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Synthesis of New Derivatives of 1-(4-(5-(3,4-substituted phenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indoles and their antibacterial & antifungal activity

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Abstract*: Ten new derivatives of 1-(4-(5-(3,4-substitutedphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indoles(**3a-j**) have been synthesized, and most of the derivatives were promisingly active towards antibacterial and antifungal strains as compared with Ampicillin and fluconazole as positive controls due to the presence of triazole and is indole heterocyclic ring systems. All the new derivatives were prepared from 3,4-substituted phenylamidine hydrochlorides (**1a-j**) salts were reacted with 4-Iodobenzonitrile in presence of cuprous chloride and cesium carbonate in DMSO yields 3-(3,4-substituted phenyl)-5-(4-iodophenyl)-4H-1,2,4-triazoles (**2a-j**). Finally, 2-methylindole reacts with 3-(3,4-substituted phenyl)-5-(4-iodophenyl)-4H-1,2,4-triazoles(**2a-j**) to form 1-(4-(5-(3,4-substitutedphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole(**3a-j**). The structures of newly synthesized derivatives were confirmed by IR, ^{1}H NMR,^{13}CNMR, MS spectral data and elemental analysis.*

Key words: *4-Iodobenzonitrile; Substituted phenyl triazole derivatives; 2-methyl indole; antibacterial activity; antifungal activity.*

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I. Introduction

The chemistry of 1, 2, 4-triazole nucleus is an important unit present In a large number of functionalized molecules with wide variety of uses, including applications in medicinal chemistry, material science and organocatalysis. 1, 2, 4-Triazole derivatives are known to possess antimicrobial[1-4], antitubercular [5-9] and anticancer [10-12]. Some of the drugs containing this heterocycle are Ribavirin(antiviral)[13], Rizatriptan(antimigrane)[14], Estazolam and Alprazolam(anxiolytic)[15-17], Letrozole and Anastrozole (breast cancer)[18,19].There are number of drugs which are containing 1, 2, 4-triazole nucleus such as Itraconazole, Fluconazole and Posaconazole, that have been used for the treatment of fungal infection disease [20-23].

The indole ring system has become an important structural component in many pharmaceutical agents. This is exemplified by the amino acid tryptophan, hormones serotonin and melatonin, the psychotropic drug LSD, the antitumour agent vinblastine [24]. Chai et al. synthesized some new ethyl 6-bromo-5-hydroxy-1*H*-indole-3-carboxylates and disclosed their favorable anti-HBV [25] activities. Indomethacin [26], Etodolac [27] and Tenidap [28] are NSAIDs, and have been shown to exert anti-inflammatory effects. Several alkyl-substituted propanoic acids of indomethacin were prepared by Black et al. [29] It was found that the alkyl, aryl, aralkyl and heterocyclic esters **(Figure 1)** and amides **(Figure 2),** which are modified from indomethacin, exhibit high potency and selectivity [30].

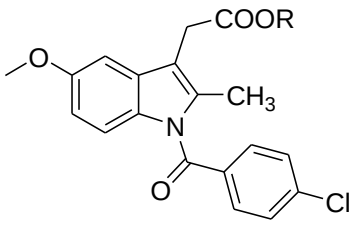


Figure-1

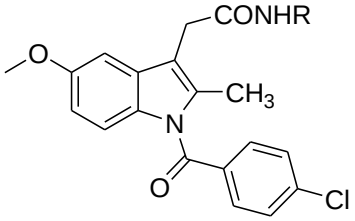


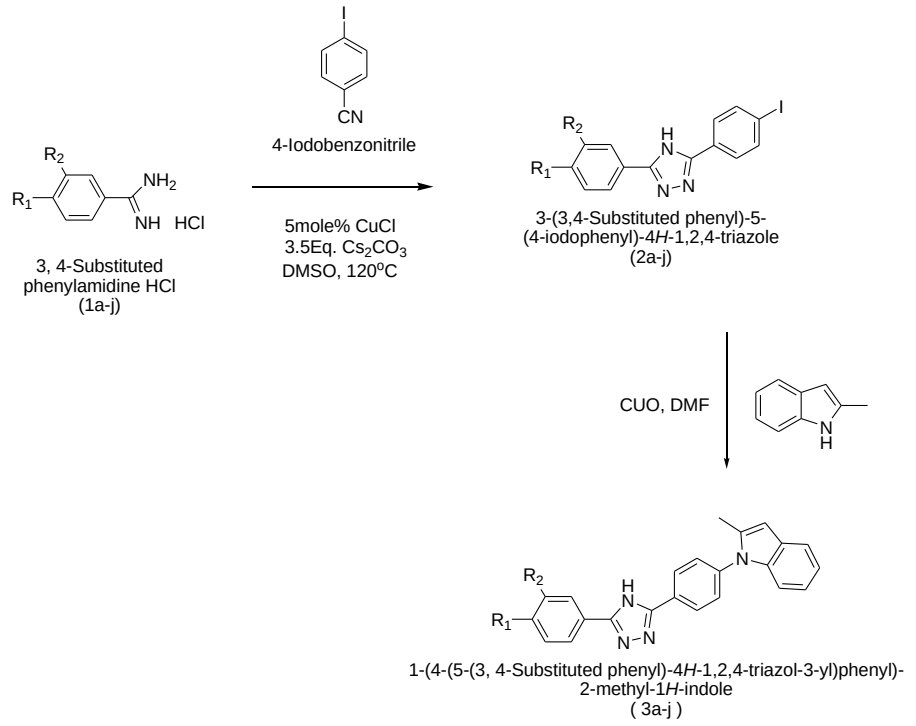
Figure-2

The chemistry of 1, 2, 4-triazole derivatives and Indole derivatives have been of significant interest because of their synthetic and extensive biological applications in the field of medicinal chemistry. The reaction scheme for the synthesis of title compounds is depicted in the following scheme.

II. Materials and Method:

Materials: All the melting points are determined on a Gallenkamp melting point apparatus and are uncorrected. The completion of the reaction and purity of synthesized compounds were checked on thin layer chromatography with silicagel 60Gf 254 merk-pre-coated plates (0.25 mm) was visualized under ultraviolet (UV) light or iodine vapour. All compounds were purified by flash chromatography on silica gel (particle size 100-200 mesh) and characterized by spectral studies. The IR spectra were recorded on Shimadzu FTIR model 8010 spectrophotometer and are given in cm^{-1} in KBr. The ^{1}HNMR & ^{13}CNMR spectra were recorded on Bruker AM-400 MHz NMR spectrometer in $CDCl_3$ & DMSO-d_6. The chemical shifts are reported in δ (ppm) relative to tetramethylsilane as internal standard. Mass spectra analyses performed with an Agilent-6400 series equipped with an electrospray ionization source.

Method: A new derivatives of 1-(4-(5-(3, 4-substitutedphenyl)-4H-1, 2, 4-triazol-3-yl)phenyl)-2-methyl-1H-indole (**3a-j**) from 3,4-substituted phenylamidine hydrochlorides (**1a-j**) salts. The reaction of 3, 4-substituted phenylamidine hydrochlorides (**1a-j**) salts with 4-Iodobenzonitrile in presence of cuprous chloride and cesium carbonate in DMSO yields 3-(3, 4-substituted phenyl)-5-(4-iodophenyl)-4H-1,2,4-triazoles (**2a-j**). The coupling of 3-(3,4-substituted phenyl)-5-(4-iodophenyl)-4H-1,2,4-triazoles (**2a-j**) with 2-methylindole in presence of cupric oxide in DMF produces final compounds 1-(4-(5-(3,4-substitutedphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole (**3a-j**). All the final compounds were characterized and identified by their FT-IR, ^{1}HNMR, ^{13}C NMR, mass spectra and elemental analyses.



Scheme

Compound	R_1	R_2
3a	H	H
3b	CH_3	H
3c	H	CH_3
3d	Cl	H
3e	H	Cl
3f	Br	H
3g	H	Br
3h	OCH_3	H
3i	H	NO_2
3j	NO_2	H

General procedure for synthesis of 3-(3, 4-Substituted phenyl)-5-(4-bromophenyl) -4H-1, 2, 4-triazole (2a-j):

A solution of 3, 4-substituted phenylamidine hydrochloride (0.01 mole), cuprous chloride (5mole%) and cesium carbonate (3.5 m.eq) in demethylsulfoxide (100 ml) was heated at 120-125^{o}C. Add 4-Iodo benzonitrile(1.0m.eq) to the mixture at 120-125^{o}C and stir for 12-30hrs. After completion of the reaction distill off DMSO under vacuum and then cool the residue to room temperature and add ethylacetate(5vol) and water to the residue. Stir the mixure for 15-20minutes and separate the layers. Distill off organic layer and crystallized the compound in isopropyl alcohol.

General procedure for synthesis of 1-(4-(5-(3,4-disubstitutedphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indoles (3a-j):

Dissolve 3-(3,4-Substituted phenyl)-5-(4-bromophenyl) -4H-1,2,4-triazoles (**2a-j**, 0.025moles) in N,N-dimethylformamide (50 ml). Add cupric oxide (0.5 m.eq) and 2-methylindole (1.0 m. eq) to the mixture and raise the temperature to 120-125^{o}C for 24-36 hrs. Filter the cupric oxide through hyflo and quench the filtrate in water (150 ml) and stir for 30 mimutes. Filter the solid and wash it with water (20 ml). Dry the compound at 60-65^{o}C. Yield: 40-60%.

Biological activity:

Antibacterial activity:

The antibacterial activity of synthesized compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram +ve bacteria screened were *Staphylococcus aureus* (S.A) and *Bacillus subtilis* (B.S). The gram _ve bacteria screened were *Escherichia coli* (E. coli) and *Pseudomonas aeruginosa* (P.A).

The synthesized compounds were used at the concentration of 250 µg/ml using DMSO as a solvent. The Ampicilin 10 µg/disc used as a standard (Himedia laboratories limited. Mumbai).

Antifungal activity: The antifungal activity of the all synthesized compounds **3a-j** against Aspergillus Niger (A.N) and Candida albicans (C.A) by disc diffusion method using fluconazole as standard.

The synthesized compounds were used at the concentration of 250µg/ml using DMSO as a solvent. The fluconazole 50 µg/disc used as a standard (Himedia laboratories limited. Mumbai).

III. Results and Discussion:

The physical and spectral data of scheme of compounds 3-(3, 4-Substituted phenyl)-5-(4-bromophenyl) -4H-1, 2, 4-triazole (2a-j) and 1-(4-(5-(3,4-disubstitutedphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indoles (**3a-j**) is as follows

2a : 3-(4-iodophenyl)-5-phenyl-4H-1,2,4-triazole

Yield: 57%, M.P: 169-171^{0}C, IR(cm^{-1}):3341,3069, 3055, 1592, 1550, 503. ^{1}H-NMR (δ) : 7.48-7.58 (5H, m, -Ar-H), 7.94-7.97 (2H, t, -Ar-H), 8.08-8.11(2H, t, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.5, 127.1, 127.8, 128.9, 129.4, 131.3, 131.8, 132.5, 138.7, 157.9, FAB Mass: m/z 348.99(M$^+$), CHN Analysis: Found C(48.47%), H (2.85%), N (12.15%), Calc: C (48.44%), H (2.90%), N (12.10%).

2b : 3-(4-iodophenyl)-5-(p-tolyl)-4H-1,2,4-triazole

Yield: 57%, M.P: 169-171^{0}C, IR(cm^{-1}):3429, 3091,3063, 2998, 1607, 1570, 510. 1H-NMR (δ) : 2.34(6H, s, -CH_3), 7.45-7.47 (2H, dd, -Ar-H), 7.52-7.56(2H, dd, -Ar-H), 7.96-7.99(2H, dd, -Ar-H), 8.55-8.56(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 21.5, 94.1, 125.6, 128.3, 129.7, 131.6, 131.4, 138.3, 157.9, FAB Mass: m/z 362.01(M$^+$), CHN Analysis: Found C(49.83%), H (3.31%), N (11.65%), Calc: C (49.88%), H (3.35%), N (11.63%).

2c : 3-(4-iodophenyl)-5-(m-tolyl)-4H-1,2,4-triazole
Yield: 60%, M.P: 154-156^{0}C, IR(cm^{-1}):3325, 3083,3059, 2988, 1589, 1563, 502. 1H-NMR (δ) : 2.46 (3H, s, -CH_3), 7.17-7.19 (1H, d, -Ar-H), 7.51-7.55(3H, m, -Ar-H), 7.77(1H, s, -Ar-H), 7.95-7.99(2H, dd, -Ar-H), 8.18-8.2(1H, d, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 21.5, 94.5, 124.2, 128.1, 129.3, 130.9, 131.3, 131.6, 137.5, 138.4, 157.8. FAB Mass: m/z 362.01(M^+), CHN Analysis: Found C(49.85%), H (3.34%), N (11.63%), Calc: C (49.88%), H (3.35%), N (11.63%).

2d : 3-(4-chlorophenyl)-5-(4-iodophenyl)-4H-1,2,4-triazole
Yield: 50%, M.P: 191-193^{0}C, IR(cm^{-1}): 3458, 3043, 3038, 2985, 1610, 1555, 768, 505. 1H-NMR (δ) : 7.56-7.59 (4H, m, -Ar-H), 7.95-7.99(2H, dd, -Ar-H), 8.1-8.14(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.5, 128.3, 128.9, 129.1, 130.5, 131.6, 134.5, 138.7, 157.9, FAB Mass: m/z 381.95(M^+), CHN Analysis: Found C(44.09%), H (2.36%), N (11.07%), Calc: C (44.07%), H (2.38%), N (11.01%).

2e : 3-(3-chlorophenyl)-5-(4-iodophenyl)-4H-1,2,4-triazole
Yield: 55%, M.P: 175-177^{0}C, IR(cm^{-1}): 3448, 3073, 3052, 2995, 1590, 1565, 760, 500. 1H-NMR (δ) : 7.46-7.52 (4H, m, -Ar-H), 7.93-7.95(3H, m, -Ar-H), 8.16-8.18(2H, d, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.4, 125.4, 126.7, 128.3, 129.2, 131.6, 132.2, 134.7, 138.7, 157.9, FAB Mass: m/z 381.95(M^+), CHN Analysis: Found C(44.05%), H (2.35%), N (11.05%), Calc: C (44.07%), H (2.38%), N (11.01%).

2f : 3-(4-Bromophenyl)-5-(4-iodophenyl)-4H-1,2,4-triazole
Yield: 62%, M.P: 220-223^{0}C, IR(cm^{-1}): 3467, 3075, 3042, 2975, 1603, 1565, 1093, 508. 1H-NMR (δ) : 7.54-7.59 (4H, dd, -Ar-H), 7.60-7.64(4H, m, -Ar-H), 7.92-7.96(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.5, 123.2, 128.9, 131.2, 131.6, 132.2, 138.9, 157.9, FAB Mass: m/z 425.9(M^+), CHN Analysis: Found C(39.45%), H (2.10%), N (9.89%), Calc: C (39.47%), H (2.13%), N (9.86%).

2g : 3-(3-Bromophenyl)-5-(4-iodophenyl)-4H-1,2,4-triazole
Yield: 58%, M.P: 158-160^{0}C, IR(cm^{-1}):3473, 3066, 3058, 2984, 1608, 1570, 1082, 510. 1H-NMR (δ) : 7.54-7.59 (4H, dd, -Ar-H), 7.60-7.64(4H, m, -Ar-H), 7.93-7.95(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.5, 122.5, 126.3, 128.2, 128.6, 131.5, 131.8, 138.5, 157.9, FAB Mass: m/z 425.9(M^+), CHN Analysis: Found C(39.48%), H (2.14%), N (9.82%), Calc: C (39.47%), H (2.13%), N (9.86%).

2h : 3-(4-Iodophenyl)-5-(4-methoxyphenyl)-4H-1,2,4-triazole
Yield: 54%, M.P: 147-149^{0}C, IR(cm^{-1}): 3480, 3072, 3050, 2992, 1595, 1564, 1020,512. 1H-NMR (δ) : 3.81(3H, s, -OCH_3), 7.03-7.07(2H, dd, -Ar-H), 7.50-7.54(2H, dd, -Ar-H), 7.93-7.97(2H, dd, -Ar-H), 8.05-8.09(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 55.7, 94.2, 114.6, 124.4, 128.3, 130.4, 131.6, 138.4, 157.9, 160.6, FAB Mass: m/z 378(M^+), CHN Analysis: Found C(47.80%), H (3.25%), N (11.11%), Calc: C (47.77%), H (3.21%), N (11.14%).

2i : 3-(4-Iodophenyl)-5-(3-nitrophenyl)-4H-1,2,4-triazole
Yield: 52%, M.P: 162-164^{0}C, IR(cm^{-1}): 3330,3073,2841,2762 1528, 1370, 506. 1H-NMR (δ) : 7.52-7.56(2H, dd, -Ar-H), 7.86-7.95(2H, m, -Ar-H), 8.32-8.34(2H, d, -Ar-H), 8.64-8.65(2H, t, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.4, 122.9, 123.2, 128.1, 130.1, 131.2, 133.8, 138.5, 148.5, 157.9, FAB Mass: m/z 378(M^+), CHN Analysis: Found C(47.80%), H (3.25%), N (11.11%), Calc: C (47.77%), H (3.21%), N (11.14%).

2j : 3-(4-Iodophenyl)-5-(4-nitrophenyl)-4H-1,2,4-triazole
Yield: 59%, M.P: 159-161^{0}C, IR(cm^{-1}): 3440, 3068, 1527, 1365, 502. 1H-NMR (δ) : 7.52-7.56(2H, dd, -Ar-H), 7.97-8.05(4H, m, -Ar-H), 8.27-8.31(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 94.5, 124.6, 125.9, 127.3, 128.6, 131.2, 138.7, 147.5, 157.9, FAB Mass: m/z 393.16(M^+), CHN Analysis: Found C(42.85%), H (2.34%), N (14.30%), Calc: C (42.88%), H (2.31%), N (14.29%).

3a : 2-methyl-1-(4-(5-phenyl-4H-1,2,4-triazol-3-yl)phenyl)-1H-indole
Yield: 45%, M.P: 152-156^{0}C, IR(cm^{-1}):3386, 1548, 1617. 1H-NMR (δ) : 2.14(3H, s, -CH_3), 6.25(1H, s, -Ar-H), 6.91-6.94(1H, t, -Ar-H), 7.34-7.49(5H, m, -Ar-H), 7.64(1H, d, -Ar-H), 7.93-7.95(4H, m, -Ar-H), 8.07-8.11(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.3, 103.7, 109.4, 114.2, 119.6, 120.5, 126.4, 127.3, 128.8, 129.3, 130.6, 131.2, 132.5, 137.8, 145.2, 151.2, 157.4, FAB Mass: m/z 351.15(M^+), CHN Analysis: Found C(78.84%), H (5.86%), N (15.96%), Calc: C (78.83%), H (5.88%), N (15.99%).

3b : 2-methyl-1-(4-(5-(p-tolyl)-4H-1,2,4-triazol-3-yl)phenyl)-1H-indole
Yield: 40%, M.P: 121-123^{0}C, IR(cm^{-1}):3390, 1555, 1610. 1H-NMR (δ) : 2.12(3H, s, -CH_3), 2.36(3H,s,-CH_3), 6.29(1H, s, -Ar-H), 6.95-6.98(1H, t, -Ar-H), 7.34-7.45(4H, m, -Ar-H), 7.62-7.64(1H, d, -Ar-H), 7.93-7.94(4H, m, -Ar-H), 8.53-8.57(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.3, 21.6, 103.7, 109.6, 114.3, 119.5, 120.4, 121.3, 125.6, 126.8, 128.2, 129.5, 129.7, 130.2, 131.5, 137.7, 145.2, 151.2, 157.9, FAB Mass: m/z 365.17(M^+), CHN Analysis: Found C(79.14%), H (5.58%), N (15.33%), Calc: C (79.10%), H (5.53%), N (15.37%).

3c : 2-methyl-1-(4-(5-(m-tolyl)-4H-1,2,4-triazol-3-yl)phenyl)-1H-indole
Yield: 55%, M.P: 115-117^{0}C, IR(cm^{-1}): 3385, 1560, 1608. 1H-NMR (δ) : 2.10(3H, s, -CH_3), 2.45(3H, s, -CH_3), 6.24(1H, s, -Ar-H), 6.95-6.98(1H, t, -Ar-H), 7.33-7.36(1H, t, -Ar-H), 7.62-7.64(1H, d, -Ar-H), 7.78(1H, s, -Ar-H), 7.92-7.93(4H, m, -Ar-H), 8.16-8.18(1H, d, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.3, 21.5, 103.7, 109.6, 114.2, 119.5, 120.4, 124.8, 126.1, 128.5, 129.1, 129.3, 130.5, 131.4, 137.7, 145.2, 151.2,157.9, FAB Mass: m/z 365.17(M^+), CHN Analysis: Found C(79.09%), H (5.53%), N (15.32%), Calc: C (79.10%), H (5.53%), N (15.37%).

3d : 1-(4-(5-(4-chlorophenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole
Yield: 46%, M.P: 127-129^{0}C, IR(cm^{-1}):3368, 1545, 1590, 768. 1H-NMR (δ) : 2.13(3H, s, -CH_3), 6.25(1H, s, -Ar-H), 6.93-6.96(1H, t, -Ar-H), 7.35(1H, s, -Ar-H), 7.46-7.48(1H, d, -Ar-H), 7.55-7.64(3H, m, -Ar-H), 7.92-7.94(4H, m, -Ar-H), 8.12-8.16(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.4, 103.4, 109.7, 114.2, 119.6, 120.5, 126.4, 128.2, 128.9, 129.3, 130.6, 134.5, 137.8, 145.2, 151.2, 157.7, FAB Mass: m/z 385.11(M^+), CHN Analysis: Found C(71.76%), H (4.42%), N (14.55%), Calc: C (71.78%), H (4.45%), N (14.56%).

3e : 1-(4-(5-(3-chlorophenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole
Yield: 40%, M.P: 134-136^{0}C, IR(cm^{-1}):3433, 1567, 1602, 763. 1H-NMR (δ) : 2.16(3H, s, -CH_3), 6.26(1H, s, -Ar-H), 6.95-6.98(1H, t, -Ar-H), 7.33(1H, s, -Ar-H), 7.48(1H, d, -Ar-H), 7.55-7.60(3H, m, -Ar-H), 7.93-7.98(4H, m, -Ar-H), 8.12-8.16(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13. 103.7, 109.6, 114.2, 119.7, 120.6, 126.5, 126., 128.2, 128.8, 129.4, 130.4, 132.1, 137.8, 145.2, 151.2, 157.9, FAB Mass: m/z 385.11(M^+), CHN Analysis: Found C(71.79%), H (4.49%), N (14.52%), Calc: C (71.78%), H (4.45%), N (14.56%).

3f : 1-(4-(5-(4-bromophenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole
Yield: 45%, M.P: 151-153^{0}C, IR(cm^{-1}): 3383, 1543,1610, 1062. 1H-NMR (δ) : 2.16(3H, s, -CH_3), 6.27(1H, s, -Ar-H), 6.92-6.95(1H, t, -Ar-H), 7.35(1H, s, -Ar-H), 7.45-7.47(1H, d, -Ar-H), 7.62-7.66(5H, m, -Ar-H), 7.92-7.93(4H, m, -Ar-H), 8.10-8.14(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.4, 103.7, 109.6, 114.2, 119.6, 120.8, 123.2, 126.4, 128.1, 129.3, 130.5, 131.2, 131.6, 132.4, 145.3, 151.2, 157.9, FAB Mass: m/z 429.06(M^+), CHN Analysis: Found C(64.30%), H (4.02%), N (13.1%), Calc: C (64.35%), H (3.99%), N (13.05%).

3g : 1-(4-(5-(3-bromophenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole
Yield: 45%, M.P: 139-141^{0}C, IR(cm^{-1}):3384,1617, 1546, 1056. 1H-NMR (δ) : 2.12(3H, s, -CH_3), 6.27(1H, s, -Ar-H), 6.94-6.97(1H, t, -Ar-H), 7.35-7.46(4H, m, -Ar-H), 7.60--7.65(2H, d, -Ar-H), 7.92-7.97(4H, m, -Ar-H), 8.13(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.3, 103.7, 109.4, 114.2, 119.5, 120.5, 122.4, 126.5, 126.7, 126.9, 128.3, 129.3, 130.6, 131.5, 132.7, 137.4, 145.2, 151.2, 157.9, FAB Mass: m/z 428.06(M^+), CHN Analysis: Found C(64.39%), H (3.97%), N (13.02%), Calc: C (64.35%), H (3.99%), N (13.05%).

3h : 1-(4-(5-(4-methoxyphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indole
Yield: 52%, M.P: 165-167^{0}C, IR(cm^{-1}): 3385, 1546, 1023. 1H-NMR (δ) : 2.12(3H, s, -CH_3), 3.81(3H,s,-Ar-H), 6.26(1H, s, -Ar-H), 6.93-6.97(3H, t, -Ar-H), 7.35(1H, s, -Ar-H), 7.46-7.48(1H, d, -Ar-H), 7.61-7.63(1H, d, -Ar-H), 7.90-7.95(4H, m, -Ar-H), 8.05-8.09(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.4, 55.9, 103.7, 109., 114.2, 114.4, 119.2, 120.5, 124.7, 126.5, 128.2, 129.4, 130.6, 137.4, 145.7, 151.2, 157.5, 160.8, FAB Mass: m/z 381.16(M^+), CHN Analysis: Found C(75.79%), H (5.32%), N (14.76%), Calc: C (75.77%), H (5.30%), N (14.73%).

3i : 2-methyl-1-(4-(5-(3-nitrophenyl)-4H-1,2,4-triazol-3-yl)phenyl)-1H-indole

Yield: 60%, M.P: 132-134^{0}C, IR(cm^{-1}): 3380, 1614, 1545, 1489,1382. 1H-NMR (δ) : 2.12(3H, s, -CH_3), 6.27(1H, s, -Ar-H), 6.95-6.98(1H, t, -Ar-H), 7.35(1H, s, -Ar-H), 7.45(1H, s, -Ar-H), 7.62-7.65(1H, t, -Ar-H), 7.86-7.92(5H, m, -Ar-H), 8.31-8.33(1H, d, -Ar-H), 8.65-8.68(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.1 103.7, 109.3, 114.2, 119.7, 120.5, 122.2 123.7, 126.5, 128.2, 129.5, 130.2, 130.4, 131.6, 133.8, 137.4, 145.2, 151.2, 157.9. FAB Mass: m/z 396.14(M^+), CHN Analysis: Found C (69.85%), H (4.34%), N (17.73%), Calc: C (69.86%), H (4.33%), N (17.71%).

3j : 2-methyl-1-(4-(5-(34-nitrophenyl)-4H-1,2,4-triazol-3-yl)phenyl)-1H-indole
Yield: 50%, M.P: 132-134^{0}C, IR (cm^{-1}): 3383, 1545, 1484,1380. 1H-NMR (δ) : 2.14(3H, s, -CH_3), 6.29(1H, s, -Ar-H), 6.94-6.97(1H, t, -Ar-H), 7.35(1H, s, -Ar-H), 7.46-7.48(1H, d, -Ar-H), 7.62-7.65(1H, m, -Ar-H), 7.92-7.93(4H, m, -Ar-H), 8.02-8.06(2H, dd, -Ar-H), 8.27-8.29(2H, dd, -Ar-H), 11.12-11.14(1H, s, -triazole amine), ^{13}C-NMR: 13.3, 103.5, 109.6, 114.2, 119.7, 120.5, 124.7, 126.6, 127.2, 128.2, 130.6, 132.2, 137.4, 138.5, 145.2, 147.5, 157.9 , FAB Mass: m/z 396.14(M^+), CHN Analysis: Found C(69.87%), H (4.31%), N (17.70%), Calc: C (69.86%), H (4.33%), N (17.71%).

Antibacterial activity:

Almost all the compounds showed promising activity that could be attributed to the presence of triazole and indole heterocyclic ring systems with their high potency. The compounds **3a-j** shows highly active with all strains of bacteria.

Table-1. The antibacterial activity against bacterial strains such as The gram +ve bacteria strains were Staphylococcus Aureus (S.A) and Bacillus Subtilis (B.S). The gram _ve bacteria strains were Escherichia Coli (E.Coli) and Pseudomonas Aeruginosa (P.A) .

S.No	Compound	R1	R2	*B.subtilis*	*S.aureus*	*P.aeruginosa*	*E.coli*
1	3a	-H	-H	22(+++)	24(+++)	21(+++)	23(+++)
2	3b	-CH_3	-H	23(+++)	24(+++)	21(+++)	24(+++)
3	3c	-H	-CH_3	22(+++)	23(+++)	22(+++)	22(+++)
4	3d	-Cl	-H	22(+++)	24(+++)	20(+++)	23(+++)
5	3e	-H	-Cl	20(+++)	24(+++)	20(+++)	20(+++)
6	3f	-Br	-H	22(+++)	21(+++)	20(+++)	23(+++)
7	3g	-H	-Br	22(+++)	22(+++)	22(+++)	24(+++)
8	3h	-OCH_3	-H	22(+++)	22(+++)	23(+++)	24(+++)
9	3i	-H	-NO_2	18(+++)	18(+++)	20(+++)	20(+++)
10	3j	-NO_2	-H	20(+++)	20(+++)	21(+++)	22(+++)
11	Ampicillin			24	26	22	25

Key to symbols: - inactive (inhibition zone < 6 mm); slightly active = + (inhibition zone 7–9 mm); moderately active = + + (inhibition zone 10-13 mm); highly active = + + + (inhibition zone > 14 mm).

Antifungal activity:

Compounds **3a-j** were active against both strains *Aspergillus Niger* and *Candida Albicans*

Table-2. . The antifungal activity against Fungal strains such as Aspergillus Niger (A.N) and Candida Albicans (C.A) .

S.No	Compound	*Aspergillus Niger*	*Candida Albicans*
1	3a	14(+++)	16(+++)
2	3b	18(+++)	16(+++)
3	3c	15(+++)	15(+++)
4	3d	18(+++)	18(+++)
5	3e	19(+++)	17(+++)
6	3f	20(+++)	16(+++)
7	3g	18(+++)	17(+++)
8	3h	18(+++)	15(+++)
9	3i	16(+++)	16(+++)
10	3j	18(+++)	17(+++)
13	Fluconazole	22(+++)	19(+++)

Key to symbols: - inactive (inhibition zone < 6 mm); slightly active = + (inhibition zone 7–9 mm); moderately active = + + (inhibition zone 10-13 mm); highly active = + + + (inhibition zone > 14 mm).

IV. Conclusions

In summary, the designation and synthesis of new derivatives of 1-(4-(5-(3,4-substitutedphenyl)-4H-1,2,4-triazol-3-yl)phenyl)-2-methyl-1H-indoles (**3a-j**), and their antibacterial and antifungal activities are

represented in this study. All of the tested compounds showed good antibacterial and antifungal activity. The results may provide a useful reference for further research on anti-microbial drugs.

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