-MS (Model-QP2010) mass spectrometer.

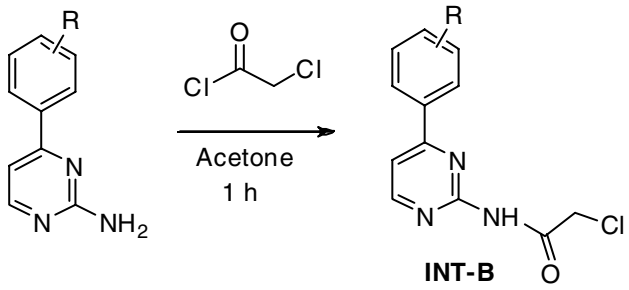
The chemicals used for the synthesis such as different substituted acetophenone, malonitrile, carbon disulphide were purchased from Spectrochem Pvt. Ltd. and used direct without further any purification. Different solvents used for reaction and anti microbial activity were purchased from Sigma-Aldrich Pvt. Ltd and used directly without any further purification.

Synthesis of 4-(4-(di(prop-2-yn-1-yl)amino)phenyl)-morpholin-3-one (INT-A): In a round bottom flask, a solution of 4-(4-aminophenyl)morpholin-3-one (0.01 mmol) was prepared in anhydrous acetone (100 mL) and to this anhydrous K_2CO_3 (0.02 mmol) was added in a single portion. The resultant solution was stirred for additional 10 min. After that propagyl bromide (0.012 mmol) was added dropwise in same experimental condition. After complete addition, shift the reaction flask in water bath and was refluxed for 12 h with constant stirring. The reaction was monitored through the preparative TLC using mixture of hexane:ethyl acetate (3:7%) as mobile phase. After the completion of reaction, the reaction mixture was poured into the crushed ice. Filtered the separated product, washed with cold water and dried under vacuum (**Scheme-I**).



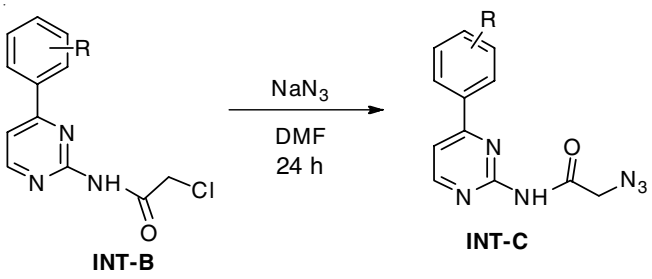
Scheme-I

Synthesis of 2-chloro-N-(4-phenylpyrimidin-2-yl)-acetamide (INT-B): Prepared a solution of substituted 4-phenylpyrimidin-2-amine (0.01 mmol) in anhydrous acetone and to this chloroacetyl chloride (0.012 mmol) was added dropwise. The resultant solution was stirred in presence of catalytic amount of triethyl amine. The reaction mixture was stirred additionally for 1 h at room temperature. After completion of reaction, checked through preparative TLC, the reaction mixture was poured into crushed ice with constant stirring. Filtered the separated product, washed with cold water and was dried under vacuum to give INT-B (**Scheme-II**).



Scheme-II

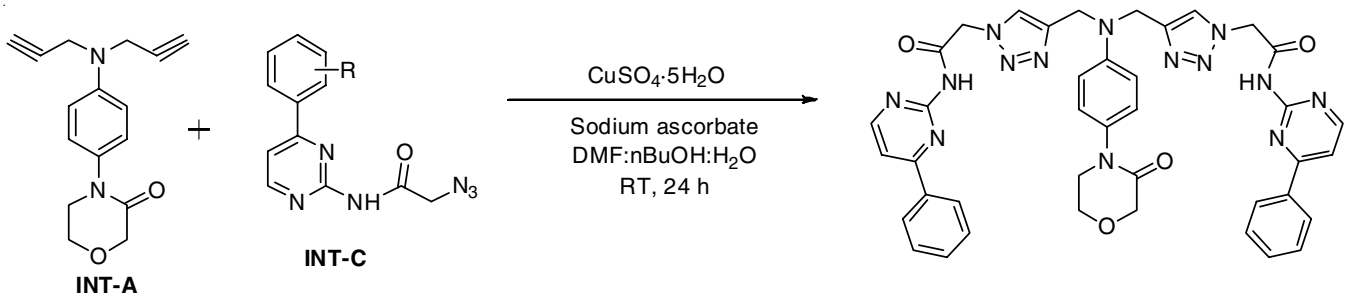
Synthesis of 2-azido-N-(4-phenylpyrimidin-2-yl)-acetamide derivatives (INT-C): INT-B (0.0.1 mmol) was dissolved in dry *N,N*-dimethyl formamide solvent and to this sodium azide (0.02 mmol) was added in single portion. The resulting mixture was stirred at room temperature for next 24 h. The reaction progress was checked through the preparative TLC using hexane:ethyl acetate (2:8%) mixture as mobile phase. After completion of reaction, the reaction mixture was poured into crushed ice with constant stirring. Solid product separated was filtered under vacuum and finally washed with cold water (**Scheme-III**).



Scheme-III

General synthesis of 2,2′-(4,4′-(((4-(3-oxomorpholino)-phenyl)azanediyl)*bis*(methylene))*bis*(1*H*-1,2,3-triazole-4,1-diyl))*bis*(*N*-(4-phenylpyrimidin-2-yl)acetamide) derivatives: In a round bottom flask, solution of **INT-A** (0.01 mmol) and **INT-C** (0.01 mmol) was prepared in ternary solvent system; *N,N*-dimethyl formamide:water:*n*-butanol (1:1:1). To this mixture of sodium ascorbate and copper sulphate was added into catalytic amount and resultant mixture was stirred at room temperature for 24 h. The completion of reaction was confirmed by preparative TLC using chloroform: methanol (8:2%) as mobile phase. After the completion of reaction, mixture poured into the crushed ice and was filtered the separated solid product (**Scheme-IV**).

JMM-1: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.610 (1.27, -CH_2-, ring), 3.914 (1.16, -CH_2-, ring), 4.134 (1.13, -CH_2-, ring), 4.736 (2.04, -CH_2-, open chain), 5.662 (1.94, -CH_2-CO-), 6.942-6.959 (1.0, Ar-H), 7.114-7.132 (1.06, Ar-H), 7.542 (3.25, Ar-H), 7.786 (1.13, Ar-H), 7.993 (1.11, Ar-H), 8.183



Scheme-IV

(2.13, Ar-H), 8.711 (1.00, Ar-H), 11.113 (0.96, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3563.73, 3508.45, 3433.48 (amides, *sec.* N-H *str.*), 3202.84, 3141.33 (=C-H *str*. aromatic ring), 1685.24, 1607.57, 1511.23 (N-H bending *sec.* amines), 1314.62, 1257.91 (C-N *str.* aromatic), 969.31, 931.70 (primary & secondary N-H wagging) *m/z* = 777.2.

JMM-2: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.613 (1.12, -CH_2-, ring), 3.916 (1.14, -CH_2-, ring), 4.135 (1.17, -CH_2-, ring), 4.738 (2.07, -CH_2-, open chain), 5.665 (2.00, -CH_2-CO-), 6.940-6.958 (1.05, Ar-H), 7.112-7.130 (1.03, Ar-H), 7.672 (3.09, Ar-H), 7.761 (1.16, Ar-H), 7.998 (1.11, Ar-H), 8.289 (1.01, Ar-H), 8.715 (1.01, Ar-H), 11.115 (0.98, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3570.71, 3512.40, 3440.91 (amides, *sec.* N-H *str.*), 3212.89, 3135.49 (=C-H *str.* aromatic ring), 1681.57, 1601.98, 1521.33 (N-H bending *sec.* amines), 1311.59, 1280.32 (C-N *str.* aromatic), 971.44, 938.76 (primary & secondary N-H wagging) *m/z* = 935.3.

JMM-3: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.614 (1.08, -CH_2-, ring), 3.918 (1.10, -CH_2-, ring), 4.138 (1.05, -CH_2-, ring), 4.741 (2.00, -CH_2-, open chain), 5.626 (2.05, -CH_2-CO-), 6.939-6.961 (1.34, Ar-H), 7.113-7.135 (1.18, Ar-H), 7.719-7.769 (3.24, Ar-H), 7.962 (1.00, Ar-H), 8.105-8.126 (1.14, Ar-H), 8.702-8.714 (1.06, Ar-H), 8.749 (1.01, Ar-H), 11.144 (1.01, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3557.61, 3499.92, 3448.05 (amides, *sec.* N-H *str.*), 3260.45, 3179.68 (=C-H *str.* aromatic ring), 1697.69, 1643.01 (N-H bending *sec.* amines), 1390.93, 1329.16, 1272.14 (C-N *str.* aromatic), 913.14 (primary & secondary N-H wagging) *m/z* = 935.3.

JMM-4: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.614 (1.11, -CH_2-, ring), 3.915 (1.13, -CH_2-, ring), 4.137 (1.09, -CH_2-, ring), 4.737 (2.12, -CH_2-, open chain), 5.664 (2.05, -CH_2-CO-), 6.943-6.963 (1.34, Ar-H), 7.116-7.134 (1.18, Ar-H), 7.611 (3.24, Ar-H), 7.762 (1.00, Ar-H), 7.995 (1.00, Ar-H), 8.245 (1.15, Ar-H), 8.720 (1.02, Ar-H), 11.118 (1.01, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3565.34, 3540.39, 3441.63 (amides, *sec.* N-H *str.*), 3240.48, 3145.36 (=C-H *str.* aromatic ring), 1686.33, 1612.14, 1535.89 (N-H bending *sec.* amines), 1394.29, 1325.34, 1289.32 (C-N *str.* aromatic), 979.12, 933.03 (primary & secondary N-H wagging) *m/z* = 846.9.

JMM-5: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.611 (1.12, -CH_2-, ring), 3.912 (1.07, -CH_2-, ring), 4.132 (1.15, -CH_2-, ring), 4.737 (2.02, -CH_2-, open chain), 5.666 (2.04, -CH_2-CO-), 6.946-6.964 (1.19, Ar-H), 7.115-7.135 (1.13, Ar-H), 7.598 (2.02, Ar-H), 7.763 (1.01, Ar-H), 7.991 (1.04, Ar-H), 8.012 (1.10, Ar-H), 8.716 (2.24, Ar-H), 11.119 (1.01, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3561.09, 3545.29, 3444.29 (amides, *sec.* N-H *str.*), 3251.29, 3148.20 (=C-H *str.* aromatic ring), 1681.03, 1615.29, 1539.99 (N-H bending *sec.* amines), 1397.21, 1321.59, 1294.30 (C-N *str.* aromatic), 983.05, 938.27 (primary & secondary N-H wagging) *m/z* = 846.9.

JMM-6: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.613 (1.18, -CH_2-, ring), 3.911 (1.14, -CH_2-, ring), 4.135 (1.11, -CH_2-, ring), 4.739 (2.10, -CH_2-, open chain), 5.663 (2.08, -CH_2-CO-), 6.949-6.968 (1.21, Ar-H), 7.117-7.137 (1.12, Ar-H), 7.684 (2.05, Ar-H), 7.765 (1.08, Ar-H), 7.996 (1.03, Ar-H), 8.711 (1.06, Ar-H), 8.989 (1.25, Ar-H), 11.111 (0.98, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3575.39, 3518.98, 3434.23 (amides, *sec.* N-H *str.*), 3258.12, 3146.02 (=C-H *str.* aromatic ring), 1689.26, 1621.39, 1545.27 (N-H bending *sec.* amines), 1390.04, 1327.72, 1298.29 (C-N *str.* aromatic), 986.29, 939.21 (primary & secondary N-H wagging). *m/z* = 915.4.

JMM-7: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 1.387 (3.01, -CH_3), 3.612 (1.18, -CH_2-, ring), 3.910 (1.14, -CH_2-, ring), 4.132 (1.11, -CH_2-, ring), 4.736 (2.10, -CH_2-, open chain), 5.662 (2.08, -CH_2-CO-), 6.943-6.962 (1.21, Ar-H), 7.119-7.139 (2.12, Ar-H), 7.666 (2.05, Ar-H), 7.977 (1.08, Ar-H), 8.102 (1.01, Ar-H), 8.714 (2.06, Ar-H), 11.114 (0.98, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3565.20, 3506.29, 3447.15 (amides, *sec.* N-H *str.*), 3218.27, 3141.92 (=C-H *str.* aromatic ring), 1684.29, 1607.27, 1515.39 (N-H bending *sec.* amines), 1319.92, 1285.23 (C-N *str.* aromatic), 977.83, 945.29 (primary & secondary N-H wagging) *m/z* = 805.9.

JMM-8: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 1.304 (3.01, -CH_3), 3.616 (1.14, -CH_2-, ring), 3.917 (1.17, -CH_2-, ring), 4.132 (1.13, -CH_2-, ring), 4.740 (2.04, -CH_2-, open chain), 5.667 (2.15, -CH_2-CO-), 6.940-6.963 (1.17, Ar-H), 7.113-7.134 (1.10, Ar-H), 7.432 (2.05, Ar-H), 7.767 (1.11, Ar-H), 7.811 (2.05, Ar-H), 7.992 (1.07, Ar-H), 8.713 (1.02, Ar-H), 11.110 (0.97, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3551.38, 3494.20, 3455.92 (amides, *sec.* N-H *str.*), 3263.29, 3182.39 (=C-H *str.* aromatic ring), 1689.29, 1648.22 (N-H bending *sec.* amines), 1399.29, 1335.28, 1278.29 (C-N *str.* aromatic), 918.29 (primary & secondary N-H wagging) *m/z* = 805.9.

JMM-9: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 1.306 (3.00, -CH_3), 1.459 (3.04, -CH_3), 3.615 (1.05, -CH_2-, ring), 3.917 (1.11, -CH_2-, ring), 4.137 (1.09, -CH_2-, ring), 4.745 (2.00, -CH_2-, open chain), 5.668 (2.09, -CH_2-CO-), 6.945-6.965 (1.31, Ar-H), 7.119-7.138 (1.01, Ar-H), 7.544 (3.14, Ar-H), 7.769 (1.10, Ar-H), 7.992 (1.03, Ar-H), 8.710 (2.03, Ar-H), 11.119 (0.98, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3569.22, 3546.29, 3442.30 (amides, *sec.* N-H *str.*), 3248.10, 3140.48 (=C-H *str.* aromatic ring), 1682.10, 1625.29, 1540.03 (N-H bending *sec.* amines), 1395.29, 1322.60, 1281.38 (C-N *str.* aromatic), 973.49, 941.06 (primary & secondary N-H wagging) *m/z* = 833.9.

JMM-10: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.056 (3.07, -OCH_3), 3.612 (1.13, -CH_2-, ring), 3.914 (1.11, -CH_2-, ring), 4.139 (1.17, -CH_2-, ring), 4.744 (2.15, -CH_2-, open chain), 5.669 (2.02, -CH_2-CO-), 6.951-6.972 (1.05, Ar-H), 7.120-7.143 (1.04, Ar-H), 7.611 (2.09, Ar-H), 7.766 (1.11, Ar-H), 7.808 (1.01, Ar-H), 7.991 (1.07, Ar-H), 8.715 (2.02, Ar-H), 11.122 (0.98, -NH-). IR (KBr, ν_{max}, cm^{-1}): 3565.24, 3555.20, 3448.46 (amides, *sec.* N-H *str.*), 3253.47, 3132.49 (=C-H *str.* aromatic ring), 1688.39, 1621.42, 1548.38 (N-H bending *sec.* amines), 1389.27, 1328.06, 1288.58 (C-N *str.* aromatic), 971.39, 945.72 (primary & secondary N-H wagging) *m/z* = 837.9.

Antimicrobial activity

Microorganisms tested: The antimicrobial activity of all the synthesized triazole-pyrimidine derivatives was tested against some selected Gram-positive and Gram-negative bacterial strains in two different solvents, *viz. N,N*-dimethyl formamide and dimethyl sulphoxide. The antifungal activity of all these derivatives was also tested against selected fungal strains in two different organic solvents. For the antimicrobial activity, agar well diffusion method was used. In this method, first of all colonies of bacteria or fungal is developed into petriplates under appropriate condition. The microorganisms were maintained on nutrient agar and MGYP medium.

The Gram-positive bacteria studied were *Bacillus cereus* (BC), *Corynebacterium rubrum* (CR), *Bacillus subtilis* (BS) and *Staphylococcus aureus* (SA). Gram-negative bacteria were *Klebsiella pneumoniae* (KP), *Staphylococcus typhimurium* (ST), *Escherichia coli* (EC), *Pseudomonas aeruginosa* (PA) and fungi were *Candida albicans* (CA), *Candida glabrata* (CG), *Candida epicola* (CE) and *Cryptococcus neoformans* (CN).

The solution of the synthesized compounds was prepared into *N,N*-dimethyl formamide and dimethyl sulphoxide solvent of 20 mg/mL concentration. For each compound in each selected solvent for a particular one strain, the experiment was repeated three times. For better understanding of antimicrobial activity of all the synthesized compounds, the standard antibiotic compounds were also tested *via* same method. For the antibacterial study, chloramphenicol and tetracycline were used as reference drugs for comparison with activity of synthesized compounds. For the antifungal strains, nystatin and itraconazole antibiotics were compared.

RESULTS AND DISCUSSION

Some physical constants such as substitution, molecular formula and molecular weight are given in Table-1.

The antibacterial activity of all the synthesized compounds along with two standard antibiotics in *N,N*-dimethyl formamide is represented in Fig. 1. It is observed that against *Bacillus cereus* in DMF, all the tested compounds showed inhibition and out of them compound **JMM-6** showed maximum, while compound **JMM-7** exhibited the minimum inhibition. The inhibition is depending on the structure of the tested molecule. In present study, the core structure; pyrimidine-triazole is common for all molecules, only side substitutions are changed. Compound **JMM-6** having 2,4-dichloro substitution whereas compound **JMM-7** possess 4-methyl substitution.

TABLE-1
SOME PHYSICAL DATA OF ALL THE SYNTHESIZED COMPOUNDS

Compd. code	Substitution (R)	m.f.	m.w.
JMM-1	-H	$C_{40}H_{36}N_{14}O_4$	776.81
JMM-2	2-Br	$C_{40}H_{34}N_{14}O_4Br_2$	934.60
JMM-3	4-Br	$C_{40}H_{34}N_{14}O_4Br_2$	934.60
JMM-4	4-Cl	$C_{40}H_{34}N_{14}O_4Cl_2$	845.70
JMM-5	2-Cl	$C_{40}H_{34}N_{14}O_4Cl_2$	845.70
JMM-6	2,4-diCl	$C_{40}H_{32}N_{14}O_4Cl_4$	914.59
JMM-7	4-CH_3	$C_{42}H_{40}N_{14}O_4$	804.86
JMM-8	2-CH_3	$C_{42}H_{40}N_{14}O_4$	804.86
JMM-9	2,4-di CH_3	$C_{44}H_{44}N_{14}O_4$	832.91
JMM-10	4-OCH_3	$C_{42}H_{40}N_{14}O_6$	836.86

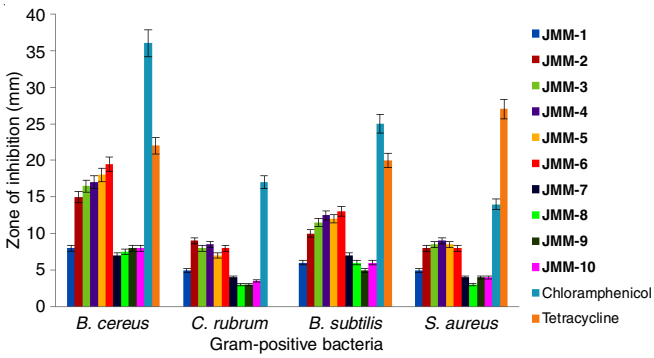


Fig. 1. Zone of inhibition of synthesized compounds against Gram-positive bacterial strains in *N,N*-dimethyl formamide

Hence, it is revealed that 2,4-dichloro substituted compound showed more inhibition than alkyl group. Rest of the synthesized compounds showed good to moderate inhibition against *Bacillus cereus* in DMF. In DMF, against *Corynebacterium rubrum,* compound **JMM-2** (2-bromo) showed maximum inhibition. In DMF, against *Bacillus subtilis*, 2,4-dichloro substitution (compound **JMM-6**) showed maximum inhibition whereas 2,4-dimethyl substituted compound (compound **JMM-9**) showed the minimum inhibition. Against *Staphylococcus aureus*, again compound **JMM-4** (4-chloro) showed the maximum inhibition. Against *Staphylococcus aureus* compounds **JMM-7**, **JMM-9** and **JMM-10** showed lower and almost same extent of inhibition in *N,N*-dimethyl formamide solvent. From the results, it was revealed that the inhibition is not depending only heterocyclic scaffolds but also depend on side substitution present in molecule. From the results, it is clear that the halogen substituted derivatives were found to be more effective against selected bacterial strains.

Fig. 2 showed the zone of inhibition of all the synthesized compounds along with two standard compounds in DMSO solvent. From Fig. 2, it is clear that all the synthesized compounds showed good to moderate inhibition against selected bacterial strains. Against *Bacillus cereus*, compound **JMM-6** (2,4-dichloro) showed the maximum inhibition whereas no substituted derivatives (compound **JMM-1**) showed minimum inhibition. In DMSO, against *Corynebacterium rubrum*, 2-bromo substituted compound (compound **JMM-2**) found to be more effective whereas 4-methyl substituted compound (compound **JMM-7**) show low inhibition. Against *Bacillus subtilis*, all the tested compounds showed good inhibition but not any

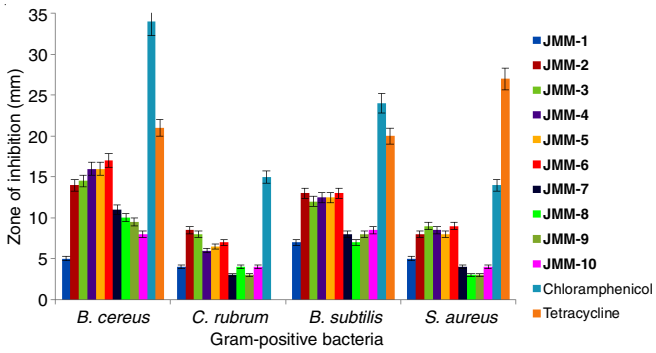


Fig. 2. Zone of inhibition of synthesized compounds against Gram-positive bacterial strains in dimethyl sulphoxide

one showed more than standard antibiotics. In DMSO, against *Staphylococcus aureus*, compound **JMM-6** showed maximum inhibition whereas compounds **JMM-8** and **JMM-9** showed the minimum and almost same extent of inhibition.

Figs. 3 and 4 showed the zone of inhibition against some selected negative bacterial strains in DMF and DMSO solvents, respectively. Against *Klebsiella pneumonia*, compound **JMM-6** (2,4-dichloro) showed the maximum inhibition whereas rest of the compounds showed good inhibition but not more than standard antibiotics. Again compound **JMM-6** showed the maximum inhibition against *Staphylococcus typhimurium*, *Escherichia coli* and *Pseudomonas aeruginosa* in DMF solvent. Hence, from the results it is cleared that the dichloro substituted compound found to be more effective against all selected Gram-negative bacterial strains in DMF solvent.

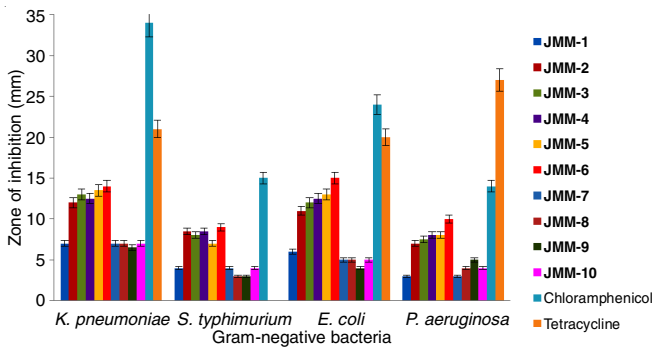


Fig. 3. Zone of inhibition of synthesized compounds against Gram-negative bacterial strains in *N,N*-dimethyl formamide

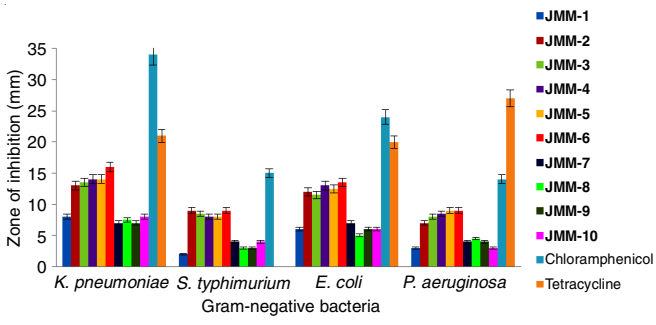


Fig. 4. Zone of inhibition of synthesized compounds against Gram-negative bacterial strains in dimethyl sulphoxide

From Fig. 4, it is observed that 2,4-dichloro substituted compound (compound **JMM-6**) possess the maximum inhibition against *Klebsiella pneumoniae*, *Staphylococcus typhimurium*, *Escherichia coli* and *Pseudomonas aeruginosa* in DMSO solvent. Against *Staphylococcus typhimurium*, compounds **JMM-7** and **JMM-9** were found to be lower effective and almost up to the same extent. In DMSO, no compound showed inhibition more than standard antibiotics drug.

Figs. 5 and 6 showed the zone of inhibition for the studied compounds and two antibiotics against some selected fungal strain in DMF and DMSO, respectively. From Fig. 5, it is observed that the most of the compounds showed good inhibition but not more than that of standard reference drugs in *N,N*-dimethyl formamide solvent. 2,4-Dichloro substituted compound (compound **JMM-6**) showed the maximum inhibition against *Candida albicans*, *Candida epicols* and *Cryptococcus neoformans* in DMF and DMSO solvents.

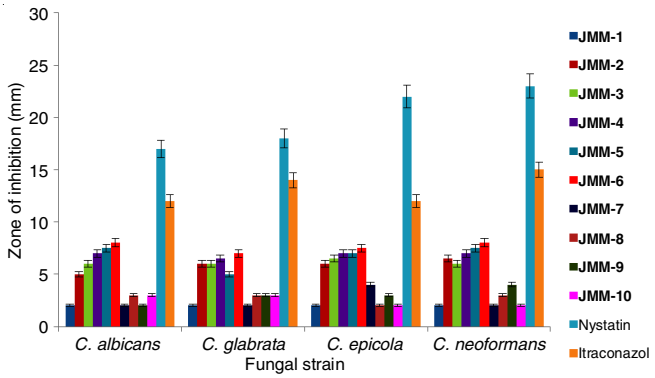


Fig. 5. Zone of inhibition of synthesized compounds against fungal strains in *N,N*-dimethyl formamide

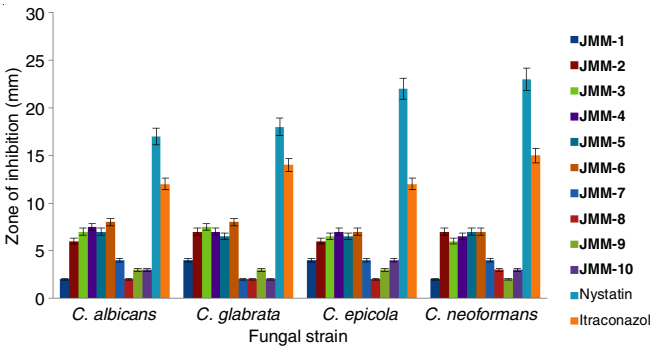


Fig. 6. Zone of inhibition of synthesized compounds against fungal strains in dimethyl sulphoxide

Conclusion

In present work, some new nitrogen based heterocyclic compounds have been synthesized by multi-step process. The conformation of synthesis of 2,2′-(4,4′-(((4-(3-oxomorpholino)-phenyl)azanediyl)*bis*(methylene))*bis*(1*H*-1,2,3-triazole-4,1-diyl))*bis*(N-(4-phenylpyrimidin-2-yl)acetamide) derivatives by different spectroscopic techniques. The antimicrobial activity of all these synthesized compounds was also tested against some selected bacterial and fungal strains in two different solvents. It was revealed that all the synthesized compounds showed good to moderate biological activity against selected strains. However, some halogen substituted compounds were showed higher inhibition then alkyl or without substituted compounds. Thus, it is clear that the halogen substitution increases antimicrobial activity of 2,2′-(4,4′-(((4-(3-oxo-

morpholino)-phenyl)azanediyl)*bis*(methylene))*bis*(1*H*-1,2,3-triazole-4,1-diyl))*bis*(N-(4-phenylpyrimidin-2-yl)acetamide) derivatives.

REFERENCES

1. N. Kerru, L. Gummidi, S. Maddila, K. Gangu and S.B. Jonnalagadda, A Review on Recent Advances in Nitrogen-Containing Molecules and their Biological Applications, *Molecules*, **25**, 1909 (2020); https://doi.org/10.3390/molecules25081909
2. T. Qadir, A. Amin, P.K. Sharma, I. Jeelani and H. Abe, A Review on Medicinally Important Heterocyclic Compounds, *The Open Med. Chem. J.*, **16**, 1 (2022); https://doi.org/10.2174/18741045-v16-e2202280
3. M.M. Heravi and V. Zadsirjan, Prescribed Drugs containing Nitrogen Heterocycles: An Overview, *RSC Adv.*, **10**, 44247 (2020); https://doi.org/10.1039/D0RA09198G
4. F. Gao, T. Wang, J. Xiao and G. Huang, Antibacterial Activity Study of 1,2,4-Triazole Derivatives, *Eur. J. Med. Chem.*, **173**, 274 (2019); https://doi.org/10.1016/j.ejmech.2019.04.043
5. M. Ellouz, N.K. Sebbar, I. Fichtali, Y. Ouzidan, Z. Mennane, R. Charof, J.T. Mague, M. Urrutigoïty and E.M. Essassi, Synthesis and Antibacterial Activity of New 1,2,3-Triazolylmethyl-2*H*-1,4-benzothiazin-3(4*H*)-one Derivatives, *Chem. Cent. J.*, **12**, 123 (2018); https://doi.org/10.1186/s13065-018-0494-2
6. T. Ni, L. Pang, Z. Cai, F. Xie, Z. Ding, Y. Hao, R. Li, S. Yu, X. Chai, T. Wang and Y. Jin Design, Synthesis, and *in vitro* Antifungal Evaluation of Novel Triazole Derivatives bearing Alkynyl Side Chains, *J. Saudi Chem. Soc.*, **23**, 576 (2019); https://doi.org/10.1016/j.jscs.2018.10.003
7. Z. Rezaei, S. K. K. Pakshir, Z. Hossaini, F. Amiri and E. Assadpour, Design, Synthesis, and Antifungal Activity of Triazole and Benzotriazole Derivatives, *Eur. J. Med. Chem.*, **44**, 3064 (2009); https://doi.org/10.1016/j.ejmech.2008.07.012
8. X.M. Chu, C. Wang, W.L. Wang, L.L. Liang, W. Liu, K.K. Gong and K.L. Sun, Triazole derivatives and their antiplasmodial and antimalarial activities. *Eur. J. Med. Chem.*, **166**, 206 (2019); https://doi.org/10.1016/j.ejmech.2019.01.047
9. H.H. Klnfe and Y.H. Belay, Synthesis and Biological Evaluation of Novel Thiosemicarbazone–Triazole Hybrid Compounds Antimalarial Agents, *S. Afr. J. Chem.*, **66**, 130 (2013).
10. G.V. Suresh Kumar, Y. Rajendraprasad, B.P. Mallikarjuna, S.M. Chandrashekar and C. Kistayya, Synthesis of Some Novel 2-Substituted-5-[isopropylthiazole] Cubbed 1,2,4-Triazole and 1,3,4-Oxadiazoles as Potential Antimicrobial and Antitubercular Agents, *Eur. J. Med. Chem.*, **45**, 2063 (2010); https://doi.org/10.1016/j.ejmech.2010.01.045
11. R.S. Upadhayaya, G.M. Kulkarni, N.R. Vasireddy, J.K. Vandavasi, S.S. Dixit, V. Sharma and J. Chattopadhyaya, Design, Synthesis and Biological Evaluation of Novel Triazole, Urea and Thiourea Derivatives of Quinoline against *Mycobacterium tuberculosis*, *Bioorg. Med. Chem.*, **17**, 4681 (2009); https://doi.org/10.1016/j.bmc.2009.04.069
12. G.R. Jadhav, M.U. Shaikh, R.P. Kale, M.R. Shiradkar and C.H. Gill, SAR Study of Clubbed [1,2,4]-Triazolyl with Fluorobenzimidazoles as Antimicrobial and Antituberculosis Agents, *Eur. J. Med. Chem.*, **44**, 2930 (2009); https://doi.org/10.1016/j.ejmech.2008.12.001
13. A.H. Banday, S.A. Shameem, B.D. Gupta and H.M.S. Kumar, D-ring Substituted 1,2,3-Triazolyl 20-Keto Pregnenanes as Potential Anticancer Agents: Synthesis and Biological Evaluation, *Steroids*, **75**, 801 (2010); https://doi.org/10.1016/j.steroids.2010.02.015
14. D.A. Ibrahim, Synthesis and Biological Evaluation of 3,6-Disubstituted [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole Derivatives as a Novel Class of Potential Anti-tumor Agents, *Eur. J. Med. Chem.*, **44**, 2776 (2009); https://doi.org/10.1016/j.ejmech.2009.01.003
15. H. Yuksek, S. Kolayli, M. Kucuk, M.O. Yuksek, Ocak, S. Ummuhan, S. Esra, E. Sivrikaya and M. Ocak, Synthesis and Antioxidant Activities of Some 4-Benzylidenamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one Derivatives, *Indian J. Chem.*, **45B**, 715 (2006).
16. S. Hussain, J. Sharma and M. Amir, Synthesis and Antimicrobial Activities of 1,2,4-Triazole and 1,3,4-Thiadiazole Derivatives of 5-Amino-2-Hydroxybenzoic Acid, *E-J. Chem.*, **5**, 963 (2008); https://doi.org/10.1155/2008/924734
17. Y.G. Sameliuk, F.A. Zedan and M. Tetyana, 1,2,4-Triazole Derivatives in Medicine and Pharmacy and Application Prospects, *Ankara Üniv. Eczacilik Fakul. Derg.*, **45**, 598 (2021); https://doi.org/10.33483/jfpau.885888
18. K.N. Mohana, B.N. Prasanna Kumar and L. Mallesha, Synthesis and Biological Activity of Some Pyrimidine Derivatives, *Drug Inven. Today*, **5**, 216 (2013); https://doi.org/10.1016/j.dit.2013.08.004
19. S.B. Patil, Biological and Medicinal Significance of Pyrimidines: A Review, *Int. J. Pharm. Sci. Res.*, **9**, 44 (2018); https://doi.org/10.13040/IJPSR.0975-8232.9(1).44-52
20. V. Sharma, N. Chitranshi and A.K. Agarwal, Significance and Biological Importance of Pyrimidine in the Microbial World, *Int. J. Med. Chem.*, **2014**, 202784 (2014); https://doi.org/10.1155/2014/202784
21. R. Sahu, S. Kumar, R.P. Aharwal and S.S. Sandhu, Antibacterial Activity of Isolated Endophytic Fungi from *Rauvolfia serpentina* (L.) benth. ex kurz, *Int. J. Pharm. Pharm. Sci.*, **8**, 38 (2016); https://doi.org/10.22159/ijpps.2016v8i11.9733
22. A.A.M. El-Reedy and N.K. Soliman, Synthesis, Biological Activity and Molecular Modeling Study of Novel 1,2,4-Triazolo[4,3-*b*][1,2,4,5]-tetrazines and 1,2,4-triazolo[4,3-*b*][1,2,4]triazines, *Sci. Rep.*, **10**, 6137 (2020); https://doi.org/10.1038/s41598-020-62977-x