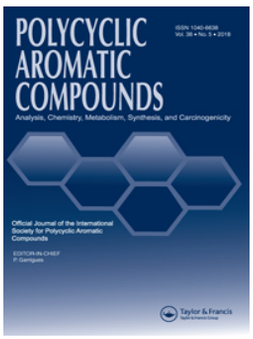

Polycyclic Aromatic Compounds

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Synthesis of New Thiazole and Pyrazole Clubbed 1,2,3-Triazol Derivatives as Potential Antimycobacterial and Antibacterial Agents

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ABSTRACT

New series of 4-methyl-2-(4-substituted phenyl)-5-(4-((4-(4-substituted phenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)thiazole, **6a-t** and 4-(1,3-diphenyl-1*H*-pyrazol-4-yl)-1-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)-1*H*-1,2,3-triazole, **11a-o** derivatives have been synthesized by applying copper-catalyzed [3 + 2] cycloaddition reaction. The newly synthesized 1,3-thiazolyl-pyrazolyl-1,2,3-triazole (**6a-t**) and bis-pyrazolyl-1,2,3-triazole (**11a-o**) derivatives were screened for *in vitro* antimycobacterial activity against *M. Tuberculosis* H37Ra dormant and active and antibacterial activity against four pathogenic bacteria, *E. coli* (NCIM 2576), *P. flurescence* (NCIM 2059), *S. aureus* (NCIM 2602) and *B. subtilis* (NCIM 2162). Compounds **6a**, **6f**, **6j**, **11e** and **11m** showed good activity against *M tuberculosis* H37Ra Active strain, also compounds **6g**, **6h**, **11f**, **11n** and **11o** showed good activity against *M tuberculosis* H37Ra Dormant strain. Compounds **6b**, **6i**, **6l**, **6o, 6r, 11k**, **11l** and **11m** showed good activity against *B. subtilis* with IC_{50} 1.99-2.96 μg/mL. The antibacterial activity of thiazolyl-pyrazolyl-1,2,3-triazole and bis-pyrazolyl-1,2,3-triazole derivatives suggested that, these derivatives could lead to new compounds for treatment against bacterial infection.

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Thiazole; Pyrazole; 123-Triazole; Antimycobacterial activity; Antibacterial activity

Introduction

The WHO raised the red flag against an inappropriate use of antibiotics during the COVID-19 pandemic.[1] Therefore, the future antibiotic resistance will become the one of the major global health emergency and the effective prevention and treatment of an increasing range of infections due to bacteria, fungi, parasites and viruses become more challenging.[2] Two or more bioactive pharmacophore tethered scaffolds plays the significant role in the discovery of new lead candidate.[3] Nitrogen and sulfur containing heterocyclic scaffolds are the precious sources that are continuously utilized in the field of drug discovery and development.[4,5]

Clubbed polycyclic pyrazole, thiazole and triazole rings are privileged pharmacophores for the construction of lead molecules and have received much attention in recent years. 1,2,3-Triazole

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containing pharmacophores have contributed significantly in drug discovery and development as it also acts as a bioisostere for the synthesis of new lead molecule.[6–8] 1,2,3-Triazole containing compounds displayed pharmacological activities such as anti-microbial,[9,10] antitubercular,[11,12] anticancer and antiproliferative,[11,13] anti-inflammatory,[14] antimalarial agents,[15,16] anti-diabetic[17] and antiviral[18] activity and many more. Thiazole pharmacophore is present in many natural and synthetic compounds.[5] It is known that thiazole derivatives many compounds have exhibited remarkable antimycobacterial activity.[19–26] Moreover, thiazole derivatives have also exhibited a wide range of other pharmacological activity such as antimicrobial,[27,28] anti-inflammatory,[29] CNS active agents,[30] antimalarial[31] and anticancer[32] activities. Additionally, compounds bearing the pyrazole skeleton have been exhibited to exhibit significant antimycobacterial activity,[33–35] as well as antimicrobial,[36] anti-inflammatory[37] anticancer[38] and antimalarial[39] activities. The structural diversity and biological importance of clubbed azoles have made them prominent target for new antimicrobial lead compounds. The clubbed 1,2,3-triazole, pyrazole and thiazole nucleus containing heterocycles have received much attention due to their promising antimicrobial activity.[40] Clubbed pyrazolyl-thiazole, pyrazolyl-triazole and thiazolyl-triazole derivatives are reported for antimycobacterial,[41–44] antimicrobial,[45–47] anti-inflammatory[48] and anticancer[49] activities.

Keeping in mind, the biological significance of clubbed azole derivatives and in continuation of our search for new anti-infection agents, we report herein the synthesis of 4-methyl-2-(4-substituted phenyl)-5-(4-((4-(4-substituted phenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)thiazole and 1-((3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methyl)-4-(3aryl-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole, **11a-o** as potential antimycobacterial agents.

Material and methods

Experimental

General procedure for synthesis of (3-(4-methyl-2-substituted phenylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methanol, 3a-e

To the solution of 3-(4-methyl-2-substituted phenylthiazol-5-yl)-1-phenyl-1H-pyrazole-4-carbaldehyde, **2a-e** (0.08 mol) in methanol, a solution of sodium borohydride (0.16 mol) in methanol (3 mL) was added drop-wise and reaction mixture was stirred at room temperature for 0.5 to 1 hour. After completion of reaction, the solvent was evaporated under reduced pressure; residue was dissolved in water and extracted with ethyl acetate afforded alcohol **3a-e** (yield 88-95%).

General procedure for synthesis of 5-(4-(azidomethyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-substituted phenylthiazole 4a-e

To the ice cold solution of (3-(4-methyl-2-substituted phenylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methanol, **3a-e** (0.06 mol) and triethyl amine (0.13 mol) in dry DCM (30 mL) methanesulfonyl chloride (0.07 mol) in DCM (10 mL) was added drop-wise for 30 minutes. The reaction mixture was stirred at room temperature for 2-3hours. The solvent was evaporated under reduced pressure, the reaction mass was dissolved in water and extracted with DCM (3 × 30 mL). The organic layer was washed with brine and dried over sodium sulfate gave (3-(4-methyl-2-substituted phenylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methylmethanesulfonate. To a solution of methanesulfonate derivative (0.05 mol) in DMSO (20 mL), sodium azide (0.06 mol) was added and reaction mixture was stirred at 60 °C for 2-5 hours. After completion of reaction (TLC) reaction mixture was quenched in water (100 mL) and extracted with ethyl acetate (3 × 30 mL). The organic layer was dried over sodium sulfate and solvent was distilled on rotary evaporator that gave 5-(4-(azidomethyl)-1-phenyl-1*H*-pyrazol-3-yl)-4-methyl-2-substituted phenylthiazole **4a-e** (70-85%).

General method for synthesis of 4-methyl-2-substituted phenyl-5-(1-phenyl-4-((4-substituted phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole (6a-t)

A solution of 5-(4-(azidomethyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-substituted phenylthiazole **4a-e** (1 mmol), substituted aryl alkyne, **5a-d** (1 mmol), sodium ascorbate (0.22 mmol) and copper sulfate (0.25 mmol) in DMF:Water (8 mL, 3:1) was stirred at room temperature for 12-24 hours. After completion of the reaction, the reaction mixture was poured in water and extracted with ethyl acetate (3 × 10 mL). Ethyl acetate layer was dried over sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using Ethyl acetate:hexane as eluent (2:8) to furnish 4-methyl-2-substituted phenyl-5-(1-phenyl-4-((4-substitutedphenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole (**6a-t**) (Yield 65-85%).

4-Methyl-2-phenyl-5-(1-phenyl-4-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6a

Yield 70%; Mp. 160-62 °C; IR: 1598, 1548, 1504, 1454, 1391, 1314, 1211, 1072, 1059, 1048, 1011, 963, 831 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H, Pyrazole-H), 7.97 − 7.91 (m, 2H, Ar-H), 7.88 (s, 1H, Triazole-H), 7.80-7.75 (m, 4H, Ar-H), 7.49 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.46-7.43 (m, 3H, Ar-H), 7.41 − 7.27 (m, 4H, Ar-H), 5.64 (s, 2H, Pyrazole-CH_2-Triazole), 2.61 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 152.7, 147.7, 143.3, 139.3, 133.2, 130.4, 130.2, 129.5, 129.0, 128.7, 128.1, 127.1, 126.4, 125.6, 121.0, 119.9, 119.8, 119.0, 116.7, 44.4, 16.6; HRMS calculated for $C_{28}H_{23}N_6S$: 475.1705; observed *m/z*: 475.1703 $(M + H)^+$

5-(4-((4-(4-Fluorophenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-phenylthiazole, 6b

Yield 75%; Mp. 212-214 °C; IR: 1599, 1549, 1500, 1451, 1334, 1253, 1221, 1176, 1069, 1029, 1019, 1005, 961, 837, 818 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H, Pyrazole-H), 7.96 (dd, $J = 6.4$, 3.2 Hz, 2H, Ar-H), 7.78 − 7.71 (m, 4H, Ar-H), 7.61 (s, 1H, Triazole-H), 7.52 − 7.44 (m, 5H, Ar-H), 7.36 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.08 (t, $J = 8.7$ Hz, 2H, Ar-H), 5.63 (s, 2H, Pyrazole-CH_2-Triazole), 2.64 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 163.70 and 161.73 ($^{1}J = 248.22$ Hz), 153.0, 147.2, 143.4, 139.3, 133.2, 130.3, 129.6, 129.1, 129.0, 128.2, 127.5, 127.44 and 127.37 ($^{3}J = 8.82$ Hz), 126.58 and 126.55 ($^{4}J = 3.78$ Hz), 126.5, 120.8, 119.1, 116.7, 115.92 and 115.75 ($^{2}J = 21.42$ Hz), 44.6, 16.7; HRMS calculated for $C_{28}H_{22}FN_6S$: 493.1611; observed *m/z*: 493.1603 $(M + H)^+$

4-Methyl-2-phenyl-5-(1-phenyl-4-((4-(p-tolyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6c

Yield 72%; Mp. 178-180 °C; IR: 1598, 1547, 1503, 1450, 1361, 1253, 1213, 1074, 1044, 1008, 947, 817 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H, Pyrazole-H), 8.00 − 7.92 (m, 2H, Ar-H), 7.73 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.68 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.63 (s, 1H, Triazole-H), 7.50 − 7.45 (m, 5H, Ar-H), 7.35 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.20 (d, $J = 8.0$ Hz, 2H, Ar-H), 5.61 (s, 2H, Pyrazole-CH_2-Triazole), 2.64 (s, 3H, Thiazole-CH_3), 2.37 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 153.0, 148.2, 143.4, 139.3, 138.2, 133.3, 130.3, 129.6, 129.5, 129.0, 128.2, 127.5, 127.3, 126.5, 125.6, 120.9, 119.1, 119.0, 116.9, 44.6, 21.3, 16.7; HRMS calculated for $C_{29}H_{25}N_6S$: 489.1861; observed *m/z*: 489.1852 $(M + H)^+$

5-(4-((4-(4-Methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-phenylthiazole, 6d

Yield 65%; Mp. 178-180 °C; IR: 1599, 1548, 1504, 1461, 1359, 1152, 1070, 1046, 1028, 1008, 980, 964 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (s, 1H, Pyrazole-H), 7.99 – 7.93 (m, 2H, Ar-H), 7.72 (t, $J = 9.2$ Hz, 4H, Ar-H), 7.58 (s, 1H, Triazole-H), 7.50-7.46 (m, 5H, Ar-H), 7.34 (t, $J = 7.4$ Hz, 1H, Ar-H), 6.92 (d, $J = 8.6$ Hz, 2H, Ar-H), 5.60 (s, 2H, Pyrazole-CH_2-Triazole), 3.83 (s, 3H, Ar-OCH_3), 2.64 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 159.7, 152.9, 148.0, 143.4, 139.3, 133.3, 130.3, 129.6, 129.0, 128.2, 127.3, 127.0, 126.5, 123.0, 120.9, 119.1, 118.6, 116.9, 114.3, 55.3, 44.6, 16.7; HRMS calculated for $C_{29}H_{25}N_6OS$: 505.1811; observed *m/z*: 505.1805 $(M + H)^+$

2-(4-Bromophenyl)-4-methyl-5-(1-phenyl-4-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6e

Yield 78%; Mp. 182-184 °C; IR: 1598, 1547, 1496, 1464, 1357, 1229, 1217, 1070, 1050, 1009, 974, 834, 808 cm^{-1}; ^1H NMR (500 MHz, DMSO) δ 8.56 (s, 1H, Pyrazole-H), 8.15 (s, 1H, Triazole-H), 7.74 (d, $J = 7.7$ Hz, 2H, Ar-H), 7.62 (d, $J = 8.6$ Hz, 2H, Ar-H), 7.59-7.55 (m, 4H, Ar-H), 7.46 (t, $J = 8.0$ Hz, 2H, Ar-H), 7.36 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.24-7.18 (m, 3H, Ar-H), 5.61 (s, 2H, Pyrazole-CH_2-Triazole), 2.48 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 152.4, 147.7, 142.9, 139.2, 134.3, 132.1, 131.7, 129.9, 129.3, 128.6, 127.7, 127.5, 127.1, 126.2, 125.8, 123.0, 121.4, 119.1, 116.7, 44.5, 16.6; HRMS calculated for $C_{28}H_{22}BrN_6S$: 553.0810; observed *m/z*: 553.0800, 555.0782 $(M + 2 + H)^+$

2-(4-Bromophenyl)-5-(4-((4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methylthiazole, 6f

Yield 82%; Mp. 198-200 °C; IR: 1599, 1563, 1501, 1450, 1331, 1249, 1220, 1176, 1029, 1020, 1009, 961, 835, 818 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.54 (s, 1H, Pyrazole-H), 8.31 (s, 1H, Triazole-H), 7.90 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.85 (dd, $J = 8.4$, 5.6 Hz, 2H, Ar-H), 7.79 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.55 (t, $J = 7.9$ Hz, 2H, Ar-H), 7.37 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.30 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.23 (t, $J = 8.8$ Hz, 2H, Ar-H), 5.65 (s, 2H, Pyrazole-CH_2-Triazole), 2.49 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.0, 163.65 and 161.64 ($^1J = 250.74$ Hz), 153.0, 147.3, 143.4, 139.3, 133.2, 132.1, 130.3, 129.8, 129.7, 129.1, 128.3, 127.46 and 127.39 ($^3J = 8.82$ Hz), 126.58 and 126.55 ($^4J = 3.78$ Hz), 123.1 120.9, 119.2, 116.8, 115.90 and 115.72 ($^2J = 22.68$ Hz), 44.6, 16.8; HRMS calculated for $C_{28}H_{21}BrFN_6S$: 571.0716; observed *m/z*: 571.0709 $(M + H)^+$, 573.0696 $(M + 2 + H)^+$

2-(4-Bromophenyl)-4-methyl-5-(1-phenyl-4-((4-(p-tolyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6g

Yield 85%; Mp. 182-184 °C; IR: 1598, 1550, 1503, 1465, 1450, 1366, 1249, 1233, 1185, 1071, 1050, 1009, 974, 962, 806 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H, Pyrazole-H), 7.86 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.79 (d, $J = 7.2$ Hz, 2H, Ar-H), 7.73 (d, $J = 7.7$ Hz, 2H, Ar-H), 7.66 (s, 1H, Triazole-H), 7.49 (t, $J = 8.0$ Hz, 2H, Ar-H), 7.40 (t, $J = 7.5$ Hz, 2H, Ar-H), 7.37 – 7.31 (m, 2H, Ar-H), 7.27 (d, $J = 8.1$ Hz, 2H, Ar-H), 5.63 (s, 2H, Pyrazole-CH_2-Triazole), 2.64 (s, 3H, Thiazole-CH_3), 2.42 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 152.9, 147.7, 143.0, 139.2, 137.8, 132.1, 132.0, 129.4, 129.3, 128.5, 127.7, 127.5, 127.1, 125.4, 124.1, 121.4, 119.3, 118.9, 116.6, 44.3, 21.1, 16.6; HRMS calculated for $C_{29}H_{24}BrN_6S$: 567.0967; observed *m/z*: 567.0955 $(M + H)^+$ 569.0937 $(M + 2 + H)^+$

2-(4-Bromophenyl)-5-(4-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methylthiazole, 6h

Yield 76%; Mp. 184-186 °C; IR: 1599, 1560, 1504, 1464, 1340, 1227, 1071, 1051, 1009, 974, 821, 818 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.83 (s, 1H, Pyrazole-H), 8.43 (s, 1H, Triazole-H), 7.90 (d, $J = 7.7$ Hz, 2H, Ar-H), 7.84 (d, $J = 8.6$ Hz, 2H, Ar-H), 7.73-7.69 (m, 4H, Ar-H), 7.55 (t, $J = 8.0$ Hz, 2H, Ar-H), 7.38 (t, $J = 7.4$ Hz, 1H, Ar-H), 6.96 (d, $J = 8.9$ Hz, 2H, Ar-H), 5.63 (s, 2H, Pyrazole-CH_2-Triazole), 3.76 (s, 3H, Ar-OCH_3), 2.50 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.2, 159.7, 152.8, 148.1, 143.5, 139.3, 130.6, 130.3, 129.7, 129.6, 128.9, 128.2, 127.4, 126.5, 120.3, 119.4, 119.1, 118.7, 116.8, 114.3, 55.4, 44.6, 16.8; HRMS calculated for $C_{29}H_{24}BrN_6OS$: 583.0916; observed *m/z*: 583.0903 $(M + H)^+$, 585.0886 $(M + 2 + H)^+$

2-(4-Chlorophenyl)-4-methyl-5-(1-phenyl-4-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6i

Yield 85%; Mp. 172-174 °C; IR: 1596, 1507, 1454, 1358, 1231, 1220, 1154, 1074, 1008, 972, 952, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H, Pyrazole-H), 7.95 − 7.90 (m, 2H, Ar-H), 7.79 − 7.75 (m, 2H, Ar-H), 7.73 − 7.71 (m, 2H, Ar-H), 7.66 (s, 1H, Triazole-H), 7.49 − 7.46 (m, 2H, Ar-H), 7.41 − 7.30 (m, 4H, Ar-H), 7.13 (t, $J = 8.6$ Hz, 2H, Ar-H), 5.61 (s, 2H, Pyrazole-CH_2-Triazole), 2.61 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 154.0, 147.4, 144.4, 137.2, 134.3, 133.2, 130.8, 129.7, 129.3, 129.1, 128.7, 128.4, 128.3, 127.4, 125.7, 123.2, 120.2 119.6, 119.3, 44.5, 16.7; HRMS calculated for $C_{28}H_{22}ClN_6S$: 509.1315; observed *m/z*: 509.1319 $(M + H)^+$, 511.1297 $(M + 2 + H)^+$

2-(4-Chlorophenyl)-5-(4-((4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methylthiazole, 6j

Yield 75%; Mp. 174-176 °C; IR: 1598, 1560, 1500, 1452, 1333, 1253, 1222, 1156, 1068, 1030, 1018, 1005, 981, 961, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.62 − 8.09 (m, 3H, Ar-H, Pyrazole-H), 7.97 (s, 2H, Ar-H), 7.83 (dd, $J = 22.5$, 11.3 Hz, 4H, Ar-H), 7.65 − 7.06 (m, 7H, Ar-H, Triazole-H), 4.63 (s, 2H, Pyrazole-CH_2-Triazole), 2.65 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 169.34 and 167.36 ($^1J = 248.48$ Hz), 156.4, 147.5, 144.5, 137.0, 136.84 and 136.81 ($^4J = 3.78$ Hz), 134.8, 134.4, 134.3, 133.10 and 133.04 ($^3J = 7.56$ Hz), 132.4, 128.7, 128.6, 127.7, 127.2, 123.4, 123.2, 121.11 and 120.95 ($^2J = 20.16$ Hz), 120.6, 44.3, 16.9; HRMS calculated for $C_{28}H_{21}ClFN_6S$: 527.1221; observed *m/z*: 527.1216 $(M + H)^+$

2-(4-Chlorophenyl)-4-methyl-5-(1-phenyl-4-((4-(p-tolyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6k

Yield 78%; Mp. 182-184 °C; IR: 1599, 1559, 1503, 1459, 1227, 1156, 1069, 1047, 1017, 1005, 1005, 844, 823, 810 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H, Pyrazole-H), 7.93 (dd, $J = 8.9$, 5.3 Hz, 2H, Ar-H), 7.73 (dd, $J = 8.6$, 1.0 Hz, 2H, Ar-H), 7.67 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.62 (s, 1H, Triazole-H), 7.48 (t, $J = 8.0$ Hz, 2H, Ar-H), 7.34 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.20 (d, $J = 7.9$ Hz, 2H, Ar-H), 7.14 (t, $J = 8.6$ Hz, 2H, Ar-H), 5.60 (s, 2H, Pyrazole-CH_2-Triazole), 2.62 (s, 3H, Thiazole-CH_3), 2.36 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 152.8, 148.1, 143.2, 139.3, 138.2, 138.2, 132.2, 130.1, 129.6, 129.5, 128.4, 128.2, 127.9, 127.3, 125.6, 123.4, 120.9, 119.1, 116.8, 44.6, 21.2, 16.7; HRMS calculated for $C_{29}H_{24}ClN_6S$ 523.1472; observed *m/z*: 523.1465 $(M + H)^+$

2-(4-Chlorophenyl)-5-(4-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methylthiazole, 6l

Yield 70%; Mp. 128-130 °C; IR: 1598, 1562, 1503, 1457, 1359, 1227, 1156, 1070, 1006, 980, 962, 831, 810 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.83 (s, 1H, Pyrazole-H), 8.43 (s, 1H, Triazole-H), 7.90 (d, $J = 7.7$ Hz, 2H), 7.87 – 7.82 (m, 2H), 7.74 – 7.67 (m, 4H), 7.55 (t, $J = 8.0$ Hz, 2H), 7.38 (t, $J = 7.4$ Hz, 1H), 6.96 (d, $J = 8.9$ Hz, 2H), 5.63 (s, 2H, Pyrazole-CH_2-Triazole), 3.76 (s, 3H, Ar-OCH_3), 2.50 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.6, 159.6, 153.9, 147.7, 144.4, 137.2, 133.9, 132.0, 130.0, 129.1, 128.3, 127.3, 127.0, 126.5, 123.0, 121.4, 119.8, 119.0, 116.9, 114.3, 55.3, 44.6, 16.8; HRMS calculated for $C_{29}H_{24}ClN_6OS$: 539.1421; observed *m/z*: 539.1416 $(M + H)^+$

2-(4-Fluorophenyl)-4-methyl-5-(1-phenyl-4-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6m

Yield 70%; Mp. 170-172 °C; IR: 1599, 1558, 1502, 1452, 1351, 1230, 1128, 1069, 1005, 958, 840, 808 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H, Pyrazole-H), 7.92 (dd, J = 8.8, 5.3 Hz, 2H, Ar-H) 7.77 (d, J = 7.2 Hz, 2H, Ar-H), 7.73 – 7.71 (m, 2H, Ar-H), 7.66 (s, 1H, Triazole-H), 7.47 (t, J = 8.0 Hz, 2H, Ar-H), 7.41 – 7.30 (m, 4H, Ar-H), 7.13 (t, J = 8.6 Hz, 2H, Ar-H), 5.61 (s, 2H, Pyrazole-CH_2-Triazole), 2.61 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 164.98 and 162.98 ($^1J = 252$ Hz), 152.9, 148.1, 143.3, 139.3, 132.2, 130.3, 129.6, 129.5, 128.9, 128.49 and 128.42 ($^3J = 8.82$ Hz), 128.29 and 128.27 ($^4J = 2.52$ Hz), 127.4, 125.8, 119.4, 119.1, 118.9, 116.7, 116.19 and 116.02 ($^1J = 21.42$ Hz), 44.6, 16.7; HRMS calculated for $C_{28}H_{22}FN_6S$: 493.1611; observed *m/z*: 493.1614 $(M + H)^+$

2-(4-Fuorophenyl)-5-(4-((4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methylthiazole, 6n

Yield 70%; Mp. 168-170 °C; IR: 1599, 1564, 1503, 1458, 1334, 1248, 1228, 1177, 1091, 1077, 1019, 1007, 966, 836, 820 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.82 (s, 1H, Pyrazole-H), 8.55 (s, 1H, Triazole-H), 7.95 – 7.87 (m, 4H, Ar-H), 7.88 – 7.78 (m, 2H, Ar-H), 7.61 – 7.50 (m, 4H, Ar-H), 7.39 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.25 (t, $J = 8.9$ Hz, 2H, Ar-H), 5.66 (s, 2H, Pyrazole-CH_2-Triazole), 2.51 (s, 3H, Thiazole-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 164.98 and 162.98 ($^1J = 252$ Hz), 163.98 and 161.99 ($^1J = 250.74$ Hz), 152.9, 148.0, 143.2, 139.3, 132.2, 130.3, 129.7, 128.9, 128.49 and 128.42 ($^3J = 8.82$ Hz), 128.29 and 128.27 ($^4J = 2.52$ Hz), 127.41 and 127.34 ($^3J = 8.82$ Hz), 126.55 and 126.52 ($^4J = 3.78$ Hz), 119.1, 118.9, 116.7, 116.19 and 116.02 ($^1J = 21.42$ Hz), 115.95 and 115.78 ($^2J = 21.42$ Hz), 44.6, 16.7; HRMS calculated for $C_{28}H_{21}F_2N_6S$: 511.1516; observed *m/z*: 511.1508 $(M + H)^+$

2-(4-Fluorophenyl)-4-methyl-5-(1-phenyl-4-((4-(p-tolyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)thiazole, 6o

Yield 70%; Mp. 194-196 °C; IR: 1598, 1560, 1502, 1454, 1325, 1229, 1074, 1049, 1008, 965, 833, 818 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H, Pyrazole-H), 7.93 (dd, $J = 8.9$, 5.3 Hz, 2H, Ar-H), 7.73 (dd, $J = 8.6$, 1.0 Hz, 2H, Ar-H), 7.67 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.62 (s, 1H, Triazole-H), 7.48 (t, $J = 8.0$ Hz, 2H, Ar-H), 7.34 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.20 (d, $J = 7.9$ Hz, 2H, Ar-H), 7.14 (t, $J = 8.6$ Hz, 2H, Ar-H), 5.60 (s, 2H, Pyrazole-CH_2-Triazole), 2.62 (s, 3H, Thiazole-CH_3), 2.36 (s, 3 H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 164.98 and 162.99 ($^1J = 250.74$ Hz), 152.9, 148.2, 143.3, 139.3, 138.2, 132.2, 130.0, 129.63 and 129.61($^4J = 2.52$ Hz), 129.5, 128.50 and 128.43 ($^3J = 8.82$ Hz), 128.2, 127.9, 127.5, 127.3, 125.6, 119.1, 119.0, 116.8, 116.19 and 116.01 ($^2J = 21.42$ Hz), 44.5, 21.3, 16.7; HRMS calculated for $C_{29}H_{24}FN_6S$: 507.1767; observed *m/z*: 507.1762 $(M + H)^+$

2-(4-Fluorophenyl)-5-(4-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methylthiazole, 6p

Yield 68%; Mp. 198-198 °C; IR: 1597, 1504, 1457, 1359, 1228, 1155, 1070, 1009, 845, 832, 810 cm^{-1};^{1}H NMR (500 MHz, DMSO-d_6) δ 8.83 (s, 1H, Pyrazole-H), 8.42 (s, 1H, Triazole-H), 7.94 − 7.88 (m, 4H, Ar-H), 7.73 (d, J = 8.9 Hz, 2H, Ar-H), 7.57-7.53 (m, 4H, Ar-H), 7.38 (t, J = 7.4 Hz, 1H, Ar-H), 6.96 (d, J = 8.9 Hz, 2H, Ar-H), 5.63 (s, 2H, Pyrazole-CH_2-Triazole), 3.76 (s, 3H, Ar-OCH_3), 2.50 (s, 3H, Thiazole-CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 164.99 and 163.00 (^1J = 250.74 Hz), 159.7, 148.0, 143.3, 132.2, 130.3, 129.0, 128.50 and 128.43 (^3J = 8.82 Hz), 128.2, 127.4, 127.0, 126.58 and 126.56 (^4J = 2.52 Hz), 126.5, 120.8, 119.1, 118.5, 116.8, 116.20 and 116.02 (^2J = 21.42 Hz), 114.3, 55.3, 44.6, 16.7; HRMS calculated for $C_{29}H_{24}FN_6OS$: 523.1716; observed *m/z*: 523.1709 $(M + H)^+$

4-Methyl-5-(1-phenyl-4-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)-2-(p-tolyl)thiazole, 6q

Yield 70%; Mp. 210-212 °C; IR: 1597, 1558, 1495, 1465, 1349, 1230, 1069, 1051, 1004, 962, 833, 804 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H, Pyrazole-H), 7.81 (d, J = 8.6 Hz, 2H, Ar-H), 7.79 (s, 1H, Triazole-H), 7.78-7.72 (m, 2H, Ar-H), 7.66 (d, J = 8.1 Hz, 2H, Ar-H), 7.57 (d, J = 8.6 Hz, 2H, Ar-H), 7.51 − 7.46 (m, 3H, Ar-H), 7.36 − 7.32 (m, 1H, Ar-H), 7.19 (d, J = 7.9 Hz, 2H, Ar-H), 5.62 (s, 2H, Pyrazole-CH_2-Triazole), 2.60 (s, 3H, Thiazole-CH_3), 2.36 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 152.9, 147.7, 143.0, 139.2, 137.8, 132.1, 132.0, 129.4, 129.3, 128.5, 127.7, 127.5, 127.1, 125.4, 124.1, 121.4, 119.3, 118.9, 116.6, 44.3, 21.1, 16.6; HRMS calculated for $C_{29}H_{25}N_6S$: 489.1861; observed *m/z*: 489.1852 $(M + H)^+$

5-(4-((4-(4-Fluorophenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-(p-tolyl)thiazole, 6r

Yield 80%; Mp. 206-208 °C; IR: 1600, 1562, 1504, 1452, 1247, 1224, 1177, 1070, 1030, 1020, 1004, 962, 835, 820 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.81 (s, 1H, Pyrazole-H), 8.54 (s, 1H, Triazole-H), 8.30 (d, J = 2.6 Hz, 1H, Ar-H), 7.90 (d, J = 8.0 Hz, 2H, Ar-H), 7.85 (dd, J = 8.4, 5.6 Hz, 2H, Ar-H), 7.79 (d, J = 8.0 Hz, 2H, Ar-H), 7.55 (t, J = 7.9 Hz, 2H, Ar-H), 7.37 (t, J = 7.4 Hz, 1H, Ar-H), 7.30 (d, J = 8.0 Hz, 2H, Ar-H), 7.23 (t, J = 8.8 Hz, 2H, Ar-H), 5.65 (s, 2H, Pyrazole-CH_2-Triazole), 2.49 (s, 3H, Thiazole-CH_3), 2.35 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 163.98 and 161.99 (^1J = 250.74 Hz), 152.9, 147.7, 143.2, 140.3, 139.3, 133.4, 130.4, 129.7, 129.1, 128.3, 127.5, 127.41 and 127.34 (^3J = 8.82 Hz), 126.55 and 126.52 (^4J = 3.78 Hz), 126.5, 121.3, 119.2, 116.7, 115.95 and 115.78 (^2J = 21.42 Hz), 44.5, 21.1, 16.6; HRMS calculated for $C_{29}H_{24}FN_6S$: 507.1767; observed *m/z*: 507.1761 $(M + H)^+$

4-Methyl-5-(1-phenyl-4-((4-(p-tolyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-pyrazol-3-yl)-2-(p-tolyl)thiazole, 6s

Yield 78%; Mp. 162-164 °C; IR: 1600, 1561, 1505, 1495, 1459, 1354, 1224, 1070, 1051, 1020, 1004, 974, 823, 808 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (s, 1H, Pyrazole-H), 7.86 (d, J = 8.1 Hz, 2H, Ar-H), 7.73 (d, J = 7.8 Hz, 2H, Ar-H), 7.68 (d, J = 8.1 Hz, 2H, Ar-H), 7.63 (s, 1H, Triazole-H), 7.48 (t, J = 7.9 Hz, 2H, Ar-H), 7.34 (t, J = 7.4 Hz, 1H, Ar-H), 7.27 (d, J = 8.1 Hz, 2H, Ar-H), 7.21 (d, J = 8.0 Hz, 2H, Ar-H), 5.61 (s, 2H, Pyrazole-CH_2-Triazole), 2.63 (s, 3H, Thiazole-CH_3), 2.42 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 152.8, 148.2, 143.5, 140.6, 139.4, 138.1, 130.6, 129.7, 129.6, 129.5, 128.2, 127.5, 127.3, 126.5, 125.6, 120.3, 119.1, 119.0, 116.8, 44.6, 21.5, 21.3, 16.7; HRMS calculated for $C_{30}H_{27}N_6S$: 503.2018; observed *m/z*: 503.2012 $(M + H)^+$

5-(4-((4-(4-Methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-(p-tolyl)thiazole, 6t

Yield 82%; Mp. 218-220 °C; IR: 1599, 1558, 1506, 1492, 1462, 1333, 1225, 1069, 1050, 1017, 1005, 979, 961, 836, 819 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.80 (s, 1H, Pyrazole-H), 8.40 (s, 1H, Triazole-H), 7.87 (d, $J = 7.7$ Hz, 2H, Ar-H), 7.84 – 7.79 (m, 2H, Ar-H), 7.71 – 7.64 (m, 4H, Ar-H), 7.52 (t, $J = 8.0$ Hz, 2H, Ar-H), 7.35 (t, $J = 7.4$ Hz, 1H, Ar-H), 6.93 (d, $J = 8.9$ Hz, 2H, Ar-H), 5.60 (s, 2H, Pyrazole-CH_2-Triazole), 3.73 (s, 3H, Ar-OCH_3), 2.47 (s, 3H, Thiazole-CH_3), 2.32 (s, 3H, Ar-CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 159.6, 152.7, 148.1, 143.4, 140.6, 139.4, 132.6, 130.6, 129.6, 129.5, 128.7, 127.5, 126.5, 125.6, 122.3, 120.4, 119.1, 116.8, 114.9, 55.3, 44.6, 21.3, 16.7; HRMS calculated for $C_{30}H_{27}N_6OS$: 519.1967; observed *m/z*: 519.1960 (M + H)+

General procedure for synthesis of 4-(azidomethyl)-3-aryl-1-phenyl-1H-pyrazole, 9a-e

To the ice cold solution of (3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methanol, **8a-e** (0.05 mol) and triethyl amine (0.11 mol) in dry DCM (25 mL), CH_3SO_2Cl (0.06 mol) in dichloromethane (10 mL) was added drop-wise for 20 minutes and stirred at room temperature for 2-3hours (TLC). The solvent was distilled on rotary evaporator; reaction mixture was dissolved in water and extracted with DCM (3 × 30 mL). The organic layer was washed with brine and dried over sodium sulfate that gave (3-aryl)-1-phenyl-1*H*-pyrazol-4-yl)methyl methanesulfonate. To a solution of methanesulfonate derivative (0.05 mol) in DMSO (20 mL), NaN_3 (0.06 mol) was added and the reaction mixture was stirred at 60 °C for 2-5 hours. The progress of reaction was monitored by TLC. The reaction mixture was quenched in water (100 mL) and extracted with ethyl acetate (3 × 30 mL). The organic layer was dried over sodium sulfate and solvent was distilled on rotary evaporator that gave 4-(azidomethyl)-3-aryl-1-phenyl-1*H*-pyrazole, **9a-e** (65-72%).

General method for synthesis of 1-((3-aryl-1-phenyl-1H-pyrazol-4-yl)methyl)-4-(3-aryl-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole (11a-o)

A solution of 4-(azidomethyl)-3-aryl-1-phenyl-1*H*-pyrazole, **9a-e** (1 mmole), 3-aryl-4-ethynyl-1-phenyl-1*H*-pyrazole, **10a-c** (1 mmole), sodium ascorbate (0.22 mmole) and $CuSO_4.5H_2O$ (0.25 mmole) in DMF:Water (6 mL, 3:1) was stirred at room temperature for 10-20 hours. After the complete consumption of starting material (TLC), the reaction mass was poured in water and extracted with ethyl acetate (3 × 10 mL). Ethyl acetate layer was dried over anhydrous Na_2SO_4 and evaporated on rotary evaporator. The crude product was purified by column chromatography using ethyl acetate:hexane as eluent (2:8) gave1-((3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methyl)-4-(3-aryl-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole (**11a-o**) (Yield 65-75%).

4-(1,3-Diphenyl-1H-pyrazol-4-yl)-1-((1,3-diphenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11a

Yield 66%; Mp. 142-144 °C; IR cm^{-1}: 1599, 1551, 1503, 1452,1351, 1215, 1061, 958, 949 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.48 (s, 1H, Pyrazole-H), 7.95 (s, 1H, Pyrazole-H), 7.81 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.73 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.63 – 7.57 (m, 4H, Ar-H), 7.52 – 7.41 (m, 7H, Ar-H), 7.33 – 7.29 (m, 5H, Ar-H), 7.21 (s, 1H, Triazole-H), 5.61 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.6, 150.7, 140.5, 139.7, 139.6, 133.0, 132.1, 129.5, 129.5, 128.9, 128.6, 128.5, 128.5, 128.5, 128.3, 127.9, 127.0, 126.7, 126.7, 120.1, 119.2, 119.0, 114.7, 112.6, 44.8; HRMS calculated for $C_{33}H_{26}N_7$ 520.2250; found HRMS m/z = 520.2242 $(M + H)^+$.

4-(3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((1,3-diphenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11b

Yield 62%; Mp. 128-130 °C; IR: 1598, 1548, 1504, 1454, 1391, 1314, 1211, 1072, 1059, 1048, 1011, 963, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H, Pyrazole-H), 8.00 (s, 1H, Pyrazole-H), 7.77 (dd, $J = 8.5$, 0.9 Hz, 2H, Ar-H), 7.74 (dd, $J = 8.6$, 1.0 Hz, 2H, Ar-H), 7.65 − 7.61 (m, 2H, Ar-H), 7.51 − 7.42 (m, 11H, Ar-H), 7.33 − 7.29 (m, 2H, Ar-H), 7.22 (s, 1H, Triazole-H), 5.64 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.6, 149.5, 140.2, 139.6, 139.5, 132.0, 131.9, 131.7, 130.1, 129.6, 129.6, 129.0, 128.7, 128.5, 127.9, 127.2, 127.2, 126.9, 122.7, 120.2, 119.2, 119.1, 114.6, 112.4, 44.8; HRMS calculated for $C_{33}H_{25}BrN_7$: 598.1355; Found HRMS m/z = 598.1344 $(M + H)^+$, 600.1323 $(M + 2 + H)^+$.

1-((1,3-Diphenyl-1H-pyrazol-4-yl)methyl)-4-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, 11c

Yield 70%; Mp. 162-164 °C; IR: 1599, 1548, 1505, 1456, 1392, 1315, 1217, 1158, 1087, 1061, 957, 949, 845 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H, Pyrazole-H), 7.97 (s, 1H, Pyrazole-H), 7.76 (dd, $J = 8.6$, 1.1 Hz, 2H, Ar-H), 7.71 (dd, $J = 8.6$, 1.1 Hz, 2H, Ar-H), 7.60 (dd, $J = 8.1$, 1.5 Hz, 2H, Ar-H), 7.54 (dd, $J = 8.8$, 5.4 Hz, 2H, Ar-H), 7.49 − 7.40 (m, 7H, Ar-H), 7.33-7.29 (m, 2H, Ar-H), 7.16 (s, 1H), 7.00 (t, $J = 8.7$ Hz, 2H, Ar-H), 5.62 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.87 and 161.90 ($^1J = 248.22$ Hz), 151.6, 149.8, 140.3, 139.7, 139.5, 132.1, 130.35 and 130.29 ($^3J = 7.56$ Hz), 129.6, 129.5, 129.06 and 129.04 ($^4J = 2.53$ Hz), 128.9, 128.7, 128.4, 127.9, 127.1, 127.0, 126.8, 120.1, 119.2, 119.0, 115.59 and 115.42 ($^2J = 21.42$ Hz), 114.6, 112.4, 44.8; HRMS calculated for $C_{33}H_{25}FN_7$: 538.2155; Found HRMS m/z = 538.2146 $(M + H)^+$.

1-((3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-4-(1,3-diphenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, 11d

Yield 75%; Mp. 146-148 °C; IR: 1598, 1546, 1501, 1451, 1353, 1217, 1051, 1007, 959, 949, 843, 827 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 1H, Pyrazole-H), 7.93 (s, 1H, Pyrazole-H), 7.80 − 7.76 (m, 2H, Ar-H), 7.70 − 7.67 (m, 2H, Ar-H), 7.59 − 7.53 (m, 4H, Ar-H), 7.49 − 7.44 (m, 6H, Ar-H), 7.35 − 7.28 (m, 5H, Ar-H), 7.17 (s, 1H, Triazole-H), 5.56 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7, 150.4, 140.6, 139.7, 139.4, 133.0, 132.1, 131.8, 131.0, 129.6, 129.5, 129.4, 129.4, 128.6, 128.5, 127.2, 126.8, 122.9, 120.0, 119.2, 119.1, 119.0, 114.7, 112.5, 44.7; HRMS calculated for $C_{33}H_{25}BrN_7$: 598.1355; Found HRMS m/z = 598.1344 $(M + H)^+$, 600.1323 $(M + 2 + H)^+$.

4-(3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11e

Yield 68%; Mp. 134-136 °C; IR: 1598, 1526, 1504, 1457, 1349, 1220, 1054, 961, 952, 843, 811 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.37 (s, 1H, Pyrazole-H), 7.85 (s, 1H, Pyrazole-H), 7.70 (d, $J = 7.6$ Hz, 2H, Ar-H), 7.61 (d, $J = 7.6$ Hz, 2H, Ar-H), 7.50 − 7.46 (m, 4H, Ar-H), 7.42 − 7.35 (m, 4H, Ar-H), 7.27 − 7.19 (m, 4H, Ar-H), 7.09 (s, 1H, Triazole-H), 7.05 (t, J = 8.0 Hz, 2H, Ar-H), 5.47 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, DMSO-d_6) δ 149.8, 149.1, 139.6, 139.4, 132.4, 132.2, 131.8, 131.7, 130.6, 130.5, 130.2, 130.1, 123.0, 129.4, 129.3, 127.3, 127.2, 123.0, 122.2, 122.1, 119.0, 118.9, 115.9, 112.7, 44.5; HRMS calculated for $C_{33}H_{24}BrFN_7$: 676.0460 HRMS m/z = 676.0458 $(M + H)^+$, 678.0443 $(M + 2 + H)^+$

1-((3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-4-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, 11f

Yield 70%; Mp. 180-182 °C; IR: 1599, 1547, 1503, 1453, 1354, 1220, 1062, 1046, 960, 948, 839, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H, Pyrazole-H), 7.87 (s, 1H, Pyrazole-H), 7.71 – 7.66 (m, 2H, Ar-H), 7.63 – 7.60 (m, 2H, Ar-H), 7.52 – 7.45 (m, 4H, Ar-H), 7.43 – 7.36 (m, 6H, Ar-H), 7.28 – 7.21 (m, 2H, Ar-H), 7.10 (s, 1H, Triazole-H), 6.96 – 6.91 (m, 2H, Ar-H), 5.51 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.89 and 161.91 (^1J = 249.48 Hz), 150.3, 149.8, 140.5, 139.6, 139.4, 132.1, 131.0, 130.40 and 130.33 (^3J = 8.82 Hz), 129.6, 129.5, 129.4, 129.09 and 129.06 (^4J = 3.78 Hz), 128.6, 127.3, 127.0, 126.9, 122.9, 120.0, 119.2, 119.1, 115.59 and 115.42 (^2J = 21.42 Hz), 114.6, 112.4, 44.8; HRMS calculated for $C_{33}H_{24}BrFN_7$: 616.1261; Found HRMS m/z = 616.1257 $(M+H)^+$, 618.1243 $(M+2+H)^+$

4-(1,3-Diphenyl-1H-pyrazol-4-yl)-1-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11g

Yield 65%; Mp. 210-212 °C (dec.); IR: 1600, 1547, 1518, 1504, 1452, 1344, 1317, 1212, 1057, 1048, 962, 826 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H, Pyrazole-H), 7.85 (s, 1H, Pyrazole-H), 7.70 (d, J = 7.6 Hz, 2H, Ar-H), 7.61 (d, J = 7.6 Hz, 2H, Ar-H), 7.50 – 7.47 (m, 4H, Ar-H), 7.40 – 7.37 (m, 4H, Ar-H), 7.26 – 7.21 (m, 5H, Ar-H), 7.09 (s, 1H, Triazole-H), 7.07 – 7.02 (m, 2H, Ar-H), 5.47 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.96 and 161.99 (^1J = 248.22 Hz), 150.7, 150.7, 140.6, 139.7, 139.5, 133.0, 129.77 and 129.71 (^3J = 7.56 Hz), 129.6, 129.5, 128.6, 128.5, 128.5, 128.21 and 128.18 (^4J = 3.78 Hz), 127.1, 126.8, 120.0, 119.2, 119.1, 116.03 and 115.85 (^2J = 22.68 Hz), 114.5, 112.5, 44.7; HRMS calculated for $C_{33}H_{25}FN_7$: 538.2155; Found HRMS m/z = 538.2155

4-(3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11h

Yield 68%; Mp. 148-150 °C; IR: 1598, 1544, 1501, 1455, 1342, 1315, 1214, 1070, 1060, 1010, 962, 844, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H, Pyrazole-H), 8.14 (s, 1H, Pyrazole-H), 7.78 – 7.73 (m, 4H, Ar-H), 7.67 – 7.62 (m, 2H, Ar-H), 7.53 – 7.44 (m, 8H, Ar-H), 7.43 (s, 1H, Triazole-H), 7.34 – 7.30 (m, 2H, Ar-H), 7.15 (t, J = 8.6 Hz, 2H, Ar-H), 5.64 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.67 and 161.70 (^1J = 248.22 Hz), 150.4, 149.2, 139.7, 139.4, 139.3, 131.8, 131.4, 129.9, 129.63 and 129.57 (^3J = 7.56 Hz), 129.4, 129.4, 128.8, 128.21 and 128.19 (^4J = 2.56 Hz), 127.3, 126.9, 126.7, 122.3, 120.6, 118.9, 118.8, 115.76 and 115.59 (^2J = 22.68 Hz), 114.4, 112.3, 44.6; HRMS calculated for $C_{33}H_{24}BrFN_7$: 616.1261; Found HRMS m/z = 616.1257 $(M+H)^+$, 618.1243$(M+2+H)^+$

4-(3-(4-Fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11i

Yield 62%; Mp. 168-170 °C; IR: 1598, 1545, 1527, 1502, 1456, 1342, 1218, 1160, 1088, 1053, 962, 843, 816 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H, Pyrazole-H), 7.98 (s, 1H, Pyrazole-H), 7.77 (dd, J = 8.6, 0.9 Hz, 2H, Ar-H), 7.71 (dd, J = 8.6, 1.0 Hz, 2H, Ar-H), 7.63 – 7.54 (m, 4H, Ar-H), 7.52 – 7.45 (m, 4H, Ar-H), 7.38 – 7.29 (m, 2H, Ar-H), 7.18 (s, 1H, Triazole-H), 7.17 – 7.11 (m, 2H, Ar-H), 7.06 – 6.99 (m, 2H, Ar-H), 5.60 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.97 and 161.99 (^1J = 249.48 Hz), 163.87 and 161.90 (^1J = 248.22 Hz), 150.6, 149.8, 140.4, 139.6, 139.4, 130.39 and 130.32 (^3J = 8.82 Hz), 129.72 and 129.66 (^3J = 7.56 Hz), 129.6, 129.5, 129.09 and 129.06 (^4J = 3.78 Hz), 128.5, 128.20 and 128.17 (^4J = 3.78 Hz), 127.2, 127.0, 126.8, 120.0, 119.1, 119.0, 116.03 and 115.86 (^{2}J = 22.68 Hz), 115.57

and 115.40 ($^2J = 22.68$ Hz), 114.4, 112.4, 44.8; HRMS calculated for $C_{33}H_{24}F_2N_7$: 556.2061; Found HRMS $m/z = 556.2065(M + H)^+$

4-(1,3-Diphenyl-1H-pyrazol-4-yl)-1-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11j

Yield 70%; Mp. 170-172 °C; IR: 1599, 1524, 1503, 1452, 1339, 1242, 1169, 1050, 1020, 1008, 944, 833, 818 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H, Pyrazole-H), 7.95 (s, 1H, Pyrazole-H), 7.78 − 7.72 (m, 4H, Ar-H), 7.56 − 7.44 (m, 11H, Ar-H), 7.32 (t, $J = 7.4$ Hz, 2H, Ar-H), 7.22 (s, 1H, Triazole-H), 7.00 (d, $J = 8.4$ Hz, 2H, Ar-H), 5.60 (s, 2H, Pyrazole-CH_2-Triazole), 3.86 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.9, 150.9, 149.9, 140.6, 139.7, 139.5, 131.9, 132.8, 130.1, 129.6, 129.2, 128.6, 128.4, 127.8, 126.8, 126.9, 124.5, 122.7, 120.1, 119.2, 119.1, 114.5, 114.3, 112.5, 55.4, 44.9; HRMS calculated for $C_{34}H_{28}N_7O$:550.2355; Found HRMS m/z = 550.2351 $(M + H)^+$

4-(3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11k

Yield 65%; Mp. 164-166 °C; IR: 1598, 1518, 1505, 1456, 1342, 1246, 1211, 1174, 1049, 1024, 1011, 962, 833 cm^{-1}; ^1H NMR (500 MHz, CDCl3) δ 8.40 (s, 1H, Pyrazole-H), 7.98 (s, 1H, Pyrazole-H), 7.77 (d, J = 7.6 Hz, 2H, Ar-H), 7.73 (d, J = 7.6 Hz, 2H, Ar-H), 7.58 − 7.53 (m, 2H, Ar-H), 7.51 − 7.44 (m, 8H, Ar-H), 7.33 (t, J = 7.4 Hz, 2H, Ar-H), 7.24 (s, 1H, Triazole-H), 7.00 (d, J = 8.8 Hz, 2H, Ar-H), 5.62 (s, 2H, Pyrazole-CH_2-Triazole), 3.87 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.0, 151.4, 149.5, 140.2, 139.6, 139.6, 131.9, 131.6, 130.1, 129.6, 129.5, 129.2, 128.4, 127.3, 126.9, 126.9, 124.5, 122.6, 120.3, 119.1, 119.1, 114.4, 114.2, 112.4, 55.4, 44.9; HRMS calculated for $C_{34}H_{27}BrN_7O$: 628.1460; Found HRMS m/z = 628.1455 $(M + H)^+$, 630.1436 $(M + 2 + H)^+$,

4-(3-(4-Fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11l

Yield 75%; Mp. 170-172 °C; IR: 1600, 1509, 1458, 1341, 1260, 1215, 1052, 1027, 959, 845, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H, Pyrazole-H), 7.96 (s, 1H, Pyrazole-H), 7.76 − 7.71 (m, 2H, Ar-H), 7.68 (dd, $J = 7.7$, 0.9 Hz, 2H, Ar-H), 7.56 − 7.49 (m, 4H, Ar-H), 7.44 (t, $J = 7.5$ Hz, 4H, Ar-H), 7.29 (dd, $J = 5.8$, 4.5 Hz, 2H, Ar-H), 7.18 (s, 1H, Triazole-H), 7.02 − 6.93 (m, 4H, Ar-H), 5.58 (s, 2H, Pyrazole-CH_2-Triazole), 3.83 (s, 3H, OCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.81 and 161.84 ($^1J = 248.22$ Hz), 159.9, 151.4, 149.7, 140.2, 139.6, 139.5, 130.32 and 130.25 ($^3J = 8.82$ Hz), 129.5, 129.5, 129.1, 129.06 and 129.03 ($^4J = 3.78$ Hz), 128.4, 127.0, 126.9, 126.8, 124.5, 120.2, 119.0, 119.0, 115.52 and 115.35 ($^2J = 21.42$ Hz), 114.3, 114.2, 112.4, 55.3, 44.9; HRMS calculated for $C_{34}H_{27}FN_7O$: 568.2261; Found HRMS $m/z = 568.2252$ $(M + H)^+$

4-(1,3-Diphenyl-1H-pyrazol-4-yl)-1-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11m

Yield 70%; Mp. 218– 220 °C; IR: 1598, 1530, 1505, 1455, 1333, 1208, 1181, 1069, 1055, 1046, 962, 863, 854 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.80 (s, 1H, Pyrazole-H), 8.75 (s, 1H, Pyrazole-H), 8.31 (d, $J = 8.9$ Hz, 2H, Ar-H), 8.08 (s, 1H, Triazole-H), 8.06 (d, $J = 8.9$ Hz, 2H, Ar-H), 7.91 (d, $J = 8.0$ Hz, 4H, Ar-H), 7.62 (dd, $J = 6.6$, 3.0 Hz, 2H, Ar-H), 7.58 − 7.50 (m, 4H, Ar-H), 7.40 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.37 − 7.30 (m, 4H, Ar-H), 5.84 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, DMSO-d_6) δ 150.3, 148.7, 147.5, 139.7, 139.6, 139.5, 139.1, 133.1, 131.3, 130.2, 130.1,

129.0, 128.9, 128.7, 128.6, 128.5, 127.6, 127.1, 124.4, 122.9, 119.2, 118.8, 116.8, 112.6, 44.4; HRMS calculated for $C_{33}H_{25}N_8O_2$: 565.2100; Found HRMS $m/z = 565.2093$ $(M + H)^+$

4-(3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11n

Yield 68%; Mp. 206-208 °C; IR: 1597, 1547, 1504, 1460, 1334, 1246, 1215, 1110, 1065, 1047, 1011, 962, 946, 857, 828 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.82 (s, 1H, Pyrazole-H), 8.76 (s, 1H, Pyrazole-H), 8.33 (d, J = 8.9 Hz, 2H), 8.16 (s, 1H, Triazole-H), 8.07 (d, $J = 8.8$ Hz, 2H, Ar-H), 7.94-7.90 (m, 4H, Ar-H), 7.62 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.58 − 7.51 (m, 6H, Ar-H), 7.41-7.34 (m, 2H, Ar-H), 5.84 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, DMSO-d_6) δ 150.4, 148.9, 147.6, 139.7, 139.6, 139.5, 139.1, 132.9, 131.4, 130.2, 130.1, 129.9, 129.2, 129.0, 128.7, 128.7, 127.7, 127.0, 125.8, 123.0, 119.2, 118.9, 114.9, 112.6, 44.6; HRMS calculated for $C_{33}H_{24}BrN_8O_2$: 643.1206; Found HRMS $m/z = 643.1195$ $(M + H)^+$ 645.1177 $(M + 2 + H)^+$

4-(3-(4-Fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methyl)-1H-1,2,3-triazole, 11o

Yield 65%; Mp. 206-208 °C; IR: 1597, 1545, 1505, 1463, 1333, 1214, 1159, 1110, 1065, 1048, 962, 947, 856, 831 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.82 (s, 1H, Pyrazole-H), 8.76 (s, 1H, Pyrazole-H), 8.32 (d, $J = 8.8$ Hz, 2H, Ar-H), 8.13 (s, 1H, Triazole-H), 8.07 (d, $J = 8.8$ Hz, 2H, Ar-H), 7.92 (dd, $J = 7.8$, 3.6 Hz, 4H, Ar-H), 7.76 − 7.68 (m, 2H, Ar-H), 7.58 − 7.52 (m, 4H, Ar-H), 7.40 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.34 (t, $J = 7.4$ Hz, 1H, Ar-H), 7.17 (t, $J = 8.8$ Hz, 2H, Ar-H), 5.84 (s, 2H, Pyrazole-CH_2-Triazole); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.81 and 161.84 ($^1J = 248.22$ Hz),150.3, 148.9, 147.8, 134.0, 139.6, 139.2, 133.2, 132.0, 130.35 and 130.28 ($^3J = 8.82$ Hz), 130.1, 129.2, 129.05 and 129.02 ($^4J = 3.78$ Hz), 128.8, 128.6, 128.5, 127.7, 127.1, 124.4, 119.2, 118.9, 115.58 and 115.41 ($^2J = 21.42$ Hz), 116.8, 112.6, 44.8; HRMS calculated for $C_{33}H_{24}FN_8O_2$: 583.2006; Found HRMS $m/z = 583.1996$ $(M + H)^+$

Antimycobacterial activity

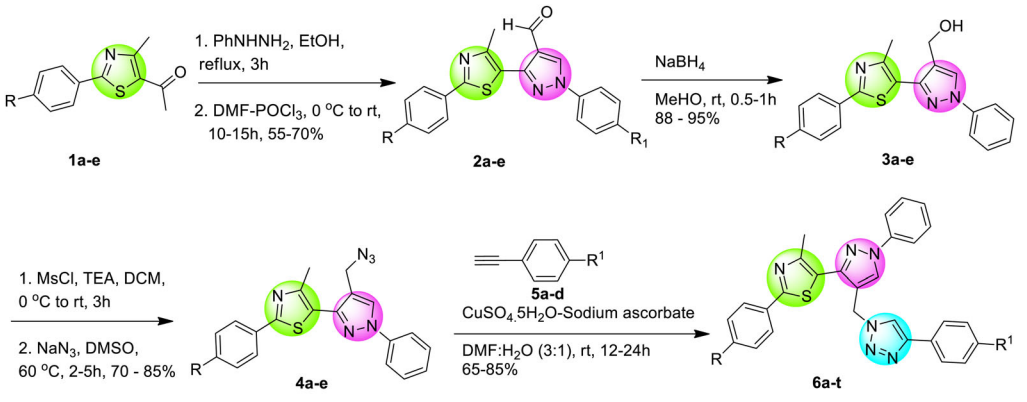
The synthesized thiazole and pyrazole clubbed 1,2,3-triazol derivatives were screened for *in vitro* activity against *M. tuberculosis* H37Ra (ATCC 25177) dormant and active strains. MTB activity was determined through the XTT reduction menadione assay (XRMA) reading absorbance at 470 nm as per the protocol given in the literature.[50–53] *In vitro* activity against MTB dormant and active (12 and 8 days, respectively) stage was performed using the XRMA. Percentage inhibition was calculated using the following formula:

$$\%\ \text{inhibition} = \left[(\text{control–CMP})/(\text{control–blank})\right] \text{ x } 100$$

Where 'control' is the activity of mycobacteria without compounds, 'CMP' is the activity of mycobacteria in the presence of compounds and 'blank' is the activity of the culture medium without mycobacteria.

Antibacterial activity

Initially, the bacterial cultures were grown in Luria Burtony media at 37 °C at 180 rpm. Once the culture reaches 1 O.D., it is used for antibacterial assay. Bacterial strains *E. coli* (NCIM 2576), *P. flurescence* (NCIM 2059) (Gram-negative) and *S. aureus* (NCIM 2602), *B. subtilis* (NCIM 2162) (Gram-positive) were obtained from NCIM (NCL, Pune) and were grown in Luria Burtony medium from Hi Media, India. The activity was performed in 96 well plates after 8 hours and 12 hours for Gram negative and Gram positive bacteria, respectivelyxx. 0.1% of 1 O.D. culture at



Comp.	R	R^1	Comp.	R	R^1	Comp.	R	R^1	Comp.	R	R^1	Comp.	R	R^1
6a	H	H	**6e**	4-Br	H	**6i**	4-Cl	H	**6m**	F	H	**6q**	CH_3	H
6b	H	F	**6f**	4-Br	F	**6j**	4-Cl	F	**6n**	F	F	**6r**	CH_3	F
6c	H	CH_3	**6g**	4-Br	CH_3	**6k**	4-Cl	CH_3	**6o**	F	CH_3	**6s**	CH_3	CH_3
6d	H	OCH_3	**6h**	4-Br	OCH_3	**6l**	4-Cl	OCH_3	**6p**	F	OCH_3	**6t**	CH_3	OCH_3

Scheme 1. Synthetic route of 4-methyl-2-aryl-5-(1-phenyl-4-((4-aryl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole, **6a-t**.

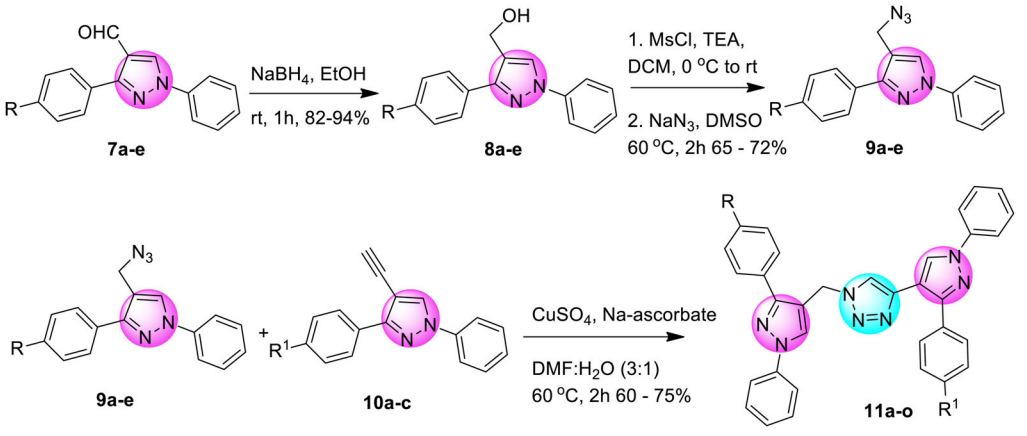
620 nm was used for screening inoculated culture was added into each well of 96 well plate containing the compounds to be tested. Optical density for each plate was measured at 620 nm after 8 hours for Gram-negative bacteria and after 12 hours for Gram- positive bacteria.[54]

Result and discussion

Chemistry

Scheme 1 represents the synthetic route for 4-methyl-2-(4-substituted phenyl)-5-(4-((4-(4-substituted phenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)thiazole, **6a-t** derivatives. 1-(4-methyl-2-substituted phenyl thiazol-5-yl)ethanone, **1a-e** on reaction with phenyl hydrazine gave phenylhydrazone derivatives which upon reaction with DMF-$POCl_3$ in DMF gave 3-(4-methyl-2-substituted phenyl thiazol-5-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde, **2a-e**.[38] Aldehyde **2a-e** was reduced to corresponding (3-(4-methyl-2-substituted phenyl thiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)methanol, **3a-e** by reaction with sodium borohydride in methyl alcohol. The alcohol **3a-e** was converted to methyl sulfonyl derivative by reaction with methyl sulfonyl chloride in DCM, which upon reaction with sodium azide in DMSO gave 5-(4-(azidomethyl)-1-phenyl-1*H*-pyrazol-3-yl)-4-methyl-2-susbtituted phenyl thiazole, **4a-e**. Azide derivatives **4a-e** on copper-catalyzed [3 + 2] azide-alkyne cycloaddition reaction with substituted alkyne, **5a-d**, in DMF:H_2O (3:1) furnished target compounds 4-methyl-2-(4-substituted phenyl)-5-(4-((4-(4-substituted phenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)thiazole, **6a-t**.

The synthesis of 1-((3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methyl)-4-(3aryl-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole, **11a-o** is presented in scheme 2. 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehyde, **7a-e** on reduction with $NaBH_4$ gave (3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methanol **8a-e**. Alcohol derivatives **8a-e** on reaction with CH_3SO_2Cl in dichloromethane gave (3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methyl methanesulfonate, which upon nucleophilic substitution reaction with NaN_3 in dimethylsulfoxide furnished 3-aryl-4-(azidomethyl)-1-phenyl-1*H*-pyrazole, **9a-e**. Azide derivatives **9a-e** upon copper-catalyzed [3 + 2] cycloaddition reaction with 3-aryl-4-ethynyl-1-phenyl-1*H*-pyrazole **10a-c** in the presence of catalytic sodium ascorbate in DMF:water (3:1) gave 1-((3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methyl)-4-(3aryl-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole, **11a-o.** The



Comp.	R	R^1	Comp.	R	R^1	Comp.	R	R^1	Comp.	R	R^1	Comp.	R	R^1
11a	H	H	**11d**	Br	H	**11g**	4-F	H	**11j**	OCH_3	H	**11m**	NO_2	H
11b	H	4-Br	**11e**	Br	4-Br	**11h**	4-F	4-Br	**11k**	OCH_3	4-Br	**11n**	NO_2	Br
11c	H	4-F	**11f**	Br	4-F	**11i**	4-F	4-F	**11l**	OCH_3	4-F	**11o**	NO_2	F

Scheme 2. Synthetic route of bis-pyrazolyl-1,2,3-triazole derivatives, **11a-o**

structure of synthesized compounds was confirmed by spectrometric analysis. All synthesized compounds screened for antimycobacterial activity.

As a representative analysis, the ^{1}H NMR spectrum of 5-(4-((4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)-4-methyl-2-phenylthiazole, **6b** showed four singlets at δ 8.10, 7.61, 5.63 and 2.61 for C-5 pyrazole, C-5 triazole, pyrazole-CH_2-triazole and thiazole-CH_3 protons, respectively. The thirteen aromatic protons resonated between δ 7.08 and 7.96. The protons attached to fluorophenyl showed H-F couplings. The ^{13}C NMR spectrum of compound **6b** showed two signals in aliphatic region at δ 44.58 and 16.73 for methylene and methyl carbon, respectively. The pyrazole, thiazole, triazole and aromatic carbons resonated from δ 115.70 to 167.02. The C-F coupling for fluorophenyl was observed with coupling constant $^1J_{C\text{-}F}$ = 248.22 Hz, $^2J_{C\text{-}F}$ = 21.42 Hz, $^3J_{C\text{-}F}$ = 8.82 Hz, $^4J_{C\text{-}F}$ = 3.78 Hz. Further, the structure of compound **6b** was confirmed by the molecular ion peak (HRMS) at *m/z*: 493.1603 [M + H]+. Structure of all synthesized compounds was ascertained accordingly.

Antimycobacterial activity

All the newly synthesized thiazolyl-pyrazolyl-1,2,3-triazole derivatives (**6a-t**) and bis-pyrazolyl-1,2,3-triazole (**11a-o**) derivatives were screened for antimycobacterial activity against *Mycobacterium Tuberculosis* H37Ra dormant and active and antibacterial activity against four pathogenic bacteria, *Escherichia coli* (NCIM 2576), *Pseudomonas flurescence* (NCIM 2059), *Staphylococcus aureus* (NCIM 2602) and *Bacillus subtilis* (NCIM 2162).[50–53]

The analysis of antimycobacterial activity (Table 1) of thiazolyl-pyrazolyl-1,2,3-triazole derivatives, **6a-t** exposed that, most of the derivatives showed moderate activity against both *M. tuberculosis* strains. It was noted that, among the compounds 4-methyl-2-phenyl-5-(1-phenyl-4-((4-substituted phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole **6a-d**, compound **6a** (R = R1 = H), showed moderate activity against M. tuberculosis H37Ra Dormant and good activity against M. tuberculosis H37Ra active strains, while compound **6 b** (R = H, R^1 = F), was found inactive against *M. tuberculosis* H37Ra Dormant and less active against *M. tuberculosis* H37Ra active. Compounds **6c** (R = H, R^1 = CH_3) and **6d** (R = H, R^1 = OCH_3) exhibited moderate activity against both *M-tb* strains. Among the compounds 2-(4-bromophenyl)-4-methyl-5-(1-phenyl-4-

Table 1. Anti-tubercular activity in % inhibition (30 μg/mL) of compounds **6a-t** and **11a-o**.

Compound	R	R^1	*M tuberculosis* H37Ra Dormant	*M tuberculosis* H37Ra Active
6a	H	H	35.41	58.35
6b	H	F	–	21.96
6c	H	CH_3	37.40	39.80
6d	H	OCH_3	32.88	36.35
6e	Br	H	30.36	36.58
6f	Br	F	36.82	51.38
6g	Br	CH_3	53.56	31.01
6h	Br	OCH_3	53.76	12.02
6i	Cl	H	39.43	30.80
6j	Cl	F	38.62	57.28
6k	Cl	CH_3	44.87	30.37
6l	Cl	OCH_3	45.29	42.78
6m	F	H	26.36	19.98
6n	F	F	–	22.22
6o	F	CH_3	40.09	31.26
6p	F	OCH_3	34.01	33.48
6q	CH_3	H	44.67	27.24
6r	CH_3	F	–	17.42
6s	CH_3	CH_3	43.16	26.22
6t	CH_3	OCH_3	30.84	–
11a	H	H	39.89	35.46
11b	H	Br	6.459	19.9
11c	H	F	16.4	22.82
11d	Br	H	46.22	42.23
11e	Br	Br	28.43	50.00
11f	Br	F	50.96	43.18
11g	F	H	35.39	31.36
11h	F	Br	28.62	22.66
11i	F	F	–	40.95
11j	OCH_3	H	nd	nd
11k	OCH_3	Br	48.07	39.32
11l	OCH_3	F	30.34	34.66
11m	NO_2	H	43.19	55.48
11n	NO_2	Br	50.12	46.31
11o	NO_2	F	53.56	24.99
Rifampicin			99.50	99.00

'-' = inactive; nd = activity not determined.

((4-substituted phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole, **6e-h**, compound **6e** (R = Br, R^1 = H) showed moderate activity against both the *M-tb* strains. Compound **6f** (R = Br, R^1 = F) exhibited moderate activity against *M. tuberculosis* H37Ra Dormant and good activity *M. tuberculosis* H37Ra active strains. Compound **6g**, (R = Br and R^1 = CH_3) exhibited good activity against *M. tuberculosis* H37Ra dormant and moderate activity against *M. tuberculosis* H37Ra active strains. It was observed that compound 6**h** (R = Br, R^1 = OCH_3), exhibited good activity against *M. tuberculosis* H37Ra dormant and was less active against *M. tuberculosis* H37Ra active strains.

Among the compounds 2-(4-chlorophenyl)-4-methyl-5-(1-phenyl-4-((4-substituted phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole **6i-l**, compound **6i** (R = Cl, R^1 = H) showed moderate activity against both *M-tb* strains. Compound **6j** (R = Cl, R^1 = F) showed moderate activity against *M-tb* dormant and good activity against *M-tb* active strains. Compounds **6k** (R = Cl, R^1 = CH_3) and **6l** (R = Cl, R^1 = OCH_3) showed moderate activity against both *M-tb* strains. Among the compounds 2-(4-fluorophenyl)-4-methyl-5-(1-phenyl-4-((4-substituted phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole **6m-p**, compounds **6m** (R = F, R^1 = H) and **6n** (R = F, R^1 = F) was less active against both *M-tb* strains. Whereas compounds **6o** (R = F, R^1 = CH_3) and **6p** (R = F, R^1 = OCH_3) showed moderate activity both *M-tb* strains. Among the compounds 4-methyl-5-(1-phenyl-4-((4-substituted phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)-2-(p-tolyl)thiazole **6q-t**, Compounds **6q** (R = CH_3, R^1 = H), **6s** (R = CH_3, R^1 = CH_3)

and **6t** (R = CH_3, R^1 = OCH_3) showed moderate activity against *M-tb* dormant and less activity against *M-tb* active strains, whereas compound **6r** (R = CH_3, R^1 = F) was found less active against both *M-tb* strains.

The antimycobacterial activity of bispyrazolyl-1,2,3-triazole, **11a-o** (Table 1), revealed that most of the compounds showed moderate to good activity against both *M. tuberculosis* H37Ra dormant (*M-tb* dormant) and *M. tuberculosis* H37Ra active (*M-tb* active) strains. Among the compounds 4-(3-aryl)-1-phenyl-1*H*-pyrazol-4-yl)-1-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)-1*H*-1,2,3-triazole **11a-c**, compound **11a** (R = R^1 = H) showed moderate activity, while compounds **11b** (R = H, R^1 = Br) and **11c** (R = H, R^1 = F), were found less active against both *M-tb* strains. Among the compounds 1-((3-(4-bromophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methyl)-4-(3-aryl-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole, **11d-f**, compounds **11d** (R = Br, R^1 = H) showed moderate activity against both *M-tb* strains, compound **11e** (R = Br, R^1 = F) showed good activity against *M-tb* active strain, whereas was less active against *M-tb* dormant strain. Compound **11f** (R = Br, R^1 = F) showed good and moderate activity against *M-tb* dormant and *M-tb* active strain, respectively. Among the compounds 4-(3-aryl-1-phenyl-1*H*-pyrazol-4-yl)-1-((3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methyl)-1*H*-1,2,3-triazole **11g-i,** compound **11g** (R = F, R^1 = H) showed moderate activity against *M-tb* dormant strain and compound **11i** (R = F, R^1 = F) showed moderate activity against *M-tb* active strain. Compound **11 h** (R = F, R^1 = Br) was less active against both *M-tb* strains.

From the compounds 4-(3-aryl-1-phenyl-1*H*-pyrazol-4-yl)-1-((3-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazol-4-yl)methyl)-1*H*-1,2,3-triazole, **11j-l**, compounds **11k** (R = OCH_3, R^1 = Br) and **11l** (R = OCH_3, R^1 = F) showed moderate activity against both *M-tb* strains. Among the compounds 4-(3-aryl)-1-phenyl-1*H*-pyrazol-4-yl)-1-((3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methyl)-1*H*-1,2,3-triazole, **11m-o**, compound **11m** (R = NO_2, R^1 = H) showed good activity against *M-tb* active strain and moderate activity against *M-tb* dormant strain. Compounds **11n** (R = NO_2, R^1 = Br) and **11o** (R = NO_2, R^1 = F) exhibited good activity against *M-tb* dormant strain and moderate activity against *M-tb* active strain.

It is also noticed that in thiazolyl-pyrazolyl-1,2,3-triazole (6a-t), R = R^1 = H, R = Br or Cl and R^1 = F in compounds **6a**, **6f** and **6j,** exhibited good activity against *M-tb* active strain also R = Br and R^1 = CH_3 or OCH_3 in compound **6g** and **6h** showed good activity against *M-tb* dormant strain. Furthermore in bispyrazolyl-1,2,3-triazole (**11a-o**) R = R^1 = Br and R = NO_2, R^1 = H in compounds **11e** and **11m** showed good activity against *M-tb* active strain, moreover R = Br or NO_2, R^1 = F and R = NO_2, R^1 = F in compound **11f**, **11n** and **11o** showed good activity against *M-tb* dormant strain.

The antibacterial activity of thiazolyl-pyrazolyl-1,2,3-triazole derivatives (**6a-t**) and bis-pyrazolyl-1,2,3-triazole (**11a-o**) was assessed against the standard Gram-negative bacteria, *E. coli* (NCIM 2576), *P. flurescence* (NCIM 2059) and Gram-positive bacteria, *S. aureus* (NCIM 2602), *B. subtilis* (NCIM 2162).[50–54] Ampicillin and Kanamycin served as positive control for antibacterial activity. The antibacterial activity results in % inhibition are summarized in Table 2 and IC_{50} in μg/mL is presented in Table 3.

The *in vitro* antibacterial activity analysis of thiazolyl-pyrazolyl-1,2,3-triazole (Table 2) revealed that, most of the thiazolyl-pyrazolyl-1,2,3-triazole (**6a-t**) derivatives were less activities against *E. coli, P. flurescence, S. aureus* and showed moderate to good activity *B. subtilis*. Against the *B. subtilis* strain, amongst the synthesized compounds **6a-d** the compound **6a** showed good activity with 30 μg/mL and moderate activity with 10 μg/mL. Compound **6b** exhibited good activity at both tested concentrations. Compound **6c** showed good activity at 30 μg/mL and moderate activity at 10 μg/mL, whereas compound **6d** showed moderate activity at 30 and 10 μg/mL.

Among the compounds **6e-h**, compounds **6e**, **6f**, and **6g** showed moderate activity and compound **6h** showed good activity at 30 μg/mL concentration. Among the compounds **6i-l**, compounds **6i** and **6l** showed good activity at both tested concentrations. At 30 μg/mL concentration,

Table 2. The *in vitro* antimicrobial screening values (% nhibition) of compounds **6a-t** and **11a-o**.

			E.coli		*P. flurescence*		*S.aureus*		*B. subtillus*	
Compd.	R	R^1	30 ug/mL	10 ug/mL	30 ug/mL	10 ug/mL	30 ug/mL	10 ug/mL	30 ug/mL	10 ug/mL
6a	H	H	4.49	–	2.24	–	–	–	62.13	45.89
6b	H	F	14.51	30.01	–	–	–	–	90.29	82.29
6c	H	CH_3	–	–	2.35	2.71	3.475	5.185	80.38	44.01
6d	H	OCH_3	–	–	10	0.43	11.28	7.875	44.22	32.12
6e	Br	H	36.91	–	12.1	2.20	–	–	47.47	39.76
6f	Br	F	–	–	–	–	–	–	33.75	32.45
6g	Br	CH_3	25.50	–	13.62	6.193	–	–	41.48	44.28
6h	Br	OCH_3	7.27	–	25.1	12.34	–	–	76.18	48.3
6i	Cl	H	15.81	10.92	–	–	–	–	82.31	80.56
6j	Cl	F	4.74	3.49	–		–	–	51.99	41.53
6k	Cl	CH_3	18.93	17.91	13.46	14.11	–	–	42.05	16.45
6l	Cl	OCH_3	5.04	3.80	–	–	–	–	87.54	81.85
6m	F	H	–		–	–	–	–	66.55	40.23
6n	F	F	16.98	8.719	12.4	6.146	–	–	53.79	37.3
6o	F	CH_3	17.64	16.75	–	–	–	–	73.34	67.42
6p	F	OCH_3	19.29	26.43	4.85	2.59	–	7.46	42.98	42.23
6q	CH_3	H	–	–	–	–	–	–	35.71	18.75
6r	CH_3	F	20.38	–	15.12	6.03	–	–	89.32	69.11
6s	CH_3	CH_3	–	–	–	–	–	–	19.29	21.16
6t	CH_3	OCH_3	–	–	8.5	–	–	–	31.42	13.95
11a	H	H	10.63	–	9.13	–	–	–	56	51.67
11b	H	Br	–	–	–	–	19.42	8.625	55.57	51.62
11c	H	F	–	–	6.31	–	–	–	53.41	50.00
11d	Br	H	41.40	40.27	9.48	–	–	–	90.35	59.72
11e	Br	Br	29.72	25.60	–	–	–	–	66.33	27.14
11f	Br	F	–	–	–	–	–	–	66.02	–
11g	F	H	36.04	32.96	8.7	–	–	–	73.8	61.55
11h	F	Br	37.79	26.89	9.51	3.865	2.38	–	58.92	51.32
11i	F	F	45.09	14.58	28.3	16.92	16.47	13.81	66.96	58.8
11j	OCH_3	H	nd	nd	nd	nd	nd	Nd	nd	nd
11k	OCH_3	Br	10.66	10.05	19.6	17.39	–	–	81.33	79.17
11l	OCH_3	F	8.81	6.012	21.4	10.47	–	–	84.4	74.3
11m	NO_2	H	40.62	24.17	17.4	15.73	–	–	81.9	72.47
11n	NO_2	Br	21.17	15.94	23	14.46	–	–	77.61	32.97
11o	NO_2	F	10.88	19.78	20	19.78	–	–	32.44	23.06
Ampicillin			99.00	98.00	98.00	97.00	99.50	98.50	99.00	89.20

compounds **6j** and **6k** showed good and moderate activity, respectively. From the compounds **6m-p**, compound **6m** and **6n** showed good activity at 30 µg/mL concentration, whereas compounds **6o** exhibited good activity against both tested concentrations. Compound **6p** showed moderate activity at 30 and 10 µg/mL concentration. Among the compounds **6q-t**, compound **6r** showed good activity at both tested concentrations, whereas compounds **6q** and **6t** were moderately active at 30 µg/mL concentration.

The *in vitro* antibacterial activity results of bispyrazolyl-1,2,3-triazole (**11a-o**) (Table 2) revealed that, most of the compounds showed less activity against *P. flurescence, S. aureus*. Compounds **11d**, **11 g**, **11h**, **11i** and **11m** showed moderate activity against *E. coli* whereas most of the tested compounds exhibited moderate to good activity *B. subtilis*. Against the *B. subtilis* strain, the trends of substituents revealed that, compounds **11a** (R = R^1 = H), **11 b** (R = H, R^1 = Br) and **11c** (R = H, R^1 = F) showed good activity at 30 µg/mL and moderate activity at 10 µg/mL. Among the compounds **11d-f**, compound **11d** (R = Br, R^1 = H) showed good activity at 30 and 10 µg/mL, whereas compounds **11e** (R = Br, R^1 = Br) and **11f** (R = Br, R^1 = F) showed good activity at 30 µg/mL. Among the compounds **11g-i**, compounds **11g** (R = F, R^1 = H), **11h** (R = F, R^1 = Br) and **11i** (R = F, R^1 = F) exhibited good activity at both the tested concentrations. Among the compounds **11j-l**, compounds **11k** (R = OCH_3, R^1 = Br) and **11l** (R = OCH_3, R^1 =

Table 3. The *in vitro* antimicrobial activity IC_{50} in μg/mL of compounds **6a-t** and **11a-o**.

Compd.	R	R^1	*E. coli*	*P. flurescence*	*S. aureus*	*B. subtillus*
6a	H	H	>30	>30	>30	>30
6b	H	F	>30	>30	>30	**2.04**
6c	H	CH_3	>30	>30	>30	>30
6d	H	OCH_3	>30	>30	>30	>30
6e	Br	H	>30	>30	>30	>30
6f	Br	F	>30	>30	>30	**26.04**
6g	Br	CH_3	>30	>30	>30	>30
6h	Br	OCH_3	>30	>30	>30	>30
6i	Cl	H	>30	>30	>30	**2.19**
6j	Cl	F	>30	>30	>30	>30
6k	Cl	CH_3	>30	>30	>30	>30
6l	Cl	OCH_3	>30	>30	>30	**1.99**
6m	F	H	>30	>30	>30	>30
6n	F	F	>30	>30	>30	>30
6o	F	CH_3	>30	>30	>30	**2.50**
6p	F	OCH_3	>30	>30	>30	>30
6q	CH_3	H	>30	>30	>30	>30
6r	CH_3	F	>30	>30	>30	**2.09**
6s	CH_3	CH_3	>30	>30	>30	>30
6t	CH_3	OCH_3	>30	>30	>30	>30
11a	H	H	>30	>30	>30	>30
11b	H	Br	>30	>30	>30	>30
11c	H	F	>30	>30	>30	>30
11d	Br	H	>30	>30	>30	>30
11e	Br	Br	>30	>30	>30	>30
11f	Br	F	>30	>30	>30	>30
11g	F	H	>30	>30	>30	>30
11h	F	Br	>30	>30	>30	>30
11i	F	F	>30	>30	>30	>30
11j	OCH_3	H	>30	>30	>30	>30
11k	OCH_3	Br	>30	>30	>30	**1.99**
11l	OCH_3	F	>30	>30	>30	**2.96**
11m	NO_2	H	>30	>30	>30	**2.29**
11n	NO_2	Br	>30	>30	>30	>30
11o	NO_2	F	>30	>30	>30	>30
Ampicillin			0.25	1.12	0.15	1.35
Kanamycin			0.30	0.15	6.20	0.35

F) showed good activity at both tested concentrations. From the compounds **11m-o**, compound **11m** ($R = NO_2$, R^1 = H) showed good activity against both tested concentrations, whereas compounds **11o** ($R = NO_2$, R^1 = Br) exhibited good activity at 30 μg/mL concentration moderate activity at 10 μg/mL concentrations. Compound **11o** ($R = NO_2$, R^1 = F) showed moderate activity at 30 μg/mL concentration.

The structure activity relationship (SAR) revealed that for thiazolyl-pyrazolyl-triazole derivatives (**6a-t**) phenyl or *p*-tolyl group at 2-position of thiazole and 4-fluorophenyl at 4-position of 1,2,3-triazole, 4-fluorophenyl at 2-position of thiazole and *p*-tolyl at 4-position of 1,2,3-triazole, similarly, 4-chlorophenyl at 2-position of thiazole and phenyl or 4-methoxy phenyl at 4-position of 1,2,3-triazole showed good activity against *B. subtillus*. Among the bispyrazolyl-1,2,3-triazole (**11a-o**) derivatives 3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methyl at 1-position of 1,2,3-triazole and (3-(4-bromo or fluorophenyl)-1-phenyl-1H-pyrazol-4-yl) at 4-position of 1,2,3-triazole showed good activity against *B. subtillus*.

It is noteworthy that, among the 4-methyl-2-substituted phenyl-5-(1-phenyl-4-((4-substituted phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1*H*-pyrazol-3-yl)thiazole (**6a-t**) and 4-(1,3-diphenyl-1*H*-pyrazol-4-yl)-1-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)-1*H*-1,2,3-triazole, (**11a-o**) derivatives compounds **6b**, **6i**, **6l**, **6o, 6r, 11k**, **11l** and **11m** exhibited good activity with IC_{50} 1.99-2.96 μg/mL.

Conclusion

In conclusion, new derivatives of 4-methyl-2-(4-substituted phenyl)-5-(4-((4-(4-substituted phenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-phenyl-1H-pyrazol-3-yl)thiazole, (**6a-t**) and 1-((3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methyl)-4-(3aryl-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole (**11a-o**) derivatives have been synthesized. The antitubercular and antibacterial screening studies of synthesized compounds were undertaken to evaluate the effects of substituent on antimycobacterial activities. Some of the synthesized thiazolyl-pyrazolyl-1,2,3-triazole and bispyrazolyl-1,2,3-triazole derivatives showed moderate to good antitubercular activity against both *M-tb* strains and *B. subtilis* strain. It is concluded that compounds **6b**, **6i**, **6l**, **6o**, **6r**, **11k**, **11l** and **11m** showed good activity with IC_{50} 1.99-2.96 µg/mL.

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