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SYNTHESIS, CHARACTERISATION, AND ANTIBACTERIAL ACTIVITY OF NOVEL PYRAZOLE-LINKED TRIAZOLE DERIVATIVES

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ABSTRACT
The present work describes the pyrazolyl alkyne by propargylation of pyrazolyl methanol. Further synthesis of pyrazole-linked 1,4-disubstituted triazole derivatives was achieved by pyrazolyl alkyne with various aryl azides via a click chemistry approach. The developed compounds were confirmed and characterised by spectroscopic techniques like IR, ^{1}H NMR, ^{13}C NMR, and Mass data, along with synthesis and characterisation, and screening of antibacterial activity was reported. Antibacterial activity for proposed new analogues(8A-8L) was tested against *S.aureus*, *B. Subtilis*, *E.Coli,* and *K. pneumonia* pathogenic strains, exhibiting moderate activity when compared to the standard drug Ampicillin. Among the compounds, 8A, 8D, 8E, 8F, 8H, and 8I showed good activity on gram-positive strains. Whereas 8E showed good antibacterial activity on both gram-positive and gram-negative bacterial strains.
Keywords: Pyrazoles, 1,2,3-triazoles, Click Chemistry, Antibacterial Activity.
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INTRODUCTION

Drug Discovery of novel antibiotics is a major challenge for human health. Although there are more potent antibiotics that can be employed to combat a variety of bacterial species, their clinical lifespan can be significantly shortened due to their high susceptibility to acquired and adaptive bacterial resistance. The primary reason for this situation is the inexorable drive of evolution that leads to antimicrobial resistance. Also, excessive use of existing antibiotics in the market, coupled with bacterial mechanisms of action and genetic modifications, contributes to the emergence of multidrug-resistant (MDR) bacterial strains.

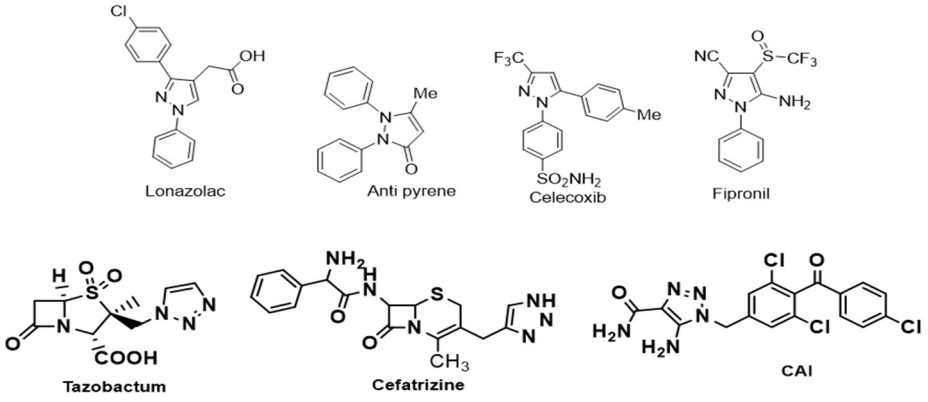

Fig.-1: A Few Triazole and Pyrazoles Containing Drugs

Hence, there is an urgent need to develop practical synthetic routes for potent antimicrobial analogues to execute comprehensive pharmacological studies, to fight adaptive and environmentally acquired bacterial resistance.[1-2] Triazoles represent a significant class of molecular scaffold widely recognised for their diverse applications in medicinal chemistry, agriculture.[3] The role of triazoles has been attracting medicinal

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chemists, due to their reactivity, pharmacological activities like antimicrobial[4], anticancer[5-6], Antitubercular[7], antimalarial[8], antifungal[9], antiproliferative[10], and antioxidant[11] properties. Various synthetic triazoles, Tazobactum, Cefatrizine are in series of β-lactam antibiotics, and CAI have potential antimicrobial activity and are already present in the market (Fig.-1).

Pyrazoles are a key class of heterocyclic moieties and hold importance in drug discovery, due to their wide range of chemical properties and biological activities.[12] Pyrazoles attracted by medicinal chemists due to their enormous pharmacological activities like antifungal[13], antibacterial[14-15], anticancer[16-18], anti-inflammatory[19], antiviral[20], and antidepressant.[21] Various biologically active pyrazoles like Lonazolac, antipyrene, Celecoxib, and Fipronil are shown in (Fig.-1), available as drugs in the market. By the hybridization approach, pyrazole-linked triazole hybrids can act as promising biologically active molecules. In the present communication, we developed novel pyrazole-linked triazole hybrids as biologically active analogues via click reaction.

EXPERIMENTAL

Materials and Methods

Phenyl hydrazine and acetophenone are purchased from BLD Pharma India. Propargyl bromide and $CuSO_4.5H_2O$, Sodium ascorbate from Avra Chemicals Hyd. Melting points were analyzed by using a Buchi melting point apparatus and are uncorrected. IR analysis was recorded on a Perkin-Elmer 100S spectrometer. Nuclear magnetic resonance spectra were detected on a Bruker 400 MHz spectrometer, and Mass data (ESI) were recorded on a Jeol JMSD-300 spectrometer.

Synthesis of 1,3-diphenyl-4-(prop-2-yn-1-yloxy)methyl)-1H-pyrazole (6)

The 1,3-diphenyl-pyrazolyl alkyne intermediate was achieved by the reaction of compound (4) (1.0 eq) with the propargyl bromide (1.5 eq) in DMF solvent(15mL) in potassium carbonate (3.0 eq) at rt, under inert condition stirred for 3h, monitor the reaction by thin layer chromatography further ice cold water mixed to the reaction pot and extracted with EtOAc. Then the ethyl acetate layers were washed with cool water and a brine solution. After that dried over Na_2SO_4, concentrated under rotavapor, and purified by column chromatography.

General Procedure for the Synthesis of Substituted Azido Benzene Derivatives (7a-l)

Various phenyl azides **7a-i** were synthesised according to the reported method (23).

Synthesis of 4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy) methyl)-1-phenyl-1H-1,2,3 triazole 8)

Combination of pyrazolyl alkyne (1.0 eq), substituted aryl azides 7a-l (1.2 eq) in tBuOH: H_2O (15mL) stirred with $CuSO_4 \cdot 5H_2O$ (0.01 eq) and sodium ascorbate (0.1eq) for about 16-20 hrs at room temperature. while the completion of the reaction, observed by TLC, the reaction contents were extracted with ice-cold water and ethyl acetate (3 x 25 mL). The organic layer was then washed with brine and dried over anhydrous sodium sulphate. Further eliminate the solvent from the reaction mixture, then the crude product was further purified by column chromatography. Final synthesized analogues 4-(((1,3-di phenyl-1H-pyrazol-4-yl)methoxy) methyl)-1-phenyl-1H-1,2,3 triazole 8a-l, in yields ranging from 70-85%. Other derivatives 8b-8l were synthesized by the same procedure.

Experimental data for 1-(4-chlorophenyl)-4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy) methyl)-1H-1,2,3-triazole (8a);

white solid ; Yield : 76%; mp 168-170^oC;IR (KBr) ν_{max} : 3060, 1500, 1272, 922, 715 cm^{-1}, ^1H NMR (400MHz, $CDCl_3$): 8.09 (1H, s), 7.94 (1H, s), 7.86 (2H, d, J=7.0 Hz), 7.84 (2H, d, J=7.0 Hz), 7.59 (2H, t, J=8.9 Hz & 6.0 Hz), 7.48-7.42 (6H, m), 7.35 (1H, d, J=7.5 Hz), 7.29 (1H, d, J=8.0 Hz), 4.87 (2H, s), 4.72 (2H, s) ppm;^{13}C NMR (100MHz, $CDCl_3$): 152.40, 144.95, 140.04, 134.99, 133.04, 130.91, 129.56, 128.93, 128.72, 128.20, 128.08, 127.90, 126.61, 124.92, 119.19, 117.41, 63.14, 63.11 ppm; ESI-MS (m/z): 442.5 (M+H)+Found, % : C, 67.75; H, 4.63; Cl, 8.07; N, 15.64; O, 3.64. $C_{25}H_{20}ClN_5O$.Calculated %; C, 67.95; H, 4.56; Cl, 8.02; N, 15.85; O, 3.62.

1-(2-chlorophenyl)-4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1H-1,2,3-triazole (8b);

pale yellow solid; Yield :78%;mp 162-164 ^{o}C; IR (KBr) ν_{max} : 3072, 1596, 1336, 1037, 812cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): 8.09 (1H, s), 7.90 (3H, m), 7.74 (2H, d, J=7.80 Hz), 7.70 (2H, d, J=7.70 Hz), 7.60 (2H, d, J=7.90 Hz), 7.50 (4H, m), 7.38 (1H, t, J=12.0 Hz &J=8.0 Hz), 7.31 (1H, t, J=12.0 Hz & 8.0 Hz), 4.84 (2H, s), 4.73 (2H, s) ppm; ^{13}C NMR (100MHz, $CDCl_3$): 152.34, 146.24, 140.01, 136.07, 133.05, 129.57, 128.94, 128.07, 128.24, 128.08, 126.67, 122.59, 122.05, 120.08, 119.18, 117.35, 63.23, 63.15 ppm. ESI (m/z): 442.5 (M+H)+Found, % : C, 67.75; H, 4.63; Cl, 8.07; N, 15.64; O, 3.64. $C_{25}H_{20}ClN_5O$.Calculated %; C, 67.95; H, 4.56; Cl, 8.02; N, 15.85; O, 3.62.

4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1-phenyl-1H-1,2,3-triazole (8c);

brown solid; Yield: 83%;mp 167-169^{o}C ; IR (KBr) ν_{max} : 3137, 1595, 1328, 1081, 818 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): 8.11(1H, s), 7.93 (1H, s), 7.88 (2H, d, J=7.50 Hz), 7.77 (2H, d, J=7.60 Hz), 7.73 (2H, d, J=7.60 Hz), 7.54 (2H, t, J=8.0 Hz & 2.0 Hz), 7.49-7.43 (6H, m), 7.38 (1H, s), 7.29 (1H, t, J=9.0 Hz & 2.0 Hz), 4.86 (2H, s), 4.73 (2H, s) ppm;^{13}C NMR (100MHz, $CDCl_3$): 152.38, 140.04, 137.14, 133.07, 131.44, 129.90, 129.57, 128.96, 128.72, 128.22, 128.09, 126.63, 121.02, 120.72, 119.20, 117.41, 63.19, 63.14 ppm; ESI (m/z): 408.3 (M+H)+. Found % : C, 73.54; H, 5.11; N, 17.28; O, 3.90; $C_{25}H_{21}N_5O$.Calculated %; C, 73.69; H, 5.19; N, 17.19; O, 3.93.

1-(4-bromophenyl)-4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1H-1,2,3-triazole(8d);

dark red solid ; Yield : 80%; mp 190-192^{o}C ; IR (KBr) ν_{max} : 2954, 1548, 1235, 1042, 818 cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): 8.10 (1H, s), 7.89-7.85 (3H, m), 7.78 (2H, d, J=8.0 Hz), 7.68 (2H, d, J=8.0 Hz), 7.52-7.40 (6H, m), 7.38 (1H, d, J=7.9 Hz), 7.29 (1H, t, J=8.0 Hz & 2.0 Hz), 4.58 (2H, s), 4.73 (2H, s), ^{13}C NMR (100MHz, $CDCl_3$): 152.32, 146.18, 139.99, 135.56, 134.70, 133.05, 130.05, 129.55, 128.92, 128.70, 128.22, 128.06, 126.64, 121.79, 120.86, 119.15, 117.33, 63.20, 63.13 ppm; ESI (m/z): 486.0 (M+H)+ Found %:C, 61.79; H, 4.08; Br, 16.49; N, 14.53; O, 3.36; $C_{25}H_{20}BrN_5O$. Calculated%;C, 61.74; H, 4.14; Br. 16.43; N, 14.40; O, 3.29.

1-(2-(4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1H-1,2,3-triazol-1-yl)phenyl)ethan-1-one(8e);

dark brown solid ; Yield : 85%;mp 160-162^{o}C ; IR (KBr) ν_{max} : 2919, 1449, 1210, 1043, 753 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): 8.27 (1H, s), 8.09 (1H, s), 8.02 (1H, s), 7.99-7.96 (2H, m), 7.86 (2H, d, J=8.0 Hz), 7.77 (2H, d, J=7.70 Hz), 7.64 (1H, t, J=8.0 Hz & 1.96 Hz), 7.48-7.42 (4H, m), 7.36 (1H, d, J=7.70 Hz), 7.27(1H, t, J=9.0 Hz & 2.0 Hz), 4.84 (2H, s), 4.72 (2H, s), 2.67 (3H, s) ppm;^{13}C NMR (100MHz, $CDCl_3$): 196.74, 152.33, 146.29, 139.99, 138.60, 137.48, 133.04, 130.36, 129.54, 128.90, 128.72. 128.56, 128.24, 128.06, 126.62, 124.85, 120.96, 119.87, 119.85, 117.34, 63.23, 63.14, 26.88 ppm; ESI (m/z): 450.1 (M+H)+Found %, C, 72.19; H, 5.08; N, 15.67; O, 7.18 , $C_{27}H_{23}N_5O_2$.Calculated %; C, 72.14; H, 5.16; N, 15.59; O, 7.12.

1-(4-(4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1H-1,2,3-triazol-1-yl)phenyl)ethan-1-one (8f);

yellow solid ; Yield: 75%; mp 170-172^{o}C; IR (KBr) ν_{max} : 3060, 1595, 1235, 933, 715 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): 8.13 (1H, s), 8.11 (1H, s), 8.08 (1H, s), 7.96 (1H, s), 7.86-7.83 (4H, m), 7.77 (2H, d, J=8.0 Hz), 7.48-7.42 (4H, m), 7.36 (1H, d, J=8.0 Hz), 7.28 (1H, t, J=8.0 Hz & 2.0 Hz), 4.84 (2H, s), 4.73 (2H, s), 2.67 (3H, s) ppm; ^{13}C NMR (100MHz, $CDCl_3$): 196.69, 152.28, 146.38, 140.06, 139.92, 136.92, 133.02, 130.19. 129.54, 128.91, 128.69, 128.22, 128.03, 126.63, 120.76, 120.92, 119.11, 117.28, 63.23, 63.07, 26.78 ppm; ESI (m/z): 450.1 (M+H)+)+ Found %, C, 72.19; H, 5.08; N, 15.67; O, 7.18 , $C_{27}H_{23}N_5O_2$. Calculated %; C,72.14; H, 5.16; N, 15.59; O, 7.12.

4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole (8g);

white solid; Yield : 80%; mp 183-185^{o}C ; IR (KBr) ν_{max} : 2889, 1548, 1358, 1043, 906 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): 8.10 (2H, d, J=8.0 Hz), 7.87 (2H, d, J=7.80 Hz), 7.77 (3H, t, J=6.80 Hz & 2.0 Hz), 7.47-7.40 (5H, m), 7.35 (1H, d, J=7.0 Hz), 7.28 (1H, d, J=7.50 Hz), 7.12-7.06 (2H, m), 4.85 (2H, s), 4.71 (2H, s), 3.85 (3H, s) ppm;^{13}C NMR (100MHz, $CDCl_3$): 152.34, 151.18, 144.39, 140.03, 133.03, 130.23, 129.51, 128.99, 128.65, 128.12. 128.03, 126.53, 126.33, 125.55, 125.13, 121.30, 119.12, 117.50, 112.31, 63.16, 62.19, 56.02 ppm; ESI (m/z): 438.0 (M+H)+Found %: C, 71.28; H, 5.33; N, 16.06; O, 7.26, $C_{26}H_{23}N_5O_2$, calculated %, C, 71.38; H, 5.30; N, 16.14; O, 7.36

4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1-(2-methoxyphenyl)-1H-1,2,3-triazole (8h);

brown solid ; Yield : 76%; mp 188-190^{o}C ; IR (KBr) ν_{max} : 3143, 1596, 1336, 1036, 814 cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): 8.10 (2H, d, J=8.0 Hz), 8.01 (1H, s), 7.87 (3H, d, J=7.70 Hz), 7.77 (3H, t, J=8.0 Hz & 2.0 Hz), 7.47-7.40 (5H, m), 7.36 (1H, d, J=8.0 Hz), 7.28 (1H, d, J=7.70 Hz), 7.12-7.06 (2H, m), 4.85 (2H, s), 4.71(2H, s), 3.85 (3H, s), 2.95 (4H, s), 2.88 (4H, s) ppm; ^{13}C NMR (100MHz, $CDCl_3$): 162.66, 152.34, 151.19, 144.40, 140.03, 133.04, 130.23, 129.51, 128.99, 128.65, 128.12, 128.04, 126.53, 126.34, 125.57, 125.13, 121.31, 119.14, 117.50, 112.31, 63.17, 62.92, 56.02 ppm; ESI (m/z): 438.19 (M+H)+Found %: C, 71.28; H, 5.33; N, 16.06; O, 7.26, $C_{26}H_{23}N_5O_2$, calculated %, C, 71.38; H, 5.30; N, 16.14; O, 7.36.

4-(4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1H-1,2,3-triazol-1-yl)benzonitrile (8i);

pale yellow solid; Yield : 74%; mp 193-195^{o}C ; IR (KBr) ν_{max} : 3100, 1546, 1365, 1063, 756 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): 8.07 (1H, s), 7.93 (1H, s), 7.87-7.81 (6H, m), 7.75 (2H, d, J=7.50 Hz), 7.48-7.42 (4H, m), 7.36 (1H, d, J=8.0 Hz), 7.28 (1H, d, J=7.70 Hz), 4.83 (2H, s), 4.72 (2H, s) ppm; ^{13}C NMR (100MHz, $CDCl_3$): 152.25, 146.75, 139.90, 139.80, 134.01, 133.02, 129.56, 128.88, 128.70, 128.23, 128.02, 126.07, 120.61, 119.08, 117.79, 117.22, 112.49, 63.33, 63.05 ppm; ESI (m/z): 433.6 (M+H)+Found %; C, 72.32; H, 4.63; N, 19.48; O, 3.64 $C_{26}H_{20}N_6O$ Calculated %, C, 72.21; H, 4.66; N, 19.43; O, 3.70.

4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1-(p-tolyl)-1H-1,2,3-triazole (8j);

brown solid; Yield : 85%;mp 182-184^{o}C ; IR (KBr) ν_{max} : 2855, 1493, 1238, 1063, 755 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): 8.11 (1H, s), 7.88 (3H, t, J=8.0 Hz & 2.0 Hz), 7.79 (2H, d, J=7.60 Hz), 7.60 (2H, d, J=6.50 Hz), 7.49-7.43 (4H, m), 7.37 (2H, d, J=8.20 Hz), 7.34 (2H, d, J=8.0 Hz), 4.85 (2H, s), 4.73 (2H, s), 2.44 (3H, s) ppm; ^{13}C NMR (100MHz, $CDCl_3$): 152.35, 145.70, 140.03, 139.05, 134.83, 133.06, 130.36, 129.54, 128.95, 128.69, 128.20, 128.06, 126.59, 121.01, 120.59, 119.17, 117.41, 63.18, 63.07, 21.22 ppm; ESI (m/z): 422.3 (M+H)+Found %; C, 74.09; H, 5.50; N, 16.62; O, 3.80, $C_{26}H_{23}N_5O$.calculated %; C, 74.18; H, 5.44; N, 16.69; O, 3.72.

4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1-(o-tolyl)-1H-1,2,3-triazole (8k);

yellow solid ; Yield :82%; mp 170-172^{o}C ; IR (KBr) ν_{max}: 3072, 1493, 1282, 920, 844 cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): 8.10 (1H, s), 7.87(2H, d, J=7.50 Hz), 7.68 (1H, s), 7.48-7.39 (5H, m), 7.31 (2H, d, J=7.50 Hz), 7.26 (3H, t, J=8.0 Hz & 2.0 Hz), 4.86 (2H, s), 4.73(2H, s), 2.20 (3H, s) ppm;^{13}C NMR (100MHz, $CDCl_3$): 152.36, 144.95, 140.02, 136.54, 133.75, 133.04, 131.59, 129.98, 129.54, 128.95, 128.69, 128.18, 128.06, 126.95, 126.59, 126.07, 124.34, 119.16, 117.41, 63.20, 63.16, 18.00 ppm; ESI (m/z): 422.19 (M+H)+Found %; C, 74.09; H, 5.50; N, 16.62; O, 3.80, $C_{26}H_{23}N_5O$.calculated %; C, 74.18; H, 5.44; N, 16.69; O, 3.72

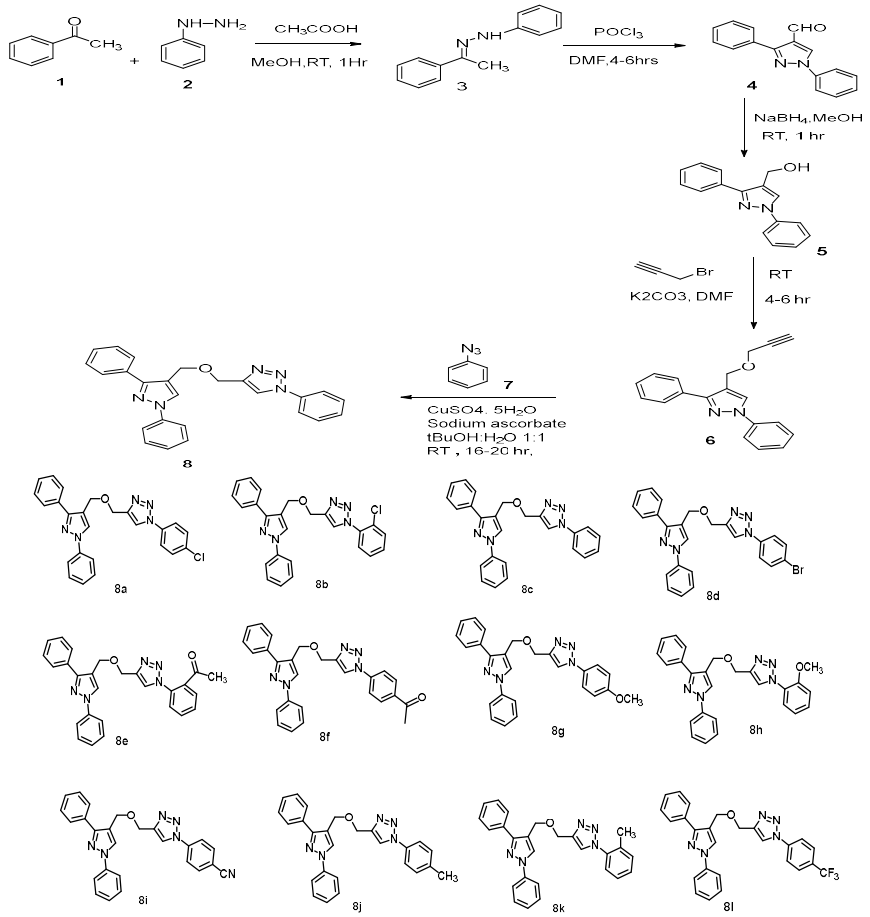
4-(((1,3-diphenyl-1H-pyrazol-4-yl)methoxy)methyl)-1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole (8l);

brown solid ; Yield : 76%;mp 194-196^{o}C ; IR (KBr) ν_{max} : 3072, 1448, 1282, 1212, 844 cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): 8.08 (1H, s), 7.87 (3H, d, J=7.50 Hz), 7.76 (3H, d, J=8.5 Hz), 7.46-7.35 (6H, m), 7.31 (1H, d, J=6.8 Hz), 7.22 (1H, d, J=7.10 Hz), 4.86 (2H, s), 4.72 (2H, s) ppm;^{13}C NMR (100MHz, $CDCl_3$): 152.29, 145.06, 139.95, 136.66, 135.21, 133.62, 132.99, 129.51, 128.89, 128.87, 128.68, 128.17, 128.03, 126.58, 124.84, 119.17, 119.10, 117.33, 63.14, 63.01 ppm; ESI (m/z):476.5 (M+H)+Found; C, 65.68; H, 4.24; F, 11.99; N, 14.73; O, 3.36, $C_{26}H_{20}F_3N_5O$; calculated %; C, 65.61; H, 4.28; F, 11.91; N, 14.64; O, 3.42.

RESULTS AND DISCUSSION

Initially, to a stirring magnetic bar, Acetophenone 1 reacted with phenyl hydrazine 2 in MeOH, with CH_3COOH under ambient conditions, forming phenyl hydrazone, then compound 3 on reaction with $POCl_3$/DMF gives pyrazole carbaldehyde 4, then compound 4 on reduction with $NaBH_4$ in ethanol, yields compound (5). Then propargylation of the compound with propargyl bromide gave 1,3-diphenyl pyrazolyl

alkyne intermediate 6. Finally1,3-dipolar cycloadditions of compound 6 with various aryl azides 7a-l afforded pyrazole-linked 1,4 di substituted triazoles (8a-8l). The newly developed molecules were analysed by Infrared spectroscopy, proton nuclear magnetic resonance spectra, ^{13}C NMR, and mass data. In the IR spectrum of 8a, the N=N band was located at 1595 cm^{-1}, the ^{1}H NMR spectrum of 8a triazole ring H appeared as a singlet at δ 8.09, and OCH_2, protons recorded as two singlets at δ 4.72 and δ 4.87 ppm, respectively. In the ^{13}C NMR data shown for 8a triazole carbon exhibits signals at δ 144.95 and δ 119.19 ppm. In the mass spectroscopy data for 8a characteristic peak at m/z 442.12 $[M+H]^+$ is reported. The developed compounds 8b-8l showed similar spectral patterns.



Scheme-1: Preparation of Pyrazole-linked Novel 1,2,3 Trizole Derivatives

Antimicrobial Assay

An antimicrobial assay was carried out to find the biologically active compounds. The MIC of compounds screened by the Broth dilution turbidometric method has been carried out in triplicate using Muller Hinton broth with two positive and negative bacterial strains.

Its efficiency to kill the bacteria and its ability to reduce its viability was confirmed by attaining the zone of clearance upon agar well diffusion assay. It was tested using Muller-Hinton agar. Each bacterial strain for every concentration was analysed in triplicate to avoid the mean variations and found with negligible standard deviation errors. Final compound concentration used in the study: 50 µg/ml. NI stands for No inhibition@250 ug/ml.

All the recently developed analogues 8a-8l antibacterial activity was screened against *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia, Escherichia Coli*, at different concentrations using ampicillin as a standard reference drug. 8A to 8L were tested against antibacterial activity at MIC/ 50 (µg/ml), where 8A, 8B, 8D, 8E, 8F, 8H, and 8I showed moderate activity on gram-positive strains. Among all 8E with (substitution $COCH_3$), exhibited significant activity with reported pathogens. Except for 8E, all the other analogues showed poor action on *E.Coli*, *K. pneumoniae* strains. The activity results are reported.

Table-1: Minimum Inhibitory Concentration Record of Compounds 8a-8l.

	MIC (µg/ml)			
	Gram Positive		Gram Negative	
Compounds	*Staphylococcus aureus*	*Bacillus subtilus*	*Escherichia coli*	*Klebsiella pneumonia*
8A	50	50	100	50
8B	50	50	100	>250
8C	>250	>250	>250	>250
8D	50	50	>250	>250
8E	50	50	50	50
8F	50	50	>250	>250
8G	>250	>250	>250	>250
8H	50	>250	>250	>250
8I	50	50	>250	>250
8J	>250	50	>250	>250
8K	>250	>250	>250	>250
8L	>250	>250	>250	>250
Ampicillin	10	10	4	10

No turbidometric inhibition has been seen at >250 µg/ml concentration

Table-2: Antibacterial activity zone of Inhibition values for compounds 8a-8l

However, compounds 8A, 8B, 8D, 8E, 8F, 8I, and 8J exhibited the maximum effectiveness against *Staphylococcus aureus* (zone of inhibition 13mm, 12 mm, 17mm, 15 mm, 15mm, 16mm, and 12 mm, respectively). The Rest of the Compounds Showed Poor Activity

	Antibacterial Activity at 50 µg/ml Compound Concentration			
	Gram Positive		Gram Negeative	
Compounds	*Staphylococcus aureus* ZOI (mm)	*Bacillus subtilis* ZOI (mm)	*Escherichia coli* ZOI (mm)	*Klebsiella pneumonia* ZOI (mm)
8A	13	15	NI	11
8B	12	13	NI	NI
8C	NI	NI	NI	NI
8D	17	9	NI	NI
8E	15	17	15	13
8F	15	14	NI	NI
8G	NI	NI	NI	NI
8H	NI	NI	NI	NI
8I	16	16	NI	NI
8J	12	13	NI	NI
8K	NI	NI	NI	NI
8L	NI	NI	NI	NI

CONCLUSION

In summary, we have synthesised the bioactive novel pyrazole-linked 1,2,3-triazole derivatives. These compounds were evaluated for their *in vitro* antibacterial activity. Among the compounds 8A, 8B, 8D, 8E, 8F, 8H, and 8I showed moderate activity on gram-positive strains. Whereas 8E showed more effectiveness on gram-positive and gram-negative bacteria.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

The present work is related to *SDG-3: Good Health and Well-being*. All the authors significantly contributed to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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REFERENCES

1. WHO report on surveillance of antibiotic consumption 2016-2018.
2. V. Economou and P. Gousia, *Infection and Drug Resistance*,**49,** 8(2015); https://https://doi.org/10.2147/IDR.S55778
3. (a) Zhi Xu, S. Jia, Zhao, Yi Liu, *European Journal of Medicinal Chemistry*, **183**, 11700(2019), https://doi.org/10.1016/j.ejmech.2019.111700; (b) D. Dheer, V.Singh, R.Shankar, *Bioorganic Medicinal Chemistry*, **71**, 30, (2017), https://doi.org/10.1016/j.bioorg.2017.01.010
4. G. Linga Goud., S. Ramesh, D. Ashok, V. Prabhakar Reddy, P. Yogeswari, D. Sriram, B. Saikrishna, M. Vijjulatha, *MedChemComm*, **8,** 559, (2017), https://doi.org/10.1039/C6MD00593D
5. (a) B.Banerji. K. Chandra Shekhar, K.Sreenath, S.Roy, S.Nag, K.D. Saha, *ACS Omega*, **3(11)**, 16134 (2018), https://doi.org/10.1021/acsomega.8b01960; (b) R.Dasari, G.Thalari, Y.J.Rao, and Ch.P.Rao, *Russian Journal of Organic Chemistry*, **57**,1519(2021), https://doi.org/10.1134/s1070428021090207
6. T. Ting Liang, X. Sun, W. Li, G. Hou, and F. Gao, *Frontiers in Pharmacology*, **12,** 161173(2021), https://doi.org/10.3389/fphar.2021.661173
7. M.H. Shaikh, D.D. Subhedar, L. Nawale, D. Sarkar, F. A. Kalam Khan, J. Nsangshetti, B.B. Shingate, *MedChemComm*, **6**, 1104 (2015), https://doi.org/10.1039/C5MD00057B
8. R. Raj, P. Singh, J. Gut, P. J. Resenthal, and V. Kumar, *European Journal of Medicinal Chemistry*, **62**, 590 (2013), https://doi.org/10.1016/j.ejmech.2013.01.032
9. Z. Cheng-He,W. Kun, Xian Long, *European Journal of Medicinal Chemistry*, **45,** 4631(2010), https://doi.org/10.1016/j.ejmech.2010.07.031
10. A. Naseem, K.K. Naveen, A. Sarfaraz, O. Mahammad, *European Journal of Medicinal Chemistry*, **82**, 552 (2014), https://doi.org/10.1016/j.ejmech.2014.06.009
11. R. D. Tajshri, S. K. Vagolu, S. Dharmaraan, N.S. Jaiprakash, B.S. Bapurao, *Chemical Papers*, **74,** 809(2020), https://doi.org/10.1007/s11696-019-00908-5
12. X. Zu, Y. Zuang, Q. Chen, *European Journal of Medicinal Chemistry*, **257**, 115495(2023), https://doi.org/10.1016/j.ejmech.2023.115495
13. S. Mert, R.Kasimogullari , T. Ica , F.Colak , A.Altun , S.Ok, *European Journal of Medicinal Chemistry*, **78**, 86 (2014), https://doi.org/10.1016/j.ejmech.2014.03.033
14. N.C. Desai, K. M. Rajpara, V. V. Joshi, *Bioorganic Medicinal Chemistry Letters*, **23**,2714(2013), https://doi.org.10.1016/j.bmcl.2013.02.077
15. O. Ebenezer, P. Awolade, N. Koorbanally, P. Singh, *Chemical Biology and Drug Design*, **95**, 162 (2020), https://doi.org. 10.1111/cbdd.13632
16. K. Suryanarayana, A.R. Robert , K. Nagaraju, T. Pooventhiran, R. Thomas, Suresh Maddila, Sreekantha B. Jonnalagadda, *Journal of Molecular Structure*, **1243,** 130865(2021), https://doi.org.10.1016/j.molstruc.2021.130865
17. A. Balbi, M. Anzaldi, C. Macciò, C. Aiello, M. Mazzei, R. Gangemi, P. Castagnola, M. Miele, C. Rosano, M. Viale, *European Journal of Medicinal Chemistry*, **46,** 5293(2011), https://doi.org/10.1016/j.ejmech.2011.08.014
18. G. M. Neitulescu, C. Draghici, O.T. Olaru, L. Matei, A. Loane, D. DraguL, C. Bleotu, *Bioorganic Medicinal Chemistry*, **21,** 4138(2011), https://doi.org/10.1016/j.bmcl.2011.05.105

19. N. Lingaiah, M. Jhanshi, H. K. Gaikwad, B. Rajashakhar, M.S. Mani, N.J. Prameela, *Bioorganic Medicinal Chemistry Letters*, **21,** 4138 (2011), https://doi.org/10.1016/j.bmcl.2011.05.105
20. El-Sabbagh OI, MM. Baraka, SM. Ibrahim , C. Pannecouque, G. Andrei, R. Snoeck , AA.Rashad, *European Journal of Medicinal Chemistry*, **44,** 3746. (2009), https://doi.org/10.1016/j.ejmech.2009.03.038
21. M. Abdel-Aziz, Abuo-Rahma Gel-D, A.A. Hassan, *European Journal of Medicinal Chemistry*, **44**, 3480 (2009), https://doi.org/10.1016/j.ejmech.2009.01.032
22. C. Dayakar, B.S. Kumar, G. Sneha, G. Sagarika, K. Meghana, S. Ramakrishna, R.S. Prakasham, B. Chinaraju, *Bioorganic Medicinal Chemistry Letters*, **25,** 5678(2017), https://doi.org/10.1016/j.bmc.2017.08.042
23. P. Srinivas, P. N. Kumar, S.Reddy, Venu, P. Shyam, and G.L.D. Krupadanam, *Russian Journal of Bioorganic Chemistry*, **44**, 244 (2018), https://doi.org/10.1134/S1068162018020097

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