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Thiazole substituted [1,2,3] Triazole: Synthesis and antimicrobial evaluation

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Novel hybrid molecules containing thiazole and triazole moieties have been efficiently synthesized and characterized by spectroscopic techniques such as IR, NMR, mass spectrometry and elemental analysis. The synthesized hybrid molecules have been screened for their antimicrobial activity against bacterial as well as fungal strains. The minimum inhibitory concentrations have been determined. The investigation of antimicrobial screening data has revealed the most of the compounds exhibited moderate to good microbial activity.

Keywords: Thiazole, Triazole, Antimicrobial, MIC

An upsurge in resistance shown by most of the pathogens to currently marketed drugs represents a great threat to the human society.[1-3] Due to this, the treatment of diseases caused by drug resistant pathogens becomes challenging, specially for the patients with suppressed immunity.[4] The emergence of the drug resistant microbial strain highlights urgent need for the development of new series of antimicrobial agents with improved pharmacological properties.[5] In this context, heterocycles with azole nucleus have received much attention owing to its wide range of pharmacological activities.[6, 7]

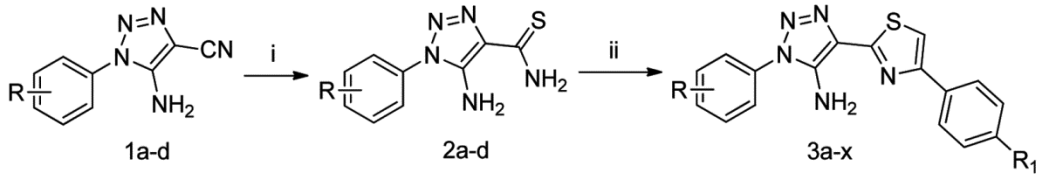
Over past few decades, triazole derivatives have been emerged as backbone of an antifungal therapy. Triazole core has been found in many therapeutically important medicines such ascefatrizine (antimicrobial), voriconazole (antifungal), trazodone (antidepressant), alprazolam (anxiolytic), ribavirin (antiviral)[8] and rizatriptan (antimigraine)[9]. Literature survey has revealed that, triazole derivatives shows wide range of biological activities including fungicidal,[10] anticancer,[11] insecticidal,[12] antiprotozaol,[13]antibacterial,[14] and plant growth regulators.[15, 16]

Thiazole derivatives have received considerable attention due to their remarkable application in medicinal chemistry.[17] Several marketed drugs such as sulfathiazole (antimicrobial),[18] tiazofurin and thianetropsin (antineoplastic),[19-23] possess thiazole moieties. In addition, thiazole derivatives are found to be useful in the treatment of allergies,[24] hypertension,[25] inflammation,[26] schizophrenia,[27] microbial infections,[28, 29] HIV infections,[30] hypnotics,[31] and for the treatment of pain.[32]

It has been shown that, the triazole clubbed thiazole molecule could be convenient candidates for investigation of their biological activity. Literature revealed that syntheses of such thiazolyl-triazole have shown antimicrobial,[33] anti-inflammatory,[34] anti-tubercular[35]and antifungal activity.[36] To the best of our knowledge, till date enough efforts have not been made to combine triazole and thiazole moieties as a single molecular scaffold and to study its biological activity. Intrigued by potential clinical applications of heterocycles and in continuation with our earlier work on heterocyclic compounds [37-44],herein we report the synthesis of new [1,2,3]-triazole embedded with thiazole derivatives **3a-x** (Scheme 1) with the aim of investigating their antimicrobial responses.

Experimental Details

Melting points are uncorrected. The ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Varian NMR Mercury 400 spectrometer. Chemical



Compd	R	R_1	Compd	R	R_1	Compd	R	R_1
3a	4-H	4-H	**3i**	4-Cl	4-Br	**3q**	3-Cl	4-CH_3
3b	4-H	4-Cl	**3j**	4-Cl	4-NO_2	**3r**	3-Cl	4-OCH_3
3c	4-H	4-Br	**3k**	4-Cl	4-CH_3	**3s**	4-Br	4-H
3d	4-H	4-NO_2	**3l**	4-Cl	4-OCH_3	**3t**	4-Br	4-Cl
3e	4-H	4-CH_3	**3m**	3-Cl	4-H	**3u**	4-Br	4-Br
3f	4-H	4-OCH_3	**3n**	3-Cl	4-Cl	**3v**	4-Br	4-NO_2
3g	4-Cl	4-H	**3o**	3-Cl	4-Br	**3w**	4-Br	4-CH_3
3h	4-Cl	4-Cl	**3p**	3-Cl	4-NO_2	**3x**	4-Br	4-OCH_3

Reagent and Condition: (i) H_2S, Pyridine, 50 °C, 1-1.5h; (ii) Phenacyl bromide, EtOH, Reflux, 20-30 min

Scheme 1 — Synthetic pathway of compounds 3a-x

shifts were reported in ppm relative to tetramethylsilane (TMS), and multiplicities are given as s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Infrared spectra were recorded as KBr pellets on a Shimadzu FTIR-408 spectrophotometer. Mass spectra were recorded on a Shimadzu LC-MS: EI QP 2010A mass spectrometer with an ionization potential of 70 eV. Elemental analyses (C, H and N) were performed on Thermo Finnigan Eager 300 EA 1112 series analyser. Reactions were monitored by thin layer chromatography (TLC), carried out on 0.2 mm silica gel 60 F254 (Merck) plates using UV light (254 and 366 nm) for detection and compounds were purified by recrystallization using solvent ethyl alcohol. Common reagent grade chemicals are commercially available and were used without further purification.

General Procedure for synthesis of compound (2a-d)

Substituted anilines **1a-d** (0.01 mol) was dissolved in 40% sulphuric acid to room temperature. Cool reaction mixture and allow to it room temperature. The temperature of reaction mixture to 0-5 °C was maintained and aqueous solution of sodium nitrite (0.011 mol) was added slowly to the above reaction mixture. Then aqueous solution of sodium azide (0.011 mol) was added slowly at the same temperature and reaction mixture was stirred for next 1 h. Exothermic reaction was observed with evolution of nitrogen gas. After completion of reaction (monitor by TLC), product was extracted with ethyl acetate and washed with water twice and treated with anhydrous sodium sulphate. The solvent was removed on rotary evaporator.

General Procedure for the synthesis of compound (1a-d)

To the mixture of substituted azide (0.01 mol) and malanonitrile (0.012 mol) in ethyl alcohol, catalytic amount of triethylamine was added and the reaction mixture stirred to room temperature for 30 min, the solid was separated. After completion of reaction (monitor by TLC), the reaction mixture was poured to ice crush water (200 mL). The solid was separated, filter, wash with aqueous alcohol and dried. The product was recrystallized from ethyl alcohol.

5-amino-1-phenyl-1H-1,2,3-triazole-4-carbonitrile (1a)

M.P.: 174-176 °**C**, Yield: 81**%,** I.R.: 3325, 3200, 2245 Cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 7.15 (s, br, 2H, NH_2), 7.63-7.56 (m, 5H, Ar-H).

5-amino-1-(4-chlorophenyl)-1H-1, 2, 3-triazole-4-carbonitrile (1b)

M.P.: 224-226 °**C**, Yield: 80**%,** I.R: 3390, 3327 2245 Cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 7.12 (s, br, 2H, NH_2), 7.57 (d, J=8.8Hz, 2H, Ar-H), 7.62 (d, J=8.8Hz, 2H, Ar-H).

5-amino-1-(3-chlorophenyl)-1H-1, 2, 3-triazole-4-carbonitrile (1c)

M.P.: 224-226 °**C**, Yield: 80% **%,** I.R: 3396, 3225, 2245 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 7.17 (s, br, 2H, NH_2), 7.41-7.56 (m, 3H, Ar-H), 7.61 (s, 1H, Ar-H), 9.06 (s, br, 2H).

5-amino-1-(4-bromophenyl)-1H-1, 2, 3-triazole-4-carbonitrile (1d)

M.P.: 228-223 °**C,**Yield: 86**%,** I.R: 3380, 33202245 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ7.18 (s,br, 2H, NH_2), 7.68 (d, J=9 Hz, 2H, Ar-H), 7.73 (d, J=9 Hz, 2H, Ar-H).

General Procedure for the synthesis of compound (2a-d)

To the solution of 5-amino-1-(substituted phenyl)-1H-1, 2, 3-triazole-4-carbonitrile **1a-d** (0.01 mol) in pyridine (15 mL) in three neck flask, catalytic amount triethyl amine was added to room temperature. Thiane (H_2S) gas was passed in the above reaction mixture to the same temperature but during the passing of H_2S the temperature of reaction was increases to 55 °C. After completion of reaction (monitor by TLC), the reaction mixture was poured to ice crush water (200 mL). The solid was separated, filter, wash with dil. HCl and water then dried. The product was recrystallized from ethyl alcohol.

5-amino-1-phenyl-1H-1, 2, 3-triazole-4-carbothioamide (2a)

M.P.: 184-186 °C**,** Yield: 85**%,** I.R.: 3352 and 3287 cm^{-1} (N-H, amine),3176 and 3110 cm^{-1}(N-H, thioamide),^{1}H NMR (400 MHz, DMSO): δ7.33 (s, br, 2H, NH_2), 7.52-7.63(m, 5H), 9.08 (s, br, 2H, NH_2).

5-amino-1-(4-chlorophenyl)-1H-1,2,3-triazole-4-carbothioamide (2b)

M.P.: 192-194**°C,**Yield: 88**%,** I.R: 3414 and 3304 cm^{-1} (N-H, amine), 3239 and 3169cm^{-1}(N-H, thioamide), ^{1}H NMR (400 MHz, DMSO): δ7.38 (s, br, 2H, NH_2), 7.60 (d, 2H, J=9 Hz, Ar-H), 7.63 (d, 2H, J=9 Hz, Ar-H), 9.07 (s, br, 2H, NH_2).

5-amino-1-(3-chlorophenyl)-1H-1, 2, 3-triazole-4-carbothioamide (2c)

M.P.: 168-170**°C,**Yield: 86**%,** I.R: 3413and 3303cm^{-1} (N-H, amine), 3238 and 3168 cm^{-1} (N-H, thioamide), ^{1}H NMR (400 MHz, DMSO): δ7.48 (s, br, 2H, NH_2), 7.54-7.61 (m, 3H, Ar-H), 7.67 (s, 1H, Ar-H), 9.06 (s, br, 2H, NH_2).

5-amino-1-(4-bromophenyl)-1H-1, 2, 3-triazole-4-carbothioamide (2d)

M.P.: 216-218 °C**,** Yield: 92**%,** I.R: 3398 and 3301 cm^{-1} (N-H, amine), 3225 and 3151cm^{-1}(N-H, thioamide), ^{1}H NMR (400 MHz, DMSO): δ 7.42 (s, br, 2H, NH_2), 7.64 (d, 2H, J=9 Hz, Ar-H), 7.70 (d, 2H, J=9 Hz, Ar-H), 9.11 (s, br, 2H, NH_2).

General Procedure for the synthesis of compound (3a-x)

The mixture of 5-amino-1-(substituted phenyl)-1H-1, 2, 3-triazole-4-carbothioamide **2a-d** (0.01 mol) and substituted phenacyl bromide (0.01 mol) was refluxed in ethyl alcohol for 30 min. After completion of reaction (monitor by TLC), the reaction mixture was cooled at room temperature, the solid separated was filtered and washed with alcohol and recrystallized from ethyl alcohol.

3-phenyl-5-(4-phenylthiazol-2-yl)-3H-1,2,3-triazol-4-amine(3a)

M.P.: 144-146 °C**,** Yield: 80**%,** I.R: 3382 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 6.63 (s, 2H, NH_2), 7.35-8.13 (m, 10 H, Ar-H), 7.76 (s, 1H, =CH), ;^{13}C NMR (75 MHz, DMSO): 110.6 (C=C), 122.5 (2C's, Ar-C), 123.5 (Ar-C), 126.8 (4C's, Ar-C), 127.3 (2C's, Ar-C), 128.9 (2C's, Ar-C), 128.2 (C=C), 130.0(C=C), 130.1 (Ar-C), 150.7 (C=C), 158.7 (C=N); MS: m/z 320.26 (M+1), 318.35 (M-1); Elemental Analysis: $C_{17}H_{13}N_5S$, Calcd.: C:63.93%; H: 4.10%; N: 21. 93%. Found: C: 63.85%; H: 4.09%; N: 21.91%.

5-(4-(4-chlorophenyl) thiazol-2-yl)-3-phenyl-3H-1,2,3-triazol-4-amine (3b)

M.P.: 196-198 °C**,** Yield: 84**%,** I.R: 3387 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.57 (s, 2H, NH_2), 7.45 (dd, 2H, J= 1.6 &6.7 Hz, Ar-H), 7.55-7.70 (m, 5 H,Ar-H), 7.88 (s ,1H,=CH), 8.03 (dd, 2H, J=1.6 & 6.7 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 111.8 (C=C), 123.4 (Ar-C), 124.2 (3C's, Ar-C), 127.9 (2C's, Ar-C), 128.8 (2C's, Ar-C), 129.2 (2C's, Ar-C), 129.9 (C=C), 132.7 (Ar-C), 134.9 (C=C), 140.7 (Ar-C), 152.9 (C=C), 160.6 (C=N); MS: m/z 354.35 (M+1); Elemental Analysis: $C_{17}H_{12}ClN_5S$, Calcd.: C:57.71%; H:3.42%; N:19.79%, Found: C:57.51%; H:3.35%; N:19.81%.

5-(4-(4-bromophenyl)thiazol-2-yl)-3-phenyl-3H-1,2,3-triazol-4-amine (3c)

M.P.: 200-202 °C**,** Yield: 87**%,** I.R: 3385 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.61 (s, 2H, NH_2), 7.57 (dd, 1H, J= 1.5 &6.5 Hz, Ar-H), 7.60-7.68 (m, 5H, Ar-H), 8.03 (s, 1H, =CH), 8.08(dd,2H, J=1.5 & 6.5 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.9 (C=C), 123.1 (Ar-C), 123.5 (Ar-C), 126.8 (3C's, Ar-C), 127.7 (2C's, Ar-C), 129.0 (2C's, Ar-C), 129.4 (C=C), 132.1 (C=C), 133.2 (2C's, Ar-C), 139.0 (Ar-C), 152.5 (C=C), 160.2 (C=N); MS: m/z 399.96 (M+1), 397.92 (M-1); Elemental Analysis: $C_{17}H_{12}BrN_5S$, Calcd.:C:51.27%; H: 3.04%; N:17.58%; Found: C:51.30%; H: 2.95%; N:17.51%.

5-(4-(4-nitrophenyl) thiazol-2-yl)-3-phenyl-3H-1,2,3-triazol-4-amine (3d)

M.P.: 264-266 °C**,** Yield: 88**%,** I.R: 3389 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.64 (s, 2H, NH_2), 7.58 (dd, 2H, J= 1.9 & 8 Hz, Ar-H), 7.66-8.28 (m, 5 H, Ar-H), 8.29 (s, 1H, =CH), 8.33 (d, 2H, J=1.9 & 8 Hz,Ar-H); ^{13}C NMR (75 MHz, DMSO): 112.6 (C=C), 124.6 (Ar-C), 126.4 (2C's, Ar-C), 128.5 (Ar-C), 129.8 (3C's, Ar-C), 130.9 (2C's, Ar-C), 131 (C=C), 134.1 (C=C), 139.2 (Ar-C), 145.8 (Ar-C),

153.5 (C=C), 162.7 (C=N); MS: m/z 365.08 (M+1); Elemental Analysis: $C_{17}H_{12}N_6O_2S$, Calcd.: C:56.04%; H:3.32%; N:23.06%; Found: C:55.98%; H:3.21%; N:22.91%.

3-phenyl-5-(4-p-tolylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3e)

M.P.: 170-172 °C**,** Yield: 84**%,** I.R: 3380 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 2.36 (s, 3H, CH_3), 6.57 (s, 2H, NH_2), 7.24 (d, 2 H, J=8.04 Hz, Ar-H), 7.52-7.68 (m, 5H, Ar-H), 7.70 (s, 1H, =CH), 7.88(d, 2H, J=8.04 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 21.1 (CH_3), 110.8 (C=C), 121.4 (2C's, Ar-C), 123.5(Ar-C), 124.8 (3C's, Ar-C), 127.6 (2C's, Ar-C), 129.9 (2C's, Ar-C), 131.9 (C=C), 132.3 (C=C), 135.4 (Ar-C), 136.2 (Ar-C), 141.7 (C=C), 154.4 (C=N); MS: m/z 334.11 (M+1); Elemental Analysis: $C_{18}H_{15}N_5S$, Calcd.: C:64.84%; H:4.53%; N:21.01%; Found: C:64.61%; H:4.44%; N:20.93%.

5-(4-(4-methoxyphenyl)thiazol-2-yl)-3-phenyl-3H-1,2,3-triazol-4-amine (3f)

M.P.: 168-170 °C**,** Yield: 83**%,** I.R: 3380 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ3.82 (s, 3 H, OCH_3), 6.63(s, 2H, NH_2), 6.98 (d, 2 H, J=8.7 Hz, Ar-H), 7.66-7.72 (m, 5 H, Ar-H), 7.78 (s, 1H, =CH), 7.94(2H, d, J=8.7 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 55.8 (OCH_3), 110.9 (C=C),115.4 (2C's, Ar-C), 124.1 (Ar-C), 126.9, (Ar-C),127.4 (2C's, Ar-C) 128.2 (3C's, Ar-C), 129.1 (2C's, Ar-C), 131.1(C=C), 134.7(C=C), 134.9 (C=C), 142.1 (Ar-C), 160.7 (C=N); MS: m/z 350.10 (M+1); Elemental Analysis: $C_{18}H_{15}N_5OS$**,** Calcd.: C: 61.87%; H: 4.33%, N: 20.4%; Found: C: 61.77%; H:4.28%, N:20.55%.

3-(4-chlorophenyl)-5-(4-phenylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3g)

M.P.: 240-242 °C**,** Yield: 85**%,** I.R: 3385 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 6.62(s, 2H, NH_2, D_2O Exchangeable), 7.33-8.00 (m, 5H, Ar-H), 7.63 (d, 2H, J=8.7 Hz, Ar-H), 7.70 (d, 2H, J=8.7 Hz, Ar-H), 7.75 (s, 1H, =CH),^{13}C NMR (75 MHz, DMSO): 110.8 (C=C), 122.8 (Ar-C), 123.9 (2C's, Ar-C), 127.5 (Ar-C) 128.5 (2C's, Ar-C), 129.3 (2C's, Ar-C), 130.3 (2C's, Ar-C), 131.1 (C=C), 131.4 (Ar-C), 134.3 (Ar-C), 139.2 (C=C), 151.4 (C=C), 160.7 (C=N); MS: m/z 354.05 (M+1); Elemental Analysis: $C_{17}H_{12}ClN_5S$, Calcd.: C:57.71%; H:3.42%; N:19.79%; Found: C:57.55%; H:3.40%; N:19.68%.

3-(4-chlorophenyl)-5-(4-(4-chlorophenyl) thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3h)

M.P.: 280-282 °C**,** Yield: 83**%,** I.R: 3433 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.69(s, 2H, NH_2), 7.67 (d,2H, J=8 Hz, Ar-H), 7.73 (d,2H, J=9 Hz, Ar-H), 7.74 (s, 1H, =CH), 8.07 (d, 2H, J=8 Hz, Ar-H), 8.11 (d, 2H, J=9 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.9 (C=C), 122.9 (Ar-C), 124.2 (2C's, Ar-C), 127.9 (2C's, Ar-C), 129.1 (2C's, Ar-C), 129.5 (Ar-C), 131.3 (2C's, Ar-C), 131.9 (C=C), 132.3 (Ar-C), 134.5 (Ar-C), 139.7 (C=C), 152.0 (C=C), 161.1 (C=N);MS: m/z 389.05 (M+1); Elemental Analysis: $C_{17}H_{11}Cl_2N_5S$, Calcd.: C:52.59%; H:2.86%;N:18.04% ;Found: C:52.44%; H:2.72%;N:17.89%.

5-(4-(4-bromophenyl) thiazol-2-yl)-3-(4-chlorophenyl)-3H-1,2,3-triazol-4-amine (3i)

M.P.: 256-258 °C**,** Yield: 84**%,** I.R: 3423 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.67 (s, 2H, NH_2), 7.64 (d, 2H, J=8.2 Hz, Ar-H), 7.66 (d, 2H, J= 8.2 Hz, Ar-H), 7.71 (s, 1H, =CH), 8.05(d, 2H, J= 9.2 Hz, Ar-H), 8.08 (d, 2H, J=9.2 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.7 (C=C), 122.7 (Ar-C), 123.9 (Ar-C), 127.5 (2C's, Ar-C), 128.9 (2C's, Ar-C), 129.0 (2C's, Ar-C), 130.8 (Ar-C), 131.2 (2C's, Ar-C), 133.1 (C=C), 134.0 (Ar-C), 139.1 (C=C), 151.0 (C=C), 160.9 (C=N); MS: m/z 430.28 (M-1); Elemental Analysis: $C_{17}H_{11}BrClN_5S$, Calcd.:C:47.19%; H:2.56%; N:16.18% ;Found: C:47.25%; H:2.43%; N:16.06%.

3-(4-chlorophenyl)-5-(4-(4-nitrophenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3j)

M.P.:268-270°C,Yield: 88%,I.R: 3389 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 6.57 (s, 2H, NH_2), 7.55 (d, 2H, J= 7.2 Hz, Ar-H), 7.60 (d, 2H, J= 8.2 Hz, Ar-H), 7.71 (s, 1H, =CH), 7.95 (d, 2H, J=7.2 Hz, Ar-H), 8.01 (d, 2H, J=8.2 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.9 (C=C), 123.1 (2C's, Ar-C), 125.6 (Ar-C), 128.4 (2C's, Ar-C), 129.5 (2C's, Ar-C), 130.3 (Ar-C), 131.9 (2C's, Ar-C), 132.2 (C=C), 133.3 (Ar-C), 135.2 (Ar-C), 139.9 (C=C), 152.3 (C=C), 161.7 (C=N); MS: m/z 399.04 (M+1); Elemental Analysis: $C_{17}H_{11}ClN_6O_2S$, Calcd.: C:51.20%; H:2.78%; N:21.07%;Found: C:51.09%; H:2.81%; N:21.17%.

3-(4-chlorophenyl)-5-(4-p-tolylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3k)

M.P.: 230-232 °C**,** Yield: 86%, I.R: 3423 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 2.34 (s, 3H, CH_3), 6.63 (s, 2H, NH_2), 7.24 (d, 2H, J=8 Hz, Ar-H),7.66 (d, 2H, J=9 Hz, Ar-H), 7.69 (d, 2H, J=9 Hz, Ar-H),7.80 (s, 1H, =CH) 7.89 (d, 2H, J=8 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 21.8 (CH_3), 111.5 (C=C), 121.2 (Ar-C), 123.4 (2C's, Ar-C), 124.4 (2C's, Ar-C), 127.2 (2C's, Ar-C), 127.1 (Ar-C), 130.3 (2C's, Ar-C), 132

(C=C), 133.3 (Ar-C), 135.4 (Ar-C), 138.2 (C=C), 142.7 (C=C), 156.7 (C=N); MS: m/z 369.06 (M+1); Elemental Analysis: $C_{18}H_{14}ClN_5S$, Calcd.: C:58.77%;H:3.84%; N:19.04%; Found: C:58.68%; H:3.72%; N:19.11%.

3-(4-chlorophenyl)-5-(4-(4-methoxyphenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3l)

M.P.: 206-208 °C,Yield: 82**%,** I.R: 3415 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 3.80 (s, 3H, OCH_3), 6.65 (s, 2H, NH_2), 7.29 (d, 2H, J=8 Hz, Ar-H), 7.70 (d, 2H, J=9 Hz, Ar-H), 7.74 (d, 2H, J=9 Hz, Ar-H), 7.83 (s, 1H, =CH), 7.92 (d, 2H, J=8 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 55.4 (OCH_3), 110.6 (C=C),114.8 (2C's, Ar-C), 124.4 (Ar-C), 126.6, (Ar-C), 127.5 (2C's, Ar-C) 129.3 (2C's, Ar-C), 130.3 (2C's, Ar-C), 131.2 (C=C), 134.3 (Ar-C), 134.7(C=C), 142.7 (C=C), 153.7 (Ar-C), 161.7 (C=N); MS: m/z 385.06 (M+1); Elemental Analysis: $C_{18}H_{14}ClN_5OS$, Calcd.:C:56.32%; H:3.68%; N:18.24%; Found: C:56.29%; H:3.55%; N:18.33%.

3-(3-chlorophenyl)-5-(4-phenylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3m)

M.P.: 190-192 °C**,** Yield: 79**%,** I.R: 3433 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.61 (s , 2H, NH_2), 7.30-(d, 1H, J=7.3 Hz , Ar-H.), 7.41 (d, 2H, J=7.4 Hz, Ar-H.), 7.63 (1H, J= 7.5 Hz, Ar-H), 7.64 (d, 1H, d, J=7.5 Hz, Ar-H), 7.75 (d, 1H, J=7.3 Hz, Ar-H), 7.83 (s, 1H, =CH) 7.92 (s ,1H, Ar-H) 7.98 (d,2H, J=7.4 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.9 (C=C), 123.4 (Ar-C), 124.5 (2C's, Ar-C), 128.0 (Ar-C), 128.8 (Ar-C), 129.9 (Ar-C), 129.8 (2C's Ar-C), 130.9 (Ar-C), 131.2 (Ar-C), 132 (C=C), 133.9 (Ar-C), 134.3 (Ar-C), 139.7 (C=C), 152.7 (C=C),161.7 (C=N); MS: m/z 354.05 (M+1); Elemental Analysis: $C_{17}H_{12}$ ClN_5S, Calcd.: C:57.71%; H:3.42%; N:19.79%. Found: 57.51%; H:3.35%; N:19.81%.

3-(3-chlorophenyl)-5-(4-(4-chlorophenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3n)

M.P.:210-212 °C**,** Yield: 87**%,** I.R: 3421 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.75 (s, 2H, NH_2), 7.60 (d, 2H, J= 7.1 Hz, Ar-H), 7.65 (d, 1H, J=7.5 Hz, Ar-H), 7.62 (d, 1H, J=7.5 Hz, Ar-H), 7.72 (d, 1H, J=7.1 Hz, Ar-H), 7.78 (s, 1H, =CH) 7.92 (1H, s, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.8 (C=C), 123.4 (Ar-C), 125.0 (Ar-C), 128.7 (Ar-C), 129.9 (2C's, Ar-C), 130.1 (2C's Ar-C), 129.9 (Ar-C), 130.2 (Ar-C), 131.2 (Ar-C), 132.7 (C=C), 133.1 (Ar-C), 134.7 (Ar-C), 140.2 (C=C), 152.7 (C=C),161.5 (C=N); MS: m/z 389.05 (M+1); Elemental Analysis: $C_{17}H_{11}$ Cl_2N_5S, Calcd.: C:52.59%; H:2.86%;N:18.04%; Found: C:52.44%; H:2.72%; N:17.89%.

5-(4-(4-bromophenyl)thiazol-2-yl)-3-(3-chlorophenyl)-3H-1,2,3-triazol-4-amine (3o)

M.P.: 212-214 °C**,** Yield: 81**%,** I.R: 3421 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 6.77 (s, 2H, NH2), 7.64 (d, 2H, J=10 Hz, Ar-H), 7.79-8.04 (m, 3H, Ar-H.), 7.83 (s, 1H, =CH), 7.92 (s , 1H, Ar-H), 8.07(d, 2H, J=10 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.9 (C=C), 123.1(Ar-C), 124.0 (Ar-C), 128.7 (Ar-C), 129.2 (2C's, Ar-C), 129.7 (2C's Ar-C), 130.1 (Ar-C), 130.7 (Ar-C), 132.1(Ar-C), 132.5 (2C's, Ar-C), 133.4 (C=C), 134.3 (Ar-C), 139.3 (C=C), 152.1 (C=C),162.1 (C=N); MS: m/z 430.28 (M+1); Elemental Analysis: $C_{17}H_{11}$ $BrClN_5S$, Calcd.: C:47.19%; H:2.56%; N:16.18%; Found: C:47.25%; H:2.43%; N:16.06%.

3-(3-chlorophenyl)-5-(4-(4-nitrophenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3p)

M.P.: 178-180 °C**,** Yield: 82**%,** I.R: 3389 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 6.60 (s, 2H, NH_2), 7.50 (d, 2H, J=10 Hz, Ar-H), 7.56-7.69 (m , 3H, Ar-H.), 7.75 (s, 1H, =CH) 7.92 (s , 1H, Ar-H), 8.01 (d, 2H, J=10 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 111.2 (C=C), 123.6 (2C's, Ar-C), 124.4 (Ar-C), 128.9 (Ar-C), 129.4 (2C's, Ar-C), 130.5 (Ar-C) ^{13}C NMR (75 MHz, DMSO): 130.9 (Ar-C), 131.2 (Ar-C), 132.4 (C=C), 133.3 (Ar-C), 139.2 (Ar-C), 139.7 (C=C), 142.4 (Ar-C), 152.7 (C=C),162.7 (C=N); MS: m/z 399.04 (M+1); Elemental Analysis: $C_{17}H_{11}ClN_6$ O_2S, Calcd.: C:51.20%; H:2.78%; N:21.07%; Found: C:51.09%; H:2.81%; N:21.17%.

3-(3-chlorophenyl)-5-(4-p-tolylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3q)

M.P.: 194-196 °C**,** Yield: 80**%,** I.R: 3423 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 2.35 (s, 3H, CH_3), 6.69 (s, 2H, NH_2), 6.99(d, 2H, J= 8.8 Hz, Ar-H), 7.59-7.68 (m, 3H, Ar-H), 7.78 (s, 1H, =CH) 7.78 (s, 1H, Ar-H), 7.98 (d, 2H, J= 8.8 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 21.3 (CH_3), 110.9 (C=C), 122.4 (Ar-C), 123.4 (2C's, Ar-C), 124.0 (Ar-C), 127.9 (Ar-C), 127.6 (2C's, Ar-C), 129.9 (Ar-C), 130.0 (Ar-C), 130.2 (Ar-C), 132.1 (C=C), 133.3 (Ar-C), 135.4 (Ar-C), 138.7 (C=C), 141.2 (C=C), 153.5 (C=N); MS: m/z 369.06 (M+1); Elemental Analysis:$C_{18}H_{14}ClN_5S$, Calcd.: C:58.77%; H:3.84%; N:19.04%; Found: C:58.68%;H:3.72%; N:19.11%.

3-(3-chlorophenyl)-5-(4-(4-methoxyphenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3r)

M.P.: 204-206 °C**,** Yield: 78**%,** I.R: 3415 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ3.80 (s, 3H, OCH_3) 6.69 (s, 2H, NH_2), 6.96(d , 2H, J= 8.8 Hz, Ar-H), 7.55-7.64 (m, 3H, Ar-H), 7.73 (s, 1H, =CH) 7.78 (s, 1H, Ar-H), 7.93 (d, 2H, J= 8.8 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 55.5 (OCH_3), 110.5 (C=C), 114.6 (2C's, Ar-C), 124.6 (Ar-C), 126.4 (Ar-C), 126.9 (Ar-C), 128.5 (2C's, Ar-C), 128.9 (Ar-C), 129.9 (Ar-C), 130.2 (Ar-C), 133.9 (C=C), 134.0 (Ar-C), 140.9 (C=C), 152.6 (C=C),157.6 (Ar-C), 161.1 (C=N); MS: m/z 385.06 (M+1); Elemental Analysis: $C_{18}H_{14}ClN_5OS$, Calcd.: C:56.32%; H:3.68%; N:18.24%; Found: C:56.29%; H:3.55%; N:18.33%.

3-(4-bromophenyl)-5-(4-phenylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3s)

M.P.: 240-242 °C**,** Yield: 84**%,** I.R: 3385 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.69 (s, 2H, NH_2), 7.36 (d, 1H, J= 6.9Hz, Ar-H), 7.47(d, 2H, J= 6.9 Hz, Ar-H.), 7.65-8.07 (m, 5H, Ar-H), 8.01(s, 1H, =CH) ^{13}C NMR (75 MHz, DMSO): 110.1 (C=C), 120.1 (Ar-C), 121.2 (Ar-C), 124.5 (2C's, Ar-C), 126.3 (Ar-C), 128.3 (2C's, Ar-C), 130.7 (2C's, Ar-C), 131.1(2C's, Ar-C), 133.8 (C=C), 136.1 (Ar-C), 140.7 (C=C), 150.0 (C=C), 160.0 (C=N); MS: m/z 399.96 (M+1), 397.92 (M-1); Elemental Analysis : $C_{17}H_{12}$ BrN_5S, Calcd.:C:51.27%; H: 3.04%; N:17.58%. Found: C:51.30%; H: 2.95%; N:17.51%.

3-(4-bromophenyl)-5-(4-(4-chlorophenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3t)

M.P.:278-280 °C**,** Yield: 86**%,** I.R: 3423cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.62 (s, 2H, NH_2), 7.44 (d, 2H, J= 8.5 Hz, Ar-H), 7.61 (d, 2H, J= 8.6 Hz, Ar-H.),7.79 (d, 2H, J= 8.6 Hz, Ar-H),7.89 (s ,1H,=CH), 8.03 (d, 2H, J=8.5 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.2 (C=C), 120.2 (Ar-C), 121.5 (Ar-C), 125.9 (2C's, Ar-C), 127.4 (2C's, Ar-C), 129.2 (Ar-C), 131.7 (2C's, Ar-C), 131.1 (2C's, Ar-C), 134.0 (C=C), 137.3 (Ar-C), 141.7 (C=C), 150.3 (C=C), 160.3 (C=N); MS: m/z 430.28 (M-1); Elemental Analysis : $C_{17}H_{11}$ $BrClN_5S$, Calcd.: C:47.19%; H:2.56%; N:16.18%; Found: C:47.07%; H:2.41%; N:16.22%.

3-(4-bromophenyl)-5-(4-(4-bromophenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3u)

M.P.: 234-236 °C**,** Yield: 90**%,** I.R: 3420 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 6.59 (s, 2H, NH_2), 7.41 (d, 2H, J= 8.5 Hz, Ar-H), 7.58 (d, 2H, J= 8.6 Hz, Ar-H), 7.75 (d, 2H, J= 8.6 Hz, Ar-H), 7.86 (s, 1H, =CH), 7.95 (d, 2H, J=8.5 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.6 (C=C), 121.8 (Ar-C), 122.4 (Ar-C), 126.7 (Ar-C), 128.0 (2C's, Ar-C), 130.1 (2C's, Ar-C), 130.7 (Ar-C), 132.4 (2C's, Ar-C), 132.6 (2C's, Ar-C), 134.5 (C=C), 139.7 (C=C), 152.9 (C=C), 160.9 (C=N); MS: m/z 476.91 (M-1), 474.91(M-2); Elemental Analysis: $C_{17}H_{11}$ Br_2N_5S, Calcd.: C:42.79%; H:2.32%; N:14.68%; Found: C:42.71%; H:2.54%; N:14.35%.

3-(4-bromophenyl)-5-(4-(4-nitrophenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3v)

M.P.: 212-214 °C**,** Yield: 89**%,** I.R: 3428 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 6.72 (s, 2H, NH_2), 7.54 (d, 2H, J= 8.5 Hz, Ar-H), 7.71 (d,2H, J= 8.6 Hz, Ar-H), 7.89 (d, 2H, J= 8.6 Hz, Ar-H), 7.99 (s, 1H, =CH), 8.13 (d, 2H, J=8.5 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 110.5 (C=C), 121.6 (2C's, Ar-C), 122.1 (Ar-C), 126.2 (Ar-C), 127.5 (2C's, Ar-C), 129.7 (2C's, Ar-C), 130.1 (2C's, Ar-C), 132.0 (C=C), 135.2 (Ar-C), 138.7 (C=C), 144.4 (Ar-C), 152.7 (C=C), 160.7 (C=N); MS: m/z 442.99 (M-1); Elemental Analysis: $C_{17}H_{11}$ BrN_6 O_2S, Calcd.: C:46.06%; H:2.50%; N:18.96%; Found: C:46.01%; H:2.38%; N:18.73%.

3-(4-bromophenyl)-5-(4-p-tolylthiazol-2-yl)-3H-1,2,3-triazol-4-amine (3w)

M.P.: 246-248°**C,**Yield: 88**%,** IR: 3425 cm^{-1},^{1}H NMR (400 MHz, DMSO): δ 2.33(s, 3H, CH_3), 6.57 (s, 2H, NH_2), 7.20 (d, 2H, J=8 Hz, Ar-H),7.59 (d, 2H, J=8.6 Hz,Ar-H), 7.60 (s, 1H, =CH), 7.74 (d, 2H, J=8.6 Hz, Ar-H), 7.82 (d, 2H, J=8 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 20.9 (CH_3), 110.2 (C=C), 120.1 (Ar-C), 122.2 (2C's, Ar-C), 123.6 (Ar-C), 126.1 (2C's, Ar-C), 126.4 (Ar-C), 129.4 (2C's, Ar-C), 131.2 (C=C), 132.8 (2C's, Ar-C), 134.1 (Ar-C), 137.5 (C=C), 140.8 (C=C), 154.3 (C=N); MS: m/z 413.01 (M+1); Elemental Analysis: $C_{18}H_{14}$ BrN_5S, Calcd.: C:52.43%; H:3.42%; N:16.99%; Found: C:52.33%; H:3.38%; N:17.08%.

3-(4-bromophenyl)-5-(4-(4-methoxyphenyl)thiazol-2-yl)-3H-1,2,3-triazol-4-amine (3x)

M.P.: 182-184 °C**,** Yield: 87**%,** IR: 3425 cm^{-1}, ^{1}H NMR (400 MHz, DMSO): δ 2.33(s, 3H, OCH_3), 6.52 (s, 2H, NH_2), 7.15 (d, 2H, J=8 Hz, Ar-H), 7.53 (d, 2H, J=8.6 Hz, Ar-H),7.58 (s, 1H, =CH), 7.68 (d, 2H, J=8.6 Hz, Ar-H), 7.76 (d, 2H, J=8 Hz, Ar-H); ^{13}C NMR (75 MHz, DMSO): 55.2(OCH_3), 110.3 (C=C), 114.1 (2C's, Ar-C), 123.6 (Ar-C), 126.1 (Ar-C), 126.7 (Ar-C), 127.5 (2C's, Ar-C), 128.1

(2C's, Ar-C), 129.8 (2C's, Ar-C), 130.4 (C=C), 133.7 (C=C), 140.8 (C=C),152.6 (Ar-C), 160.1 (C=N); MS: m/z 429.01 (M+1); Elemental Analysis: $C_{18}H_{14}BrN_5OS$, Calcd.: C:50.48%; H:3.29%; N:16.35%;Found: C:50.36%; H:3.32%; N:16.28%.

Results and Discussion

Chemistry

The synthetic route of the compounds is outlined in Scheme 1. In the present work, compounds 5-amino 4-cyno [1,2,3] triazoles (**1a-d**) were prepared by following literature method.[45] The reaction of 5-amino 4-cyno [1,2,3] triazoles (**1a-d**) with hydrogen sulfide in pyridine and catalytic amount of triethyl amine gave corresponding thioamides (**2a-d**). Latter these thioamides (2**a-d**) were subjected to Hantzsch reaction using substituted phenacyl bromide to deliver the desired 5-(4-(4-substituted phenyl)thiazol-2-yl)-3-(substituted phenyl)-3H-[1,2,3]-triazol-4-amine (**3a-x**)[46,47] as shown in Scheme 1. Analytical and spectral data (IR, ^{1}H NMR, ^{13}C NMR and EIMS) confirmed the structure of the new compounds.

The behaviour of thiocarbamoyl functional group in thioamide towards phenacyl bromide was investigated. In the literature[48] there are three sets of experimental conditions used to the reaction of thiocarbamide with phenacyl bromide using pyridine as catalyst. In the literature[49], it was reported that thiocarbamide reacted with phenacyl bromide in absolute ethanol in the presence of fused sodium acetate at room temperature. Treatment of the thiocarbamide (**2a-d**) with phenacyl bromide in anhydrous ethanol under 70 °C for 30 min gave the corresponding compounds (**3a-x**) in good yields without using catalyst (Scheme 1).

Spectroscopic analysis

The structure of intermediate (**1a-d**) was substantiated by IR spectroscopy. IR spectra of compounds (**1a-d**) revealed in each case, absorption band in the region 3395-3215 cm^{-1} and 2240 cm^{-1} corresponding to NH_2 and CN stretching frequencies, respectively. IR spectra of the compounds (**2a-d**) shows absorption band in the region 3395-3327 cm^{-1} for N-H (amine) stretching frequency, 3168-3238 cm^{-1} for N-H (thioamide) stretching frequency, and CN stretching frequency of (**1a-d**) disappeared and new stretching frequency of C=S of thioamide was appeared at 1276-1275 cm^{-1}. ^{1}H NMR spectra of the compounds (**2a-d**) showed broad singlet at 7.35-7.42 ppm due to protons of amine (-NH_2) group and broad singlet at 9.06-9.11 ppm due to protons of thiomide (-NH_2) group confirmed the structures of (**2a-d**).

The structure of the titled compounds (**3a-x)** was also confirmed by IR, NMR, MS and elemental analysis. The ^{1}H NMR spectra of these compounds exhibited broad singlet between 6.77-6.52 ppm due to -NH_2 protons confirmed by D_2O exchange experiment of representative compound **3g**, a multiplet at 6.96 to 7.87 for the aromatic and thiazole protons. The respective MS spectra, showed the molecular ion peaks of all title compounds. The presence of M + 2 peaks was the characteristic for the compound with chlorine and bromine substitution.

Antimicrobial assay

The antimicrobial activity of the synthesized compounds was evaluated by the agar cup plate method. The antibacterial and antifungal assays were performed in Muller Hinton broth and Czapek Dox broth, respectively. Evaluation was performed using the bacteria reseeded in broth for 24 h at 37 °C and the fungi were reseeded in broth for 48 h at 25 °C. The antibacterial activity of tested samples was studied against one Gram positive bacteria *Staphylococcus aureus* ATCC 25923, one Gram negative bacteria *Escherichia coli* ATCC 25922 while *Candida albicans* MTCC 277, *Aspergillus niger* MCIM was used as standard fungal strain. The compounds were diluted in DMSO with required concentration for bioassay. DMSO was also loaded as control. Streptomycin and griseofulvin were used as standards to evaluate the potency of the tested compounds under the same conditions. The zone of inhibition was determined from the diameter of the zone of inhibition using caliper. Each inhibition zone was measured three times to get average value. The minimum inhibitory concentration (MIC) values were determined on MH agar plates by pouring the molted agar in Petri dishes according to National Committee for Clinical Laboratory Standards (NCCLS, M7-A5 January 2000), containing the following concentrations (mg/mL): 0 (control), 2.5, 5, 10, 20, 40, 80. The MIC was defined as the lowest concentration of tested samples showing no visible bacterial growth after 24 h incubation period at 37 °C. Antimicrobial screening results of synthesized compounds **3a-x** are tabulated in Table 1 and 2.

Table 1 — Antimicrobial screening of synthesized compounds 3a-x (zone diameter of growth inhibition in mm)

Entry	*Escherichia coli* ATCC 25922	*Staph. Aureus* ATTC 25923	*Candida albicans* MTCC 277	*Aspergillus niger* MCIM 545
3a	16.8	16.3	21.4	19.2
3b	15.6	19.6	16.1	15.7
3c	14.4	16.5	15.6	16.1
3d	14.5	22.4	17.3	18.8
3e	13.9	25.4	19.8	20.3
3f	16.8	14.6	28.3	24.2
3g	12.6	15.5	14.8	15.2
3h	16.6	15.8	18.3	19.1
3i	12.5	14.7	12.2	12.6
3j	17.7	14.9	16.6	18.9
3k	19.2	15.6	20.4	21.1
3l	14.8	21.4	17.6	18.1
3m	17.7	18.6	17.7	18.5
3n	19.4	15.7	13.8	12.7
3o	17.9	16.7	20.6	19.8
3p	17.6	18.4	24.6	21.4
3q	17.4	15.9	22.8	24.2
3r	16.8	23.7	20.8	19.5
3s	19.4	15.2	12.8	12.5
3t	14.7	21.2	11.9	12.2
3u	12.1	13.6	11.1	11.6
3v	15.6	13.3	14.8	16.7
3w	18.6	13.8	16.1	18.8
3x	12.6	19.3	15.8	16.7
Strept.	18.4	19.8	n.t.	n.t.
Gris.	n.t.	n.t.	21.5	20.6

n.t. not tested, Strept.: Streptomycine (100 µg/disc), Gris.: Griseofulvin (100 µg /disc).
Test Compound: (80 µg /disc).

Table 2 — Antimicrobial screening of synthesized compounds 3a-x and MIC in µg/mL

Entry	*Escherichia coli* ATCC 25922	*Staph. Aureus* ATTC 25923	*Candida albicans* MTCC 277	*Aspergillus niger* MCIM 545
3a	10	10	5	5
3b	10	10	10	10
3c	10	10	10	10
3d	10	05	10	10
3e	20	05	05	05
3f	10	20	05	05
3g	20	10	20	20
3h	10	10	10	10
3i	40	20	80	40
3j	05	20	10	10
3k	05	10	10	05
3l	10	10	10	10
3m	10	10	10	10
3n	05	20	40	80
3o	10	20	05	10
3p	10	05	05	05
3q	10	10	05	05
3r	10	10	10	10
3s	05	20	40	80
3t	10	05	80	80
3u	10	10	10	10
3v	10	10	10	10
3w	10	20	10	10
3x	10	10	10	10
Strept.	05	05	n.t.	n.t.
Gris.	n.t.	n.t.	05	05

n.t. not tested. Strept.: Streptomycine (µg/mL). Gris.: Griseofulvin (µg/mL). Test compound: (µµ/mL).

Out of **3a-x**, the compounds **3k, 3n, 3s** and **3w** shows excellent zone of inhibition against *E. coli* and compound **3b, 3d-e, 3j-m**, **3r, 3s, 3t** and **3x** excellent zone of inhibition against *S.aurius* as compared to standard antibacterial agent Streptomycin. Compounds **3a, 3f, 3k, 3o-r** show excellent antifungal activity against *C. albicans* and compounds **3e-f, 3k** and **3o-r** shows excellent antifungal activity against *A.niger*.

MICs were observed against *E. coli* for each of the compounds **3a-d, 3f, 3h, 3l-m, 3o-r, 3t-x** required 10 µg/mL and for **3j-n, 3n** and **3s** required 05 µg/mL which are very excellent. Against *S.aureus* good activity were observed with MIC of 10 µg/mL for each of the **3a-c, 3g-h, 3k-m, 3q-r, 3u-v** and **3x**. Excellent activity was observed with MIC of 05 µg/mL for **3d-e, 3p** and **3t**. In case of *C. albicans* compounds, **3b-d, 3h, 3j-m, 3r** and **3u-x** exhibited good activity which required 10 µg/mL and compound **3a, 3e-f** and **3o-q** required 5 mg/mL which are excellent. About *A. niger* the compound **3b-d, 3h, 3j, 3l-m, 3o, 3r** and **3u-x** shows MIC of 10 µg/mL and **3a, 3e-f, 3k, 3p-q** shows MIC of 05 µg/mL. The comparative study of all these synthesized compounds indicates that the compounds show very excellent antifungal activity.

From the data, it is clear that antimicrobial activity of the compounds is influenced by changing the substituent on the aromatic ring. Either highly electron withdrawing or highly electron donating group shows excellent activity.

Conclusion

A series of novel molecules **3a-x** were synthesized and their antimicrobial activities were screened

against two pathogenic bacteria *E. coli* and *S. Aureus* and two pathogenic fungi *C. albicans* and *A.niger*. Most of the synthesized compounds exhibited good to excellent activity towards Gram positive and Gram-negative bacteria as well as both the fungi species. The present study therefore would be very useful to get lead antimicrobial agents.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/58776.

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