Research Article

Synthesis and Antimicrobial Evaluation of Some Novel Trisubstituted s-Triazine Derivatives Based on Isatinimino, Sulphonamido, and Azacarbazole

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A study directed towards exploring the temperature-dependent reactivity of the chlorine atoms of 2,4,6-trichloro-s-triazine (TCT) in the nucleophilic displacement reaction, allowed a facile replacement of its chlorine atoms in succession with (i) N-amino methyl substituted isatin-3-hydrazones, (ii) N₁-substituted-4-amino benzene sulphonamides, and (iii) 8-amino-4-oxo-N-benzyl-azacarbazole to produce the corresponding 2,4,6-trisubstituted-s-triazine, namely; 2-(N-amino methyl substituted isatin-3-hydrazinyl)-4-(N₁-substituted-4'-amino benzenesulfonamidyl)-6-(8'-amino-4'-oxo-N-benzylazacarbazolyl)-1,3,5-triazine derivatives in acceptable yields. The compounds prepared were further evaluated for their antibacterial activity against *E. coli* and *B. subtilis* and antifungal activities against *A. niger* and *A. flavus*, and some of them showed promising activity profile.

1. Introduction

Due to rapid development in drug resistance, tolerance, and side effects, there is a critical need for the development of a new generation of antimicrobial agents that exhibit improved pharmacological properties and drug-resistance profiles. In this aspect substituted s-triazine derivatives have been received central attention due to their significant antimicrobial [1], antibacterial [2], antifungal [3], anti-HIV [4], anticancer [5], and a wide array of other biological activities [6, 7]. Our hypothesis is to incorporate the certain pharmacophoric features and scaffolds on the templates of s-triazine molecule in order to design as a novel antimicrobial agents.

Mannich bases of isatin derivatives have been reported to form an integral part of the bioactive molecules exhibiting wide range of activities such as cytotoxic [8], anticonvulsant [9], antidepressant [10], and anti-inflammatory [11] agents. Sulphonamides have been widely known in the literature to exhibit a broad range of biological activities [12, 13]. The SO₂-NH group of sulphonamide constitutes a key structural motif shared by a large number of bioactive compounds

spanning a variety of effects such as the microbial activities [14], specific enzyme inhibition [15] and hormonal regulation [16].

The ubiquitous presence of azacarbazoles and pyridocarbazoles in a vast array of biologically active molecules (such as ellipticine, olivacine and carbaquinacine [17], to name a few) have stimulated as intense research efforts to the synthesis of their structural analogues where different constitution and biological activity of new materials could allow them to be used as novel chemotherapeutic agents.

Greatly encouraged by the biological profiles of these heterocyclic scaffolds, we aimed in the present work to synthesize 2,4,6-trisubstituted-s-triazine molecules incorporating in them the structural features of (i) N-Mannich's bases of isatin-3-hydrazones, 2(a-f), (ii) established sulpha drugs, 4(a,b), (iii) N-benzyl-4-oxo azacarbazole derivatives (6), on the premise that their presence in tandem in a single molecular framework in 7(a-l) should contribute significantly to the biological activity in the resulting molecules and should allow them to be used as novel chemotherapeutic agents.

2. Experimental Section

2.1. General Remarks. Melting points were determined in open glass capillaries and are uncorrected. The reactions were monitored by the TLC on silica gel "G" plates and were visualized with UV light and by exposing to iodine. The purity of the compounds was checked by spectral data, namely, IR, NMR, mass and elemental analysis. IR spectra were recorded on CE (SIMADZU) FTIR-8400S. ¹H-NMR spectra were recorded on model Avance 300 (Bruker 300 MHz) using DMSO-*d*₆ as solvent and TMS as an internal reference.

3. Chemical Synthesis

3.1. General Methods for the Preparation of 3(a-f), 5(a-l), 7(a-l)

3.1.1. Preparation of 3-(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazono)-1-(morpholinomethyl)indolin-2-one (3a). Cyanuric chloride (**1**) (0.5 g, 0.002 moles) was taken in dry THF containing K₂CO₃ (0.1 g). 1-(morpholinomethyl)indolin-2-one-3-hydrazone (**2a**) (0.7 g, 0.002 moles) was added to it. Reaction was kept on stirring at 0–5°C for 2–3 hr. Reaction mixture was poured in crushed ice and neutralized with dil. HCl. The resulting solid was filtered, washed with dil. Ethanol. The resultant solid was dried and recrystallized from ethanol: water (1:9) mixture to give **3a**, 0.48 g (yield 68.8%) m.p. 180–181°C. Anal. Calcd. C, 47.07; H, 3.70; N, 24.02; Cl, 17.37 (C₁₆H₁₅Cl₂N₇O₂). Found: C 47.01; H, 3.75; N, 23.98; Cl, 17.31 IR (KBr) cm⁻¹ 3400 (NH), 3100 (arom. Str.), 1711 (C=O), ¹H-NMR (DMSO-*d*₆)—δ, 10.7 (1H, s, NH), 7.77–6.81 (4H, m, Ar-H), 4.03 (2H, s, CH₂), 3.65 (4H, t, CH₂, J = 1.1 Hz), 2.47 (4H, t, CH₂, J = 1.8 Hz).

Compound **3(b-f)** was prepared by a similar method using appropriate reactants with required change in stirring time.

3-(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazono)-1-(piperidin-1-ylmethyl)indolin-2-one (3b). Yield 70%; m.p. 205–206°C; Anal. Calcd. C 50.26; H, 4.22; N, 24.13; Cl, 17.45 (C₁₇H₁₇Cl₂N₇O). Found: C 50.20; H, 4.02; N, 24.01; Cl, 17.41; IR (KBr) cm⁻¹ 3390(NH), 3100 (arom. Str.), 1675 (C=O), 1602 (C=N str.), 1425 (C=C aromatic str.), ¹H-NMR (DMSO-*d*₆)—δ, 10.5 (1H, s, NH), 7.86–6.78 (4H, m, Ar-H), 4.05 (2H, s, CH₂), 2.45 (4H, d, CH₂, J = 1.8 Hz), 1.59 (2H, m, CH₂), 1.53 (4H, m, CH₂).

3-(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazono)-1-(pyrrolidin-1-ylmethyl)indolin-2-one (3c). Yield 69%; m.p. 220–221°C; Anal. Calcd. C, 48.99; H, 3.85; N, 25.00; Cl, 18.08 (C₁₆H₁₅Cl₂N₇O). Found: C 48.91; H, 3.81; N, 24.87; Cl, 18.02 IR (KBr) cm⁻¹ 3410 (NH), 1710 (C=O), 3200 (aromatic Str.), 1610 (C=N), 1425 (C=C), ¹H-NMR (DMSO-*d*₆)—δ, 10.2 (1H, s, NH), 7.67–6.52 (4H, m, Ar-H), 4.03 (2H, s, CH₂), 2.51 (4H, t, CH₂, J = 2.2 Hz), 1.68 (4H, m, CH₂).

3-(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazono)-1-((4-methylpiperazin-1-yl)methyl)indolin-2-one (3d). Yield 69%; m.p.

225–226°C; Anal. Calcd. C, 48.47; H, 4.31; N, 26.60; Cl, 16.83 (C₁₇H₁₈Cl₂N₈O). Found: C 48.41; H, 4.25; N, 26.50; Cl, 16.72; IR (KBr) cm⁻¹ 3386 (NH), 3050 (aromatic Str.), 1700 (C=O), 1602 (C=N), 1420 (C=C aromatic Str.), ¹H-NMR (DMSO-*d*₆)—δ 10.8 (1H, s, NH), 7.86–6.45 (4H, m, Ar-H), 4.03 (2H, s, CH₂), 2.35 (8H, t, CH₂, J = 2.1 Hz), 2.26 (3H, s, CH₃).

3-(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazono)-1-((4-ethylpiperazin-1-yl)methyl)indolin-2-one (3e). Yield 71%; m.p. 232–233°C; Anal. Calcd. C, 49.66; H, 4.63; N, 25.74; Cl, 16.29 (C₁₈H₂₀Cl₂N₈O). Found: C 49.50; H, 4.55; N, 25.65; Cl, 16.10; IR (KBr) cm⁻¹ 3390 (NH), 3050 (aromatic str.), 1715 (C=O), 1602 (C=N), 1425(C=C str.), ¹H-NMR (DMSO-*d*₆)—δ 10.7 (1H, s, NH), 7.86–6.91 (4H, m, Ar-H), 4.03 (2H, s, CH₂), 2.35 (8H, t, CH₂, J = 2.4 Hz), 2.38 (2H, m, CH₂), 1.02 (3H, t, CH₃, J = 1.2 Hz).

3-(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazono)-1-((4-phenylpiperazin-1-yl)methyl)indolin-2-one (3f). Yield 72%; m.p. 228–229°C; Anal. Calcd. C, 54.67; H, 4.17; N, 23.18; Cl, 14.67 (C₂₂H₂₀Cl₂N₈O). Found: C 54.55; H, 4.07; N, 23.10; Cl, 14.52; IR (KBr) cm⁻¹ 3245 (NH), 3010 (aromatic Str.), 1720 (C=O), 1602 (C=N str.), 1425 (C=C str.), ¹H-NMR (DMSO-*d*₆)—10.8 (1H, s, NH), 7.86–6.79 (9H, m, Ar-H), 4.03 (2H, s, CH₂), 3.44 (4H, t, CH₂, J = 5.6 Hz), 2.48 (4H, t, CH₂, J = 1.6 Hz).

3.1.2. Preparation of 4-(4-chloro-6-(2-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide 5(a). Compound **3a** (0.3 g, 0.00073 moles) was taken in dry THF and K₂CO₃ (0.1 g). Sulphathiazole **4a** (0.187 g, 0.00073 moles) was added to this. Reaction mixture was kept on stirring at 30–35°C for 2–3 hr and was then poured in to crushed ice and neutralized with dil. HCl. The resulting solid was filtered, washed with dil. Ethanol. The resultant solid was dried and recrystallized from ethanol: water (1:9) mixture to give **5a**, 0.182 g (yield 58.8%) m.p. 200–201°C. Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3300 (NH), 3011 (aromatic Str.), 1695 (C=O), 1602 (C=N str.), 1425 (C=C str.), 1360, 1162 (S=O), ¹H-NMR (DMSO-*d*₆)—12.64 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 7.61–7.18 (9H, m, Ar-H), 3.87 (1H, t, CH, J = 0.9 Hz), 3.65 (4H, q, CH₂), 3.11 (2H, s, CH₂), 2.67 (4H, q, CH₂).

Compound **5(b-l)** were prepared by a similar method using appropriate reactants with required change in temperature and stirring time.

4-(4-chloro-6-(2-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide (5b). Yield 67%; m.p. 221–222°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3337 (NH), 3015 (aromatic str.), 1710 (C=O), 1587 (C=N), 1450 (C=C str.), 1311, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—11.22(1H, s, NH), 10.79(1H, s, NH), 9.44(1H,

s, NH), 7.35–6.93(10H, m, Ar-H), 3.65(4H, t, CH₂, J = 1.3 Hz), 2.67(4H, q, CH), 2.33(3H, s, CH₃).

4-(4-chloro-6-(2-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**5c**). Yield 68%; m.p. 299–300°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3180(NH), 3020(aromatic Str.), 1712 (C=O), 1590 (C=N), 1480 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—12.64 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 7.86–6.75(10H, m, Ar-H), 4.03 (2H, s, CH₂), 2.45 (4H, t, CH₂, J = 0.9 Hz), 1.59 (2H, q, CH₂), 1.53 (4H, m, CH₂).

4-(4-chloro-6-(2-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide (**5d**). Yield 69%; m.p. 291–292°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3180 (NH), 3025 (aromatic str.), 1712 (C=O), 1595 (C=N), 1490 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—11.27 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 8.11 (1H, s, Ar-H), 7.86–7.24 (9H, m, Ar-H), 4.03 (2H, s, CH₂), 2.45 (4H, t, CH₂, J = 0.78 Hz), 2.33 (3H, s, CH₃), 1.59 (2H, q, CH₂), 1.53 (4H, m, CH₂).

4-(4-chloro-6-(2-(2-oxo-1-(pyrrolidin-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**5e**). Yield 70%; m.p. 240–241°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3180 (NH), 3125 (aromatic str.), 1712 (C=O), 1480 (C=N str.), 1505 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—12.64(1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 7.86–6.75 (10H, m, Ar-H), 4.03 (2H, s, CH₂), 2.51 (4H, t, CH₂, J = 5.6 Hz), 1.68 (4H, m, CH₂).

4-(4-chloro-6-(2-(2-oxo-1-(pyrrolidin-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide (**5f**). Yield 65%; m.p. 250–251°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3225 (NH), 3120 (aromatic str.), 1715 (C=O), 1485 (C=N str.), 1510 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—11.27 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 8.11 (1H, s, Ar-H), 7.86–7.24 (9H, m, Ar-H), 4.03 (2H, s, CH₂), 2.51 (4H, t, CH₂, J = 0.9 Hz), 2.33 (3H, s, CH₃), 1.68 (4H, m, CH₂).

4-(4-chloro-6-(2-(1-((4-methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**5g**). Yield 65%; m.p. 233–234°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3195 (NH), 3230 (aromatic str.), 1712 (C=O), 1490 (C=N str.), 1525 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—10.67 (1H, s, NH), 10.04 (1H, s,

NH), 9.44 (1H, s, NH), 7.86–6.38 (10H, m, Ar-H), 4.03(2H, s, CH₂), 2.35(8H, t, CH₂, J = 0.88 Hz), 2.26 (3H, s, CH₃).

4-(4-chloro-6-(2-(1-((4-methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide (**5h**). Yield 62%; m.p. 245–246°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3210 (NH), 3235 (aromatic str.), 1712 (C=O), 1500 (C=N str.), 1520 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—11.27 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 8.11 (1H, s, Ar-H), 7.86–7.24 (9H, m, Ar-H), 4.03 (2H, s, CH₂), 2.35 (8H, t, CH₂, J = 0.85 Hz), 2.33 (3H, s, CH₃), 2.26 (3H, s, CH₃).

4-(4-chloro-6-(2-(1-((4-ethylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**5i**). Yield 65%; m.p. 234–235°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3210 (NH), 3235 (aromatic str.), 1712 (C=O), 1500 (C=N str.), 1520 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—12.64 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 7.86–6.75 (10H, m, Ar-H), 4.03 (2H, s, CH₂), 2.38 (2H, q, CH₂), 2.35 (8H, t, CH₂, J = 2.1 Hz), 1.02 (3H, t, CH₃, J = 2.09 Hz).

4-(4-chloro-6-(2-(1-((4-ethylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide (**5j**). Yield 71%; m.p. 255–256°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3115 (NH), 3225 (aromatic str.), 1712 (C=O), 1510 (C=N str.), 1525(C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—11.27 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 8.11 (1H, s, Ar-H), 7.86–7.24 (9H, m, Ar-H), 4.03 (2H, s, CH₂), 2.38 (2H, q, CH₂), 2.35 (8H, t, CH₂, J = 2.3 Hz), 2.33 (3H, s, CH₃), 1.02 (3H, t, CH₃, J = 2.4 Hz).

4-(4-chloro-6-(2-(2-oxo-1-((4-phenylpiperazin-1-yl)methyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**5k**). Yield 65%; m.p. 245–246°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3150 (NH), 3225 (aromatic str.), 1712 (C=O), 1540 (C=N str.), 1560 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—12.64 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 7.86–6.75 (14H, m, Ar-H), 4.03 (2H, s, CH₂), 3.44 (4H, t, CH₂, J=1.2 Hz), 2.48 (4H, t, CH₂, J = 0.8 Hz).

4-(4-chloro-6-(2-(2-oxo-1-((4-phenylpiperazin-1-yl)methyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide (**5l**). Yield 60%; m.p. 234–235°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3180 (NH), 3235 (aromatic str.), 1712

(C=O), 1545 (C=N str.), 1565 (C=C str.), 1357, 1134 (S=O), ¹H-NMR (DMSO-*d*₆)—11.27 (1H, s, NH), 10.67 (1H, s, NH), 9.44 (1H, s, NH), 8.11 (1H, s, Ar-H), 7.86–6.79 (14H, m, Ar-H), 4.03 (2H, s, CH₂, J = 1.1 Hz), 3.44 (4H, t, CH₂, J = 0.9 Hz), 2.48 (4H, t, CH₂, J = 0.92 Hz), 2.33 (3H, s, CH₃).

3.1.3. Preparation of *N*-benzyl-8-amino-azacarbazole-4-one (6). A solution of *p*-aminoacetanilide (0.76 g, 0.050 mol) in aqueous HCl (2 mL conc. HCl in 5 mL water) was treated with a cold saturated solution of sodium nitrite (0.7 gm in 5 mL water). The solution was kept aside for 10 min. It was then added in portion wise to an ice cooled mixture containing 1-benzyl-3-(hydroxymethylidene)-piperidin-4-one (**9**) (1.26 g, 0.05 mole), sodium acetate trihydrate (1.78 g), methanol (10 mL), and water (20 mL) over a period of 30 minutes with stirring. The contents were allowed to stand for further 30 minutes and the resulting solid was filtered, washed with water, dried, and recrystallised from ethanol. The solid was refluxed with acetic acid (5 mL) and HCl (1 mL) to get the cyclized product (**10**). The contents were then cooled and poured into cold water with stirring. The separated brown solid was purified by Silica column chromatography (benzene/pet ether, 50/50) to yield cyclized intermediate. The cyclized intermediate was hydrolysed by heating it in aq. HCl (5 mL) for 30 min to yield **6**. M.P. 305°C.

3.1.4. Preparation of 4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-*b*] indol-7-ylamino)-6-(2-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-*N*-(thiazol-2-yl)benzenesulfonamide **7(a).** Compound **5a** (0.1 g, 0.00015 moles) was taken in dry THF and K₂CO₃ (0.1 g). *N*-benzyl-8-amino-azacarbazole-4-one (**6**) (0.046 g, 0.00015 moles) was added to this. Reaction mixture was refluxed at 60–65°C for 6 hrs and was then poured in to crushed ice and neutralized with dil. HCl. The resulting solid was filtered, washed with dil. Ethanol. The resultant solid was dried and recrystallized from ethanol: water (1 : 9) mixture to give **7a**, 0.05 g (yield 48.8%) m.p. 249–250°C. Anal. Calcd. C, 58.56; H, 4.46; N, 20.65; S, 7.27 (C₄₃H₃₉N₁₃O₅S₂). Found: C, 58.50; H, 4.33; N, 20.55; S, 7.21; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3050 (aromatic str.), 1710 (C=O), 1602 (C=N str.), ¹H-NMR (DMSO-*d*₆)—δ, 12.04 (1H, s, NH), 11.62 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 7.81–6.38 (16H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.65 (4H, t, CH₂, J = 5.1 Hz), 3.39 (2H, t, CH₂, J = 3.6 Hz), 2.63 (2H, t, CH₂, J = 5.2 Hz), 2.50 (4H, t, CH₂, J = 4.6 Hz).

Compound **7(b–l)** were prepared by a similar method using appropriate reactants.

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-*b*] indol-7-ylamino)-6-(2-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-*N*-(6-methylpyrazin-2-yl) benzenesulfonamide (7b**).** Yield 56%; m.p. 320°C; Anal. Calcd. C, 60.66; H, 4.75; N, 22.01; S, 3.60 (C₄₅H₄₂N₁₄O₅S). Found: C, 60.40; H, 4.65; N, 21.97; S, 3.56; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3050 (aromatic str.), 1650 (C=O), 1612 (C=N str.), ¹H-NMR (DMSO-*d*₆)—δ,

11.63 (1H, s, NH), 10.64 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 8.6–6.38 (18H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.65 (4H, t, CH₂, J = 6.6 Hz), 3.39 (2H, t, CH₂, J = 5.9 Hz), 2.63 (2H, t, CH₂, J = 2.2 Hz), 2.50 (4H, t, CH₂, J = 3.6 Hz), 2.33 (3H, s, CH₃).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-*b*] indol-7-ylamino)-6-(2-(2-oxo-1-(piperidine-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (7c**).** Yield 62%; m.p. 315°C; Anal. Calcd. C, 60.05; H, 4.70; N, 20.69; S, 7.29 (C₄₄H₄₁N₁₃O₄S₂). Found: C, 60.50; H, 4.20; N, 20.47; S, 7.22; IR (KBr) cm⁻¹ 3100 (NH symm. str.), 3050 (aromatic str.), 1610 (C=O), 1610 (C=N str.), ¹H-NMR (DMSO-*d*₆)—δ, 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 7.86–6.38 (17H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 3.6 Hz), 2.63 (2H, t, CH₂, J = 2.6 Hz), 2.50 (4H, t, CH₂, J = 5.2 Hz), 1.59 (2H, m, CH₂), 1.53 (4H, m, CH₂).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-*b*] indol-7-ylamino)-6-(2-(2-oxo-1-(piperidine-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-*N*-(6-methylpyrazin-2-yl)benzenesulfonamide (7d**).** Yield 57%; m.p. 340°C; Anal. Calcd. C, 62.15; H, 4.99; N, 22.06; S, 3.61 (C₄₆H₄₄N₁₄O₄S). Found: C, 62.10; H, 4.45; N, 22.16; S, 3.55; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3050 (aromatic str.), 1700 (C=O), 1600 (C=N str.), ¹H-NMR (DMSO-*d*₆)—δ, 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 8.6–6.30 (18H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 7.2 Hz), 2.63 (2H, t, CH₂, J = 7.7 Hz), 2.50 (4H, t, CH₂, J = 5.1 Hz), 2.33 (3H, s, CH₃), 1.59 (2H, m, CH₂), 1.53 (2H, m, CH₂).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-*b*] indol-9-ylamino)-6-(2-(2-oxo-1-(pyrrolidine-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (7e**).** Yield 60%; m.p. 313°C; Anal. Calcd. C, 59.64; H, 4.84; N, 21.03; S, 7.41 (C₄₃H₃₉N₁₃O₄S₂). Found: C, 59.34; H, 4.34; N, 20.97; S, 7.22; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3050 (aromatic str.), 1680 (C=O), 1622 (C=N str.), ¹H-NMR (DMSO-*d*₆)—δ, 11.63 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 7.86–6.38 (18H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 5.1 Hz), 2.63 (2H, t, CH₂, J = 3.6 Hz), 2.50 (4H, t, CH₂, J = 1.6 Hz), 1.66 (4H, m, CH₂).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-*b*] indol-9-ylamino)-6-(2-(2-oxo-1-(pyrrolidine-1-ylmethyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-*N*-(6-methylpyrazin-2-yl)benzenesulfonamide (7f**).** Yield 63%; m.p. 330°C; Anal. Calcd. C, 61.77; H, 4.73; N, 22.41; S, 7.41 (C₄₅H₄₂N₁₄O₄S). Found: C, 61.52; H, 4.23; N, 22.22; S, 7.22; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3050 (aromatic str.),

FIGURE 1: Antibacterial activity against *B. subtilis*. FIGURE 2: Antibacterial activity against *E. coli*.

1690 (C=O), 1625 (C=N str.), $^1\text{H-NMR}$ (DMSO- d_6)— δ , 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 8.6–6.75 (18H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 3.6 Hz), 2.63 (2H, t, CH₂, J = 2.6 Hz), 2.51 (4H, t, CH₂, J = 2.2 Hz), 2.33 (3H, s, CH₃), 1.66 (4H, m, CH₂).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-b] indol-9-ylamino)-6-(2-(1-((4-methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(6-thiazol-2-yl)benzenesulfonamide (**7g**). Yield 64%; m.p. 318°C; Anal. Calcd. C, 59.05; H, 5.02; N, 21.91; S, 7.17 (C₄₄H₄₂N₁₄O₄S₂). Found: C, 58.45; H, 4.95; N, 22.86; S, 7.07; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3000 (aromatic

str.), 1675 (C=O), 1590 (C=N str.), $^1\text{H-NMR}$ (DMSO- d_6)— δ , 11.63 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 7.86–6.30 (18H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 3.3 Hz), 2.53 (2H, t, CH₂, J = 1.4 Hz), 2.35 (8H, t, CH₂, J = 2.2 Hz), 2.26 (3H, s, CH₃).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-b] indol-9-ylamino)-6-(2-(1-((methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(6-methylpyrazin-2-yl)benzenesulfonamide (**7h**). Yield 58%; m.p. 314°C; Anal. Calcd. C, 61.12; H, 4.88; N, 23.24; S, 3.55 (C₄₆H₄₅N₁₅O₄S). Found: C, 61.52; H, 4.77; N, 23.04; S, 3.51; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3005 (aromatic str.), 1710 (C=O), 1600 (C=N str.), $^1\text{H-NMR}$ (DMSO- d_6)— δ , 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 8.6 (1H, s, Ar-H), 8.4 (1H, s, Ar-H), 7.5–6.2 (17H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 2.2 Hz), 2.63 (2H, t, CH₂, J = 2.6 Hz), 2.35 (8H, t, CH₂, J = 3.6 Hz), 2.33 (3H, s, CH₃), 2.26 (3H, s, CH₃).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-b] indol-9-ylamino)-6-(2-(1-((4-ethylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**7i**). Yield 65%; m.p. 321°C; Anal. Calcd. C, 59.46; H, 5.16; N, 21.57; S, 7.05 (C₄₅H₄₄N₁₄O₄S₂). Found: C, 59.16; H, 5.06; N, 21.37; S, 6.99; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 2990 (aromatic str.), 1670 (C=O), 1595 (C=N str.), $^1\text{H-NMR}$ (DMSO- d_6)— δ , 11.63 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 7.77–6.31 (18H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 4.2 Hz), 2.53 (2H, t, CH₂, J = 3.8 Hz), 2.35 (8H, t, CH₂, J = 2.5 Hz), 2.33 (2H, q, CH₂).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-b] indol-9-ylamino)-6-(2-(1-((4-ethylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(6-methylpyrazin-2-yl)benzenesulfonamide (**7j**). Yield 64%; m.p. 320°C; Anal. Calcd. C, 61.49; H, 4.63; N, 22.89; S, 3.49 (C₄₅H₄₄N₁₄O₄S₂). Found: C, 61.19; H, 4.13; N, 22.84; S, 3.43; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3005 (aromatic str.), 1690 (C=O), 1692 (C=N str.), $^1\text{H-NMR}$ (DMSO- d_6)— δ , 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 8.6–6.38 (17H, s, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.39 (2H, t, CH₂, J = 2.1 Hz), 2.63 (2H, t, CH₂, J = 3.1 Hz), 2.35 (8H, t, CH₂, J = 3.3 Hz), 2.33 (3H, s, CH₃), 2.30 (2H, q, CH₂), 1.02 (3H, s, CH₃).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-b] indol-9-ylamino)-6-(2-(2-oxo-1-((4-phenylpiperazin-1-yl)methyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(thiazol-2-yl)benzenesulfonamide (**7k**). Yield 64%; m.p. 345°C; Anal. Calcd. C, 61.49; H, 4.54; N, 20.49; S, 6.70 (C₄₉H₄₄N₁₄O₄S₂). Found: C, 61.09; H, 4.34; N, 20.29; S, 7.56; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3000 (aromatic str.), 1690 (C=O), 1595 (C=N str.), $^1\text{H-NMR}$

FIGURE 3: Antifungal activity against *A. niger*. FIGURE 4: Antifungal activity against *A. flavus*.

(DMSO- d_6)— δ , 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 7.86–6.79 (22H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.44 (4H, t, CH₂, J = 1.6 Hz), 3.39 (2H, t, CH₂, J = 1.9 Hz), 2.63 (2H, t, CH₂, J = 1.9 Hz), 2.48 (4H, t, CH₂, J = 2.6 Hz).

4-(4-(1-benzyl-4-oxo-2,3,4,5-tetrahydro-1H-pyrido [3,2-b] indol-9-ylamino)-6-(2-(2-oxo-1-((4-phenylpiperazin-1-yl)methyl)indolin-3-ylidene)hydrazinyl)-1,3,5-triazin-2-ylamino)-N-(6-methylpyrazin-2-yl)benzenesulfonamide (**7l**). Yield 65%; m.p. 335°C; Anal. Calcd. C, 63.41; H, 4.90; N, 21.75; S, 3.32 (C₅₁H₄₇N₁₅O₄S). Found: C 63.01; H, 4.75; N, 21.55; S, 3.02; IR (KBr) cm⁻¹ 3300 (NH symm. str.), 3010 (aromatic str.), 1680 (C=O), 1610 (C=N str.), ¹H-NMR (DMSO- d_6)— δ , 11.53 (1H, s, NH), 10.67 (1H, s, NH), 10.04 (1H, s, NH), 9.44 (1H, s, NH), 8.91 (1H, s, NH), 8.4–6.28 (23H, m, Ar-H), 4.51 (2H, s, CH₂), 4.03 (2H, s, CH₂), 3.44(4H, t, CH₂, J = 7.2 Hz), 3.39 (2H, t, CH₂, J = 2.2 Hz), 2.63 (2H, t, CH₂, J = 5.9 Hz), 2.48 (4H, t, CH₂, J = 6.6 Hz), 2.33 (3H, s, CH₃).

4. Biological Assay

Among all of the synthesized compounds, compounds **7(a–l)** were screened for antimicrobial activity by disc diffusion method [18]. The test compounds **7(a–l)**, in measured quantities, were dissolved in dimethyl formamide (DMF) to get the final concentrations 400 mg/L, 200 mg/L, 100 mg/L respectively. The bacterial (24 h) and fungal (48 h) cultures from the slants were diluted with sterile water and mixed thoroughly to prepare a clear homogeneous suspension. These suspensions were spread on solidified agar (NA—nutrient agar—for bacteria and PDA—potato dextrose agar for fungi)

medium. The filter paper disks [18] prepared by only DMF (as a negative control) and with solutions of different concentrations of test compounds **7(a–l)** as well as standard compounds (ciprofloxacin and fluconazole as positive control) were carefully placed over the spread cultures and incubated at 37°C for 24 hr for bacteria and at 28–30°C for 48 hr for fungi. After the incubation period, the plates were examined for the zone of inhibition. The diameter for the zones of inhibition were measured including the diameter of disk also. All determinations were made in triplicate for each of the compound and the average value was taken. The antibacterial and antifungal activity was evaluated against *E. coli*, *B. subtilis*, *A. niger*, and *A. flavus* against the standard drugs ciprofloxacin for bacteria and fluconazole for fungi. The outcome of this study is presented in Table 1 and in Figures 1–4.

5. Results and Discussion

The synthetic approach which allowed the incorporation of the aforementioned bioactive heterocyclic systems on to the 2, 4, and 6 positions of s-triazine molecule was confined to three series outlined in Schemes 1, 2, and 3. The first series was derived from isatin which afforded its hydrazone from the reaction with hydrazine hydrate. Scheme 1 shows the synthetic strategy applied to obtain **3(a–f)** by replacing one of the chlorine atoms of s-triazine (**1**) with isatinyl-3-hydrazone Mannich's bases **2(a–f)**, by conducting the reaction in Dry THF/K₂CO₃ at 0–5°C for 2–3 hrs. Replacement of chlorine atoms of s-triazine is a temperature dependent nucleophilic substitution reaction [19]. While the second series was derived by the replacement of one of the chlorine atoms of **3(a–f)** with two established sulpha drugs **4(a,b)**, consisting of sulphathiazole and sulphamerazine respectively, to yield of **5(a–l)** by conducting the reaction in THF/K₂CO₃ at 30–35°C for 2–3 hrs.

SCHEME 1: Monosubstitution reaction (i) Dry THF, 0–5°C, K_2CO_3 . **3a**, R = morpholinyl, **3b**, R = piperidinyl, **3c**, R = pyrrolidinyl, **3d**, R = N-methyl piperazinyl, **3e**, R = N-ethyl piperazinyl, **3f**, R = N-phenyl piperazinyl.

SCHEME 2: Disubstitution (ii) dry THF, 30–35°C, K_2CO_3 . **5a**, R = morpholinyl, R' = thiazolyl, **5b**, R = morpholinyl, R' = methyl pyrimidinyl, **5c**, R = piperidinyl, R' = thiazolyl, **5d**, R = piperidinyl, R' = methyl pyrimidinyl, **5e**, R = pyrrolidinyl, R' = thiazolyl, **5f**, R = pyrrolidinyl, R' = methyl pyrimidinyl, **5g**, R = N-methyl piperazinyl, R' = thiazolyl, **5h**, R = N-methyl piperazinyl, R' = methyl pyrimidinyl, **5i**, R = N-ethyl piperazinyl, R' = thiazolyl, **5j**, R = N-ethyl piperazinyl, R' = methyl pyrimidinyl, **5k**, R = N-phenyl piperazinyl, R' = thiazolyl, **5l**, R = N-phenyl piperazinyl, R' = methyl pyrimidinyl.

SCHEME 3: Trisubstitution (iii) dry THF, reflux (60–65°C), K_2CO_3 .

SCHEME 4: Synthesis of N-benzyl-8-amino-azacarbazole-4-one (**4**) (a) Japp-Klingemann-sodium acetate trihydrate, methanol, water (b) Fischer-indolization-acetic acid, HCl (5) hydrolysis, Dil. HCl.

TABLE 1: Antibacterial and antifungal activities of synthesized compounds using disc diffusion method.

S. number	Zone of inhibition (mm)											
	<i>B. subtilis</i>			<i>E. coli</i>			<i>A. niger</i>			<i>A. flavus</i>		
	400 mg/L	200 mg/L	100 mg/L	400 mg/L	200 mg/L	100 mg/L	400 mg/L	200 mg/L	100 mg/L	400 mg/L	200 mg/L	100 mg/L
7a	20	12	7	27	16	12	16	9	3	26	18	13
7b	15	10	6	18	10	8	18	10	4	22	17	10
7c	17	13	8	21.5	11	9	22	16	6	25	15	11
7d	16	9	3	22	12	8	20	12	8	28	20	15
7e	19	10	2	25	15	11	13	9	6	22	14	9
7f	22	16	6	19	13	9	18	6	8	15	10	10
7g	18	10	4	22	17	10	15	10	6	18	10	10
7h	15	8	5	26	18	13	13	9	8	18	10	8
7i	20	12	8	28	20	15	17	13	8	22	12	8
7j	13	9	6	22	14	9	19	10	2	19	13	9
7k	12	8	7	21	15	10	20	12	7	21.5	11	9
7l	18	6	8	20	15	10	12	8	7	27	16	12
Cipro. (Std.)	28	22	16	30	23	17	—	—	—	—	—	—
Fluco. (Std.)	—	—	—	—	—	—	26	20	15	29	23	18

The third series which consisted of the target compounds **7(a–l)**, was derived by replacement of the last chlorine atom of **5(a–l)** with N-benzyl-8-amino-azacarbazole-4-one derivative (**6**). The reaction was carried out in THF/K₂CO₃ medium at 60–65°C for 6 hrs. as shown in Scheme 3.

Compound, N-benzyl-8-amino-azacarbazole-4-one (**6**) required in the preparation of the target compounds, **7(a–l)**, was synthesized from p-acetamido benzene diazonium chloride (**8**) following the strategy shown in Scheme 4. The reaction of **8** when allowed to take place with 3-hydroxy methylidene-N-benzyl-4-piperidone (**9**) under the conditions of Japp-Klingeman [20] reaction afforded the corresponding hydrazone **10**, from which **6** resulted on Fischer indolization with Kent's reagent [AcOH : HCl, 4 : 1, v/v] followed by subsequent hydrolysis with acid.

The antibacterial and antifungal activity was evaluated against *E. coli*, *B. subtilis*, *A. niger*, and *A. flavus* against the standard drugs ciprofloxacin for bacteria and fluconazole for fungi. The zone of inhibition was measured in mm, on three different concentrations 400 mg/L, 200 mg/L, 100 mg/L. Maximum inhibitory activity was observed for 400 mg/L and compounds showed their effect in a dose-dependent manner. The compound **7f** was found to be most potent against *B. subtilis*, while the compound **7a** and **7i** these were found to be equipotent remaining compounds also showed the promising antibacterial activity. The compounds **7a**, **7i** these were most potent against *E. coli* while the compound **7e** and **7h** these were equipotent against the same strain as shown in Figures 1 and 2. The compounds **7c** and **7d**, these showed promising activity against *A. niger* and *A. flavus* respectively, while the remaining compounds also showed promising inhibitory activity as shown in Figures 3 and 4. The morpholine, pyrrole ring, and thiazole ring were found more potent in their inhibitory effect on growth of both bacterial and fungal strains which indicates the positive modulator effect of electro negativity on activity in these molecules.

6. Conclusion

We developed novel trisubstitute triazine derivatives containing, N-Mannich bases of isatin-3-hydrazone, established sulphadiazine drugs and N-benzyl-4-oxo azacarbazole derivatives using nucleophilic substitution reaction, Japp-Klingmann, Fischer-indolization, and other reactions. Furthermore, it was found that the morpholine, pyrrole ring, and thiazole ring derivatives **7a**, **7i**, and **7h** were more potent in their inhibitory effect on growth of both bacterial and fungal strains which indicates the positive modulator effect of electronegativity on activity in these molecules. Their further quantitative structure relationship (QSAR) studies are currently under investigation.

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