Synthesis and Antimicrobial Activities of Novel 1,2,4-Triazole Clubbed Pyrazole Derivatives

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Abstract

A new series of 2-((4-ethyl-5-phenyl-4H-1,2,4-triazol-3-yl)thio)-1-(3-(4-subphenyl)-5-(sub.phenyl)-4,5-dihy dro-1H-pyrazol-1-yl)ethan-1-one derivatives (6a-6j) have been synthesized from 4-ethyl-5-phenyl-4H-1,2,4-triazole-3-thiol and 2-chloro-1-(4,5-dihydro-5-(3-aryl)-3-arylpyrazol-1-yl)ethanone (5a-5j) in the presence of anhydrous K_2CO_3. All novel compounds (6a-6j) have been characterized by spectroscopy techniques such as ^{1}HNMR, ^{13}CMR, FTIR and LCMS.

All newly synthesized derivatives were investigated for their antimicrobial activity against Gram-positive and Gram-negative bacterial strains as well as fungal strains. Compound 6j possessing methoxy and nitro group has shown highest antibacterial activities while 3,4 di methoxy and methyl bearing compound 6g displayed excellent antifungal activities.

Keywords: Antibacterial, Antifungal, Pyrazole, 1,2,4-Triazole.

Introduction

Among the most prominent classes of heterocyclic compounds, those featuring a fusion of 1,2,4-triazole and pyrazole moieties have garnered considerable attention in recent years[7,17]. These nitrogen-rich frameworks serve as pivotal structural units in a variety of bioactive natural products and synthetic therapeutic agents. The remarkable versatility of these heterocycles arises from their ability to engage biological targets through diverse molecular interactions, establishing them as pharmacologically significant scaffolds in medicinal chemistry.

Derivatives of triazole and pyrazole are well-documented for their extensive range of biological activities including antimicrobial and antioxidant properties[19,20]. Compounds bearing these moieties have demonstrated efficacy in combating microbial infections by inhibiting key enzymatic pathways and protecting biological systems from oxidative stress by neutralizing reactive oxygen species[4,9].

Although naturally occurring examples exist, significant research has been devoted to the synthesis of triazole- and pyrazole-based compounds, as synthetic derivatives frequently exhibit superior pharmacological properties compared to their natural analogs[14]. Over the past few decades, triazole- and pyrazole-containing compounds have been shown to possess a diverse array of therapeutic activities. These include antibacterial[13], antifungal[8,18], anti-inflammatory[5,10], antitumor[11] and antiviral[6] effects, highlighting their potential for addressing various unmet medical needs. Notably, many synthetic derivatives have demonstrated dual or multi targeted mechanisms of action, further enhancing their pharmacological significance.

In light of their broad biological potential, the present study focuses on the synthesis and detailed characterization of novel compounds incorporating both 1,2,4-triazole and pyrazole moieties. The antimicrobial efficacy of these compounds was evaluated against a spectrum of pathogenic microorganisms, while their antioxidant activity was assessed using established free radical scavenging assays.

This investigation underscores the potential of triazole-pyrazole hybrids as promising therapeutic agents with significant applications in biomedicine.

Material and Methods

All the reagents and solvents used were purchased from Sigma-Aldrich. All melting points were determined in open capillary tube and are uncorrected. Infrared spectra were recorded in KBr on Perkin– Elmer RX1 spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded using $CDCl_3$ at 500 MHz through Brucker spectrometer. Mass spectra were recorded on a QP-2010 simadzu instrument. Elemental analysis was carried out by ElementarVario EL III elemental analyzer.

Synthesis of 4-ethyl-5-phenyl-4*H*-1,2,4-triazole-3-thiol, 3: 4-ethyl-5-phenyl-4*H*-1,2,4-triazole-3-thiol was prepared as per reported method[3].

Synthesis of chloro acetyl pyrazoline derivatives, 5a-j: Pyrazolines were prepared as per reported method [1,2].

General Procedure for Synthesis of 2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(3-(4-subphenyl)-5-(substi tutedphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one derivatives: 4-ethyl-5-phenyl-4H-1,2,4-triazole-3-thiol (0.0 05mol), 2-chloro-1-(4,5-dihydro-5-(3-aryl)-3-arylpyrazol-1-yl)ethanone (0.005mol) and potassium carbonate were mixed in 100 ml dimethyl formamide in FBF. Reaction mass was stirred for 8-9 hours at room temperature and progress was monitored through TLC**.** Then mixture was poured into chilled water. Product was filtered off as well as recrystallized with ethyl alcohol.

Physical and Spectral Data

1-(3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)ethan-1-one (6a): White solid, Yield: 69 %; Melting Point (M.p.): 118°C; Molecular Formula:$C_{27}H_{25}N_5OS$; FTIR (cm^{-1}, KBr): 3061, 2937, 2836 (C-H Str), 1662 (C=O amide), 1602 (C=C str- aromatic ring), 1427 (C=N str– triazole), 698 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.33 (s, CH_3), 3.11, 3.84 (dd, H, Pyrazoline), 4.00 (q,CH_2), 4.81 (s,CH_2), 5.63 (dd, H,CH), 6.68 – 7.83 (15H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.62, 37.50, 39.81, 42.32, 60.17, 126.62, 126.83, 127.26, 127.32, 128.58, 130.12, 130.79, 130.32, 133.28, 150.72, 155.37, 155.54, 159.21, 165.01; Elemental Analysis: C 69.35%, H 5.39%, N 14.98 %, S 6.86%; Found: C 69.3 %, H 5.32%, N 14.91 %, S 6.80%; Mass: M^+ 468

1-(5-(4-chlorophenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)ethan-1-one (6b): White solid, Yield: 70%, M.p.: 126°C, Molecular Formula:$C_{27}H_{24}ClN_5OS$; FTIR (cm^{-1}, KBr): 3068, 2941, 2835 (C-H Str), 1671 (C=O amide), 1609 (C=C str- aromatic ring), 1426 (C=N str – triazole), 696 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.32 (s, CH_3), 3.14, 3.86 (dd, H, Pyrazoline) 4.06(q,CH_2), 4.79 (s,CH_2), 5.62 (dd,H,CH), 6.78 – 7.97 (14H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.62, 37.51, 39.82, 42.87, 60.11, 126.67, 126.89, 127.24, 127.26, 128.64, 130.07, 130.68, 130.33, 133.21, 150.69, 155.32, 155.54, 159.14, 165.02; Elemental Analysis: C 64.60%, H 4.82%, N 13.95 %, S 6.39%; Found: C 64.55 %, H 4.80%, N 13.90 %, S 6.30%; Mass: M^+ 502

2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(3-phenyl-5-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (6c): White solid, Yield: 56%, M.p.: 132°C,Molecular Formula:$C_{28}H_{27}N_5OS$; FTIR (cm^{-1}, KBr): 3061, 2941, 2842 (C-H Str), 1662 (C=O amide), 1599 (C=C str- aromatic ring), 1427 (C=N str – triazole), 697 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.33 (s, CH_3), 2.45 (s, CH_3) 3.13, 3.85 (dd, H, Pyrazoline), 4.03(q,CH_2), 4.84 (s,CH_2), 5.58 (dd,H,CH), 6.85 – 8.1 (14H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.61, 21.54, 37.44, 39.77, 42.26, 60.04, 126.59, 126.83, 127.22, 127.23, 128.54, 130.08, 130.70, 130.39, 133.31, 150.74, 155.32, 155.55, 159.21, 165.11; Elemental Analysis: C 69.83%, H 5.65%, N 14.54 %, S 6.66%; Found: C 69.75 %, H 5.60%, N 14.45 %, S 6.56%; Mass: M^+ 482

2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (6d): White solid, Yield: 78%, M.p.: 76°C, Molecular Formula:$C_{28}H_{27}N_5O_2S$; FTIR (cm^{-1}, KBr): 3060, 2935 (C-H Str), 1665 (C=O amide), 1607 (C=C str- aromatic ring), 1428 (C=N str – triazole), 695 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.29 (s, CH_3), 3.17, 3.79 (dd, H, Pyrazoline), 3.79 (s, OCH_3), 4.01(q,CH_2), 4.69 (s,CH_2), 5.54 (dd,H,CH), 6.82 - 7.76 (14H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.62, 37.47, 39.87, 42.34, 55.28, 60.10, 114.32, 126.90, 127.11, 127.34, 128.64, 130.08, 130.70, 130.95, 133.32, 150.72, 155.30, 155.50, 159.17, 165.04; Elemental Analysis: C 67.58 %, H 5.47%, N 14.07 %, S 6.44%; Found: C 67.51 %, H 5.41%, N 14.01 %, S 6.35 %; Mass : M^+ 498

2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(5-phenyl-3-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (6e): White solid, Yield: 70%, M.p.: 102°C, Molecular Formula:$C_{28}H_{27}N_5OS$; FTIR (cm^{-1}, KBr): 3069, 2937 (C-H Str), 1661 (C=O amide), 1607 (C=C str- aromatic ring), 1426 (C=N str – triazole), 691 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.32 (s, CH_3), 2.42(s, CH_3) 3.12, 3.80 (dd,H,Pyrazoline), 4.00(q,CH_2), 4.76 (s,CH_2), 5.54 (dd,H,CH), 6.71 – 7.89 (14H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.61, 21.55, 37.45, 39.76, 42.25, 60.03, 126.61, 126.85, 127.21, 127.25, 128.54, 130.07, 130.71, 130.38, 133.32, 150.71, 155.30, 155.56, 159.19, 165.10; Elemental Analysis: C 69.83%, H 5.65%, N 14.54 %, S 6.66%; Found: C 69.8 %, H 5.5%, N 14.45 %, S 6.55%; Mass: M^+ 482

1-(5-(4-chlorophenyl)-3-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)ethan-1-one (6f): White solid, Yield: 72%, M.p.: 116°C, Molecular Formula:$C_{28}H_{26}ClN_5OS$; FTIR (cm^{-1}, KBr): 3066, 2941 (C-H Str) 1667 (C=O amide), 1605 (C=C str- aromatic ring), 1427 (C=N str– triazole), 691 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.33 (s, CH_3), 2.44 (s, CH_3) 3.14, 3.81 (dd,H,Pyrazoline), 4.05(q,CH_2), 4.81 (s,CH_2), 5.59 (dd,H,CH), 6.81 – 8.06 (13H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.61, 21.44, 37.49, 39.80, 42.29, 60.01, 126.64, 126.88, 127.21, 127.21, 128.59, 130.05, 130.71, 130.35, 133.29, 150.73, 155.31, 155.52, 159.18, 165.07; Elemental Analysis: C 65.17%, H 5.08%, N 13.57 %, S 6.21%; Found: C 65.12 %, H 5.0%, N 13.49 %, S 6.15%; Mass: M^+ 516

1-(5-(3,4-dimethoxyphenyl)-3-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)ethan-1-one (6g): White solid, Yield: 75%, M.p.: 94°C, Molecular Formula:$C_{30}H_{31}N_5O_3S$; FTIR (cm^{-1}, KBr): 3061, 2935, 2837 (C-H Str), 1664 (C=O amide), 1601 (C=C str- aromatic ring), 1427 (C=N str – triazole), 688 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.31 (s, CH_3), 2.41(s, CH_3) 3.10, 3.82 (dd,H,Pyrazoline), 3.89 (s, OCH_3), 4.01(q,CH_2), 4.77 (s,CH_2), 5.61 (dd,H,CH), 6.79 – 7.99 (12H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.63, 21.42, 37.40, 39.84, 42.32, 55.22, 59.95, 109.54, 117.42, 122.83, 127.09, 127.54, 128.47, 130.15, 130.60, 133.32, 141.64, 150.84, 155.25, 155.60, 159.24, 165.02; Elemental Analysis: C 66.52%, H 5.77%, N 12.93 %, S 5.92%; Found: C 66.45 %, H 5.65%, N 12.80 %, S 5.80%; Mass: M^+ 542

1-(5-(4-(dimethylamino)phenyl)-3-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)ethan-1-one (6h): White solid, Yield: 65%, M.p.: 100°C, Molecular Formula:$C_{30}H_{32}N_6OS$; FTIR (cm^{-1}, KBr): 3059, 2939 (C-H Str), 1662 (C=O amide), 1603 (C=C str-

aromatic ring), 1427 (C=N str – triazole), 692 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.30 (s, CH_3), 2.4, 2.96 (s, CH_3), 3.11, 3.81 (dd,H,Pyrazoline), 4.00(q,CH_2), 4.69 (s,CH_2), 5.56 (dd,H,CH), 6.83 – 7.99 (13H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.61, 21.43, 37.44, 39.81, 42.30, 42.65, 60.02, 112.61, 126.83, 127.05, 127.45, 128.65, 130.15, 130.60, 133.2, 141.52 150.62, 155.28, 155.54, 159.26, 165.07; Elemental Analysis: C 68.68%, H 6.15%, N 16.02 %, S 6.11%; Found: C 68.6%, H 6.04%, N 15.95 %, S 6.00%; Mass : M^+ 525

2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(3-(4-methoxyphenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl) ethan-1-one (6i): White solid, Yield: 69%, M.p.: 114°C, Molecular Formula:$C_{28}H_{27}N_5O_2S$; FTIR (cm^{-1}, KBr): 3067, 2939, 2832 (C-H Str), 1667 (C=O amide), 1601 (C=C str- aromatic ring), 1427 (C=N str – triazole), 689 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.32 (s, CH_3), 3.12, 3.81 (dd,H,Pyrazoline), 3.81 (s, OCH_3), 4.03(q,CH_2), 4.75 (s,CH_2), 5.60 (dd,H,CH), 6.78 – 7.96 (14H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.62, 37.46, 39.85, 42.33, 55.25, 60.08, 114.29, 126.88, 127.10, 127.31, 128.62, 130.09,130.63, 130.92, 133.26, 150.67, 155.31, 155.53, 159.21, 165.03; Elemental Analysis: C 67.58%, H 5.47%, N 14.07 %, S 6.44%; Found: C 67.5 %, H 5.40%, N 14.00 %, S 6.35%; Mass: M^+ 498

2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(3-(4-methoxyphenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (6j): White solid, Yield: 66%, M.p.: 80°C, Molecular Formula:$C_{25}H_{19}ClN_4O_2S$; FTIR (cm^{-1}, KBr): 3259, 3039, 2935 (C-H Str), 2839 (methoxy), 1666 (C=O amide), 1604 (C=C str- aromatic ring), 1431 (C=N str – triazole), 1346 (NO_2), 686 (str of S-C); ^{1}H NMR (500 MHz, δ ppm $CDCl_3$): 1.33 (s, CH_3), 3.15, 3.85 (dd,H,Pyrazoline), 3.86 (s, OCH_3), 4.02(q,CH_2), 4.71 (s,CH_2), 5.66 (dd,H,CH), 6.93 - 8.12 (13H, Ar-H); ^{13}C NMR (500 MHz, δ ppm $CDCl_3$): 15.53, 36.82, 40.03, 42.35, 55.46, 59.90, 114.33, 121.06, 122.98, 126.64, 128.99, 130.24, 130.33, 132.10, 143.16, 148.59, 150.67, 154.85, 155.41, 161.91, 165,08; Elemental Analysis: C 61.98%, H 4.83%, N 15.49 %, S 5.91%; Found: C 61.92 %, H 4.65%, N 15.40 %, S 5.80%; Mass : M^+ 543

Antimicrobial screening: Standard ATCC strains of bacterial strain were used for the antimicrobial screening of the compounds (6a-6j) at 150 mg/ml concentration using the agar disk diffusion method[15]. In the present investigation, *S. aureus*, *B. subtilis*, *E. coli* and *E. aerogenes* as well as two fungal strains *A. niger* and *C. albicans* were used for the antimicrobial evaluation. Amoxicillin, ciprofloxacin and fluconazole were used as standard drugs for antibacterial and fungal activity.

Results and Discussion

Chemistry: The target compound, 1-(3,5-di-aryl- 4,5-dihydro-1H-pyrazol-1-yl)-2-((4-ethyl-5-phenyl-4H-1,2,4-triazol-3-yl)thio)ethan-1-one, was successfully synthesized via a multi-step synthetic procedure. The synthetic route presented in scheme 1. It involved the condensation of 4-ethyl-5-phenyl-4*H*-1,2,4-triazole-3-thiol with 2-chloro-1-(4,5-dihydro-5-(3-aryl)-3-arylpyrazol-1-yl)ethanone in the presence of a suitable base. The reactions proceeded with satisfactory yields and were monitored using thin-layer chromatography (TLC). The purity of the synthesized compounds was confirmed through TLC, which showed single spot. This indicates the absence of significant impurities. The structure and purity of the synthesized compound were thoroughly characterized using elemental analysis, ^{1}HNMR, ^{13}CMR, FTIR and LCMS.

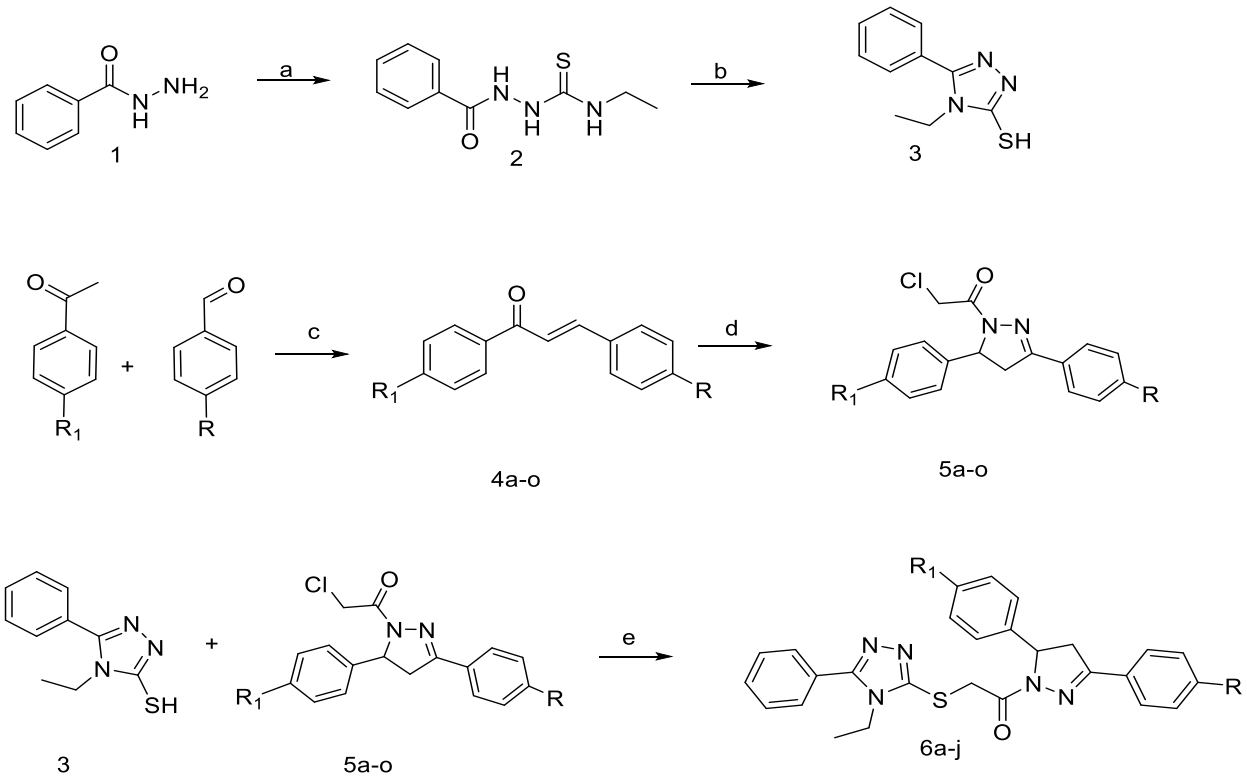
The FT-IR spectral data of the synthesized derivatives (6a-6j) revealed key characteristic absorption bands. A strong band at 698 cm^{-1} was observed for the ν(S-C) linkage. The presence of nitrogen in the triazole ring was confirmed by a band at 1427 cm^{-1}, corresponding to C=N stretching vibrations. Notable additional peaks included a strong absorption at ~1680 cm^{-1}, indicating the presence of the carbonyl (C=O) group; peaks around 2920–2850 cm^{-1}, attributed to aliphatic C-H stretching vibrations, a band at ~1600 cm^{-1} associated with aromatic C=C stretching vibrations and a sharp peak near 1220 cm^{-1}, characteristic of C-S stretching. The 1H-NMR spectrum provided substantial evidence supporting the structure of the synthesized compound.

The chemical shift values and splitting patterns are consistent with the expected structure. The pyrazoline moiety was characterized by double doublets observed at 3.11 and 3.84 δ ppm. A distinct double doublet at 5.63 δ was assigned to the methine of pyrazoline. The ethyl group attached to the triazole ring exhibited a quartet at 4.00 δ ppm for the two protons of the N-CH_2 group and a triplet at 1.33 δ for the three protons of the CH_3 group. Additionally, aromatic protons were observed as multiplets in the region of 6.9–7.8 δ ppm. The mass spectrum exhibited a molecular ion peak (M+) at 468m/z consistent with the molecular weight of the synthesized compound, further confirming its identity. The molecular ion peak (m/z) corresponded precisely to the molecular weight of the proposed compounds.

Antibacterial activities: The synthesized compounds were screened against *S. aureus*, *B. subtilis*, *E. coli* and *E. aerogenes* using disk siffusion method.[12] Significant inhibition zones were observed for Gram-positive strains, particularly *Staphylococcus aureus*, while moderate to low activity was recorded against Gram-negative bacteria.

The promising antibacterial activity of these compounds may be attributed to the presence of the triazole and pyrazole moieties, known to enhance interactions with microbial targets. The data indicate that compound 6j exhibits significant antibacterial activity against *S. aureus* with an MIZ value of 35 µg/mL, comparable to that of amoxicillin and ciprofloxacin (both have MIZ: 40 µg/mL).

In contrast, the compound demonstrates moderate activity against *B. subtilis* (Gram-positive bacteria) and Gram-negative bacteria such as *E. coli* and *E. aerogenes*, with MIZ values of 22 µg/mL and 21 µg/mL respectively. This differential activity could be attributed to the structural features of compound 6j, including methoxy and nitro groups, which may interact effectively with Gram-positive bacteria cell walls. However, the reduced activity against Gram-negative bacteria could result from the permeability barrier posed by their outer membrane. The findings suggest that compound 6j holds potential as a lead compound for further optimization and development of novel antibacterial agents, particularly against Gram-positive pathogens like *S. aureus*.



(a) ethyl isothiocyanate, Ethanol **(b)** Ethanol, aq. NaOH **(c)** CH_3OH, KOH
(d) (1)$NH_2NH_2.2H_2O$,(2) chloro acetyl chloride **(e)** DMF , K_2CO_3

Scheme 1: Reaction scheme of 6a-6j

Table 1
Antimicrobial activity of 6a-6j

Compound	Zone of Inhibition (mm)					
	Gram Positive		Gram negative		Fungal strains	
	S. aureus	***B. subtilis***	***E. coli***	***E.aerogenes***	***C.albican***	***A.niger***
6a	15	16	11	12	15	13
6b	22	17	16	14	16	15
6c	19	18	14	13	17	15
6d	26	22	16	17	19	18
6e	22	20	16	18	19	18
6f	24	18	12	14	15	14
6g	23	21	15	17	24	24
6h	29	21	18	19	22	23
6i	27	22	17	17	19	18
6j	35	24	22	21	20	19
Amoxicillin	40	28	22	24	-	-
Ciprofloxacin	40	36	28	30	-	-
Fluconazole	-	-	-	-	28	26

Antifungal Activity: The antifungal activity of the synthesized compounds was evaluated against *Aspergillus niger* (*A. niger*) and *Candida albicans* (*C. albicans*) using the agar disk diffusion method[16]. The results are presented in table 1 and compared with the standard antifungal drug fluconazole. The antifungal activity of the synthesized compounds was evaluated against *Candida albicans* (yeast) and *Aspergillus niger* (filamentous fungus). Compound 6g exhibited impressive antifungal activity, with MIZ values of 24 µg/mL against both *C. albicans* and *A. niger*. These results indicate that 5g is slightly more effective than the standard antifungal drug fluconazole which showed MIZ values of 28 µg/mL and 26 µg/mL for *C. albicans* and *A. niger* respectively.

The structural features of compound 6g including a methyl group and 3,4-dimethoxy substitution, may play a critical role in its antifungal activity. The electron-donating methoxy groups can enhance lipophilicity, potentially improving membrane permeability and interaction with fungal targets. Additionally, the methyl group might contribute to optimal spatial orientation, facilitating binding to fungal enzymes or disrupting critical biosynthetic pathways such as ergosterol synthesis. The consistent activity of 6g against both yeast and filamentous fungi highlights its broad-spectrum potential. However, its moderate efficacy suggests that further optimization of the methyl and dimethoxy moieties could enhance binding affinity and potency.

Conclusion

In present work, we have reported 2-((4-ethyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)thio)-1-(3-(4-subphenyl)-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one derivatives (6a-j) through condensation of 4-ethyl-5-phenyl-4*H*-1,2,4-triazole-3-thiol (3) and pyrazolines in presence of anhydrous K_2CO_3 at room temperature. These new derivatives (6a-j) were then tested as antimicrobial agents against a variety of types of bacteria and fungi. The most effective antibacterial agents were compounds 6j and 6i while compound 6g showed a surprisingly high level of antifungal activity.

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