

Novel s-Triazinyl Schiff Base/Chalcone Congeners: Rational, Synthesis, Antimicrobial and Anti-TB Evaluation

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ABSTRACT

The occurrence of Multi Drug Resistant (MDR) infectious microbial strains has been increased upto alarming level which affects the public health worldwide. To cure this problem, a library of s-triazinyl derivatives comprising schiff base or chalcone motif have been rationalized, synthesized and screened for their *in vitro* antibacterial activity against five bacterial strains (*Staphylococcus aureus* MTCC 96, *Bacillus subtilis* MTCC 441, *Escherichia coli* MTCC 739, *Pseudomonas aeruginosa* MTCC 741 and *Klebsiella pneumoniae* MTCC 109) and four fungal strains (*Aspergillus niger* MTCC 282, *Aspergillus fumigates* MTCC 343, *Aspergillus clavatus* MTCC 1323, *Candida albicans* MTCC 183) using broth dilution technique. All the newly synthesized scaffolds were further evaluated for their *in vitro* anti-TB efficacy against the tubercular strain (*Mycobacterium tuberculosis* H37Rv) using Lowenstein-Jensen MIC method. All the derivatives were well characterized by IR, ¹H NMR, ¹³C NMR, elemental analysis as well as mass spectroscopy.

Keywords: Antimicrobial; Anti-TB; s-Triazine; Schiff Base; Chalcone

1. INTRODUCTION

Multidrug resistant strength of a variety of infectious microbial flora towards existing standard drugs has been increased in recent decade which is serious health problem worldwide. Antimicrobial resistant (AMR) is a phenomenon of infectious microbial flora to resist antimicrobial agents to which it was previously sensitive [1]. Various multidrug resistant microbes including bacteria, fungi, viruses, parasites etc. exhibit such type of resistant profile against traditional standard drugs including antibiotics, antifungals, antivirals, antimalarials etc. which results in failure or ineffectiveness of the standard treatment, so that the rate of spread of infectious disease also increases. The appearance of methicillin-resistant *Staphylococcus aureus* (MRSA), a multidrug resistant gram-positive bacterial strain, poses infectious disease.

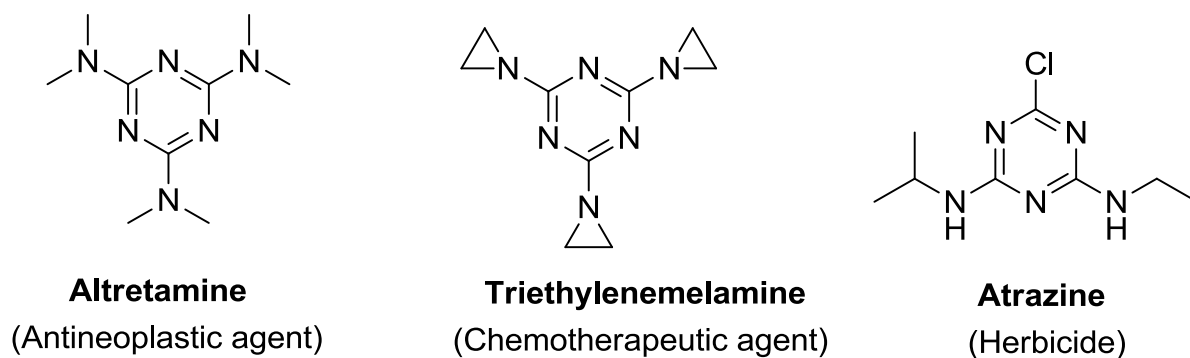
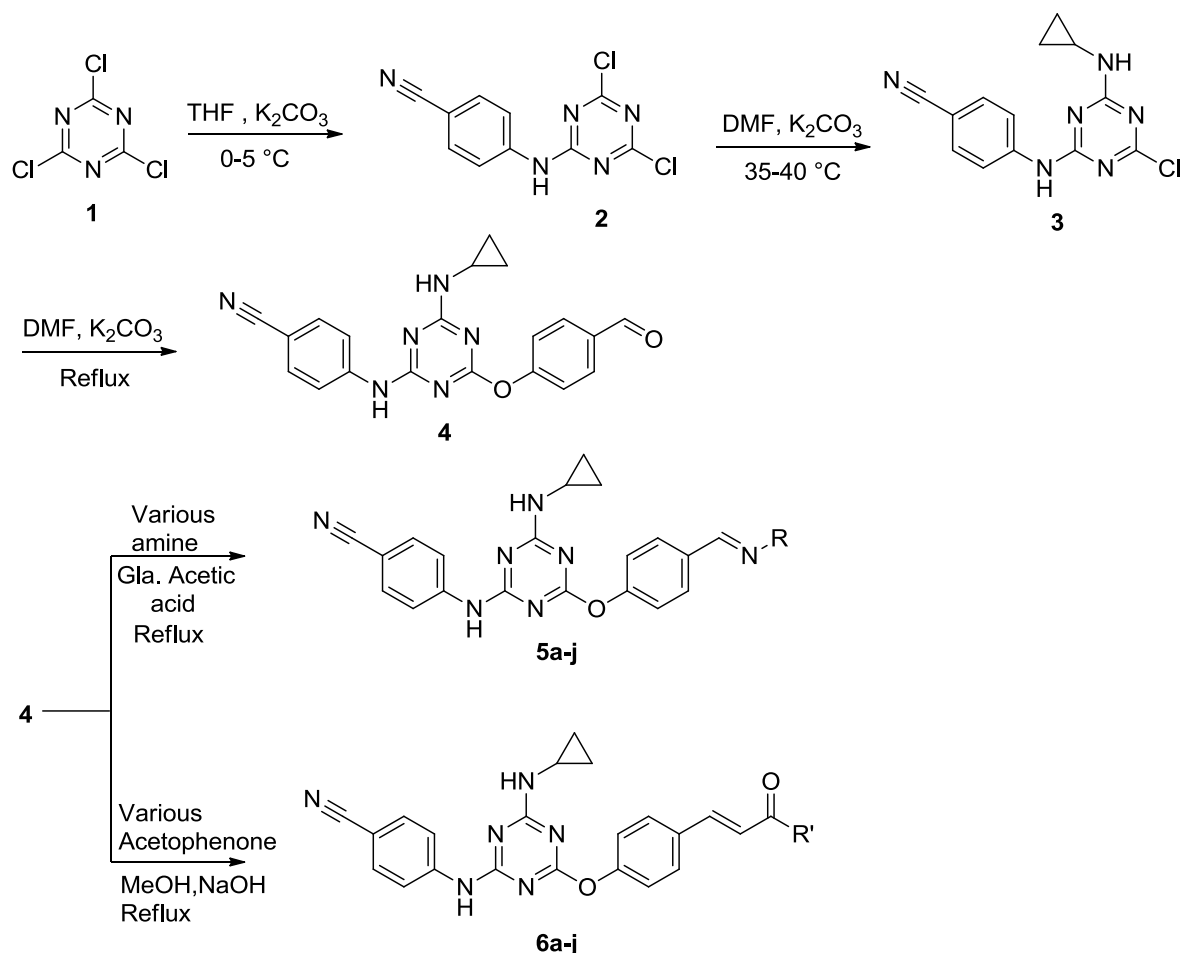


Figure 1. s-Triazine based pharmaceutical agents.



Scheme 1. Synthetic pathway for the preparation final analogues **5a-j** and **6a-j**.

In the current period, some tubercular strains of *Mycobacterium tuberculosis* cause MDR-Tuberculosis (TB) and extensively drug-resistant XDR-TB which generally affects the lungs [2]. The current figures of World Health Organization (WHO) for the year 2012 showed 8.6 million people suffered with TB and 1.3 million died from TB. An estimated 530

000 children became ill with TB and 74 000 HIV-negative children died of TB [3]. In context of the above discussion, the cost of these troubles highlights the urgent need to develop new medicinal agents which have relatively higher efficiency to sustain a pool of new bioactive scaffolds.

In context of the above discussion, the cost of these troubles indicate the urgent need to develop new medicinal agents having relatively higher potency with reference to traditional drugs to sustain a pool of novel antimicrobial agents. Hence, rational and synthesis of novel bioactive agents likely to be unaffected by existing resistance mechanisms is an area of vast implication for medicinal chemists showed the urgent need to combat such impasse. The rationalization of novel bioactive agents with more selectivity and little toxicity persist an area of intensive research in synthetic medicinal chemistry.

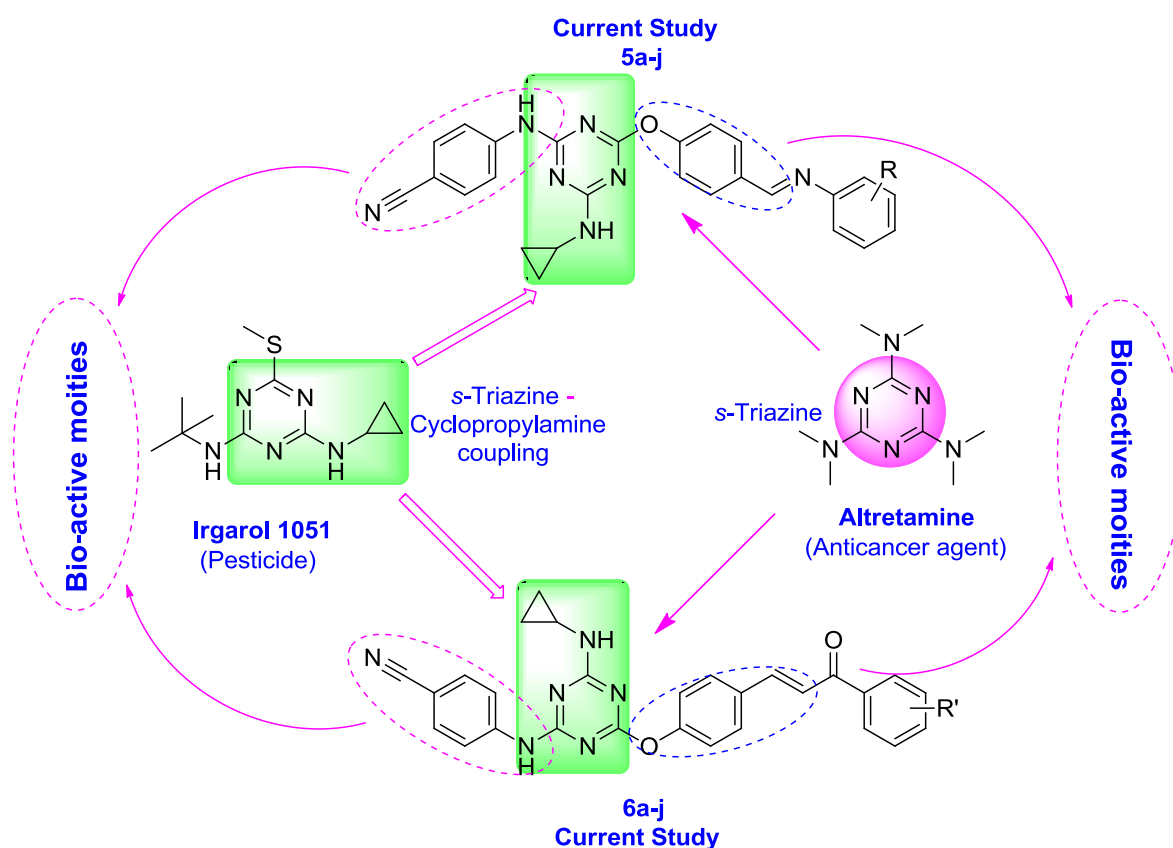


Figure 2. Rationalization of Titled Compounds.

s-Triazine derivatives represents an imperative group of drugs possessing miscellaneous medical applications by means of their widespread medicinal attribute such as antibacterial [4], antifungal [5], anti-TB [6], anticancer [7,8], antimalarial [9], anti-HIV [10] etc. Some triazine based drugs e.g. Altretamine, Triethylenemelamine and Atrazine (Fig. 1) have also been used for therapeutic purpose in clinic. Many chemists have synthesized effective antimicrobial agents containing *s*-triazine as a core moiety [11,12]. Schiff base possessing molecule having good inhibitory profile also been synthesized by many workers [13,14]. Triazine derivatives endowed with chalcone residue were also found to exhibit

superior medicinal applications [15]. In this study, we have designed and developed a variety of *s*-triazine derivatives endowed with schiff base or chalcone residue [16-20].

2. EXPERIMENTAL SECTION

2. 1. Material and methods

All the chemicals and solvents used for the synthesis work acquired from commercial sources were of analytical grade, and were used without further purification. Melting points were determined by using open capillary tubes and are uncorrected. TLC was checked on E-Merck pre-coated 60 F254 plates and the spots were rendered visible by exposing to UV light or iodine. IR spectrums were recorded on SHIMADZU HYPER IR. NMR spectra were recorded by 400 MHz BRUKER AVANCE instrument using TMS as internal standard (Chemical Shift in δ , ppm) and DMSO-*d*₆ as a solvent. Spectra were taken with a resonant frequency of 400 MHz for ¹H and 100 MHz for ¹³C NMR. The splitting patterns are designated as follows; s, singlet; d, doublet; dd, doublet of doublets; and m, multiplet. Elemental analysis was done on "Haraeus Rapid Analyser". The mass spectra were recorded on JOEL SX-102 (EI) model with 60 eV ionizing energy.

Synthesis of 4-((4,6-dichloro-1,3,5-triazin-2-yl)amino)benzonitrile (2)

To a solution of cyanuric chloride (10 g, 0.054 mol) in dry THF (150 ml) at 0-5 °C were slowly added K₂CO₃ (14.9 g, 0.108 mole) and 4-aminobenzonitrile (6.41 g, 0.054 mole). The solution was stirred for 4 hrs 0-5 °C. After completion of reaction based on TLC monitoring Toluene:Acetone (7:3), The resulted reaction mixture was then treated with crushed ice, followed by neutralization by dilute HCl and then filtered, dried and recrystallized from acetone to afford (2).

Yield- 79 %; mp 247-250 °C; IR (vmax cm⁻¹): 3277 (N-H, secondary), 2228 (C≡N), 833 (C₃N₃, *s*-triazine), 802 (C-Cl); ¹H NMR (400 MHz, DMSO-*d*₆, δ ppm): 8.61 (s, 1H, –NH 4-amino benzonitrile), 7.86-7.78 (m, 4H, Ar–H aromatic proton); ¹³C NMR (100 MHz, DMSO-*d*₆, δ ppm): 171.72, 166.61, 165.35, 140.76, 132.17, 125.38, 122.61, 120.68, 119.32, 100.82; ESI-MS (m/z): 265.9 (M⁺).

Synthesis of 4-((4-chloro-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzonitrile (3)

To a stirred solution of 2 (5 g, 0.0188 mol) in dry DMF (20 mL), slowly added a solution of cyclopropyl amine (1.07 g, 0.0188 mol) in DMF (30 mL) and K₂CO₃ (2.6 g, 0.0188 mol) at room temperature. The reaction mixture was stirred at room temperature for 9 hrs. After the completion of reaction, the reaction mass was dumped into crushed ice, solid was filtered, washed with water, dried to give crude product. The crude product was purified by column chromatography to get the pure product (3).

Yield- 70 %; mp 187-190 °C; IR (vmax cm⁻¹): 3335 (N–H, secondary), 2174 (C≡N), 821 (C₃N₃, *s*-triazine), 785 (C-Cl); ¹H NMR (400 MHz, DMSO-*d*₆, δ ppm): 7.51 (d, J = 7.5 Hz, 2H), 7.04 (d, J = 7.1 Hz, 2H), 6.85 (s, 2H), 6.35 (s, 1H), 4.80 (s, 1H), 2.36 (s, 3H), 2.23 (s, 6H); ¹³C NMR (100 MHz, DMSO-*d*₆, δ ppm): 164.27, 162.56, 161.46, 145.27, 142.48, 135.55, 133.49, 131.13, 129.57, 128.84, 127.74, 114.24, 22.25, 19.16; ESIMS (m/z): 365.8 (M⁺).

Synthesis of 4-((4-(cyclopropylamino)-6-(4-formylphenoxy)-1,3,5-triazin-2-yl)amino)benzonitrile (4)

To a stirred solution of **3** (5 g, 0.0174 mol) in dry DMF (20 mL), slowly added a solution of 4-hydroxy benzaldehyde (2.13 g, 0.0174 mol) in DMF (30 mL) and K_2CO_3 (2.4 g, 0.0174 mol). After all the reagents have been added, the temperature of reaction raised upto 150 °C. The reaction mass was refluxed for 11 hrs. After the completion of reaction, the reaction mass was cooled to room temperature, dumped into crushed ice, solid was filtered, washed with water and then dried to give crude product. It was then purified by crystallization from ethanol to give pure desired product (**4**).

Yield- 70 %; mp 153-157 °C; IR (ν_{max} cm^{-1}): 3384 (N-H, secondary), 2185 (C≡N), 1735 (Ar-CHO), 832 (C_3N_3 , s-triazine); 1H NMR (400 MHz, DMSO) δ 9.95 (s, 1H), 7.66 (d, $J = 7.43$ Hz, 2H), 7.63 (d, $J = 7.39$ Hz, 2H), 7.30 (d, $J = 7.7$ Hz, 2H), 7.13 (d, $J = 7.42$ Hz, 2H), 6.25 (s, 1H), 3.54 (s, 1H), 2.46 (m, $J = 8.7$ Hz, 1H), 1.71-1.52 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 192.00, 170.92, 162.66, 161.23, 151.56, 143.66, 134.89, 133.16, 130.37, 121.66, 119.41, 119.12, 100.31, 23.03, 8.93; ESIMS (m/z): 373.1 (M+).

General procedure for the synthesis of compounds 5a-j

A mixture of **4** (5 g, 0.0134 mol), appropriate amine (0.0134 mol) and glacial acetic acid (0.5 mL) in ethanol (50 mL) was refluxed for 12 hrs. After the completion of reaction, the reaction mass was cooled to room temperature, dumped into crushed ice, solid was filtered, washed with water and then dried to give the desired crude product. The crude was then purified by column chromatography to get pure title compound.

4-((4-(4-(((3-Chlorophenyl)imino)methyl)phenoxy)-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzonitrile (5a)

IR (ν_{max} cm^{-1}): 3364 (N-H, secondary), 2174 (C≡N), 825 (C_3N_3 , s-triazine); 1H NMR (400 MHz, DMSO) δ 8.74 (s, 1H), 7.63-7.42 (m, 5H), 7.32-7.10 (m, 5H), 6.91-6.74 (m, 2H), 6.33 (s, 1H), 3.43 (s, 1H), 2.34-2.22 (m, 1H), 1.34-0.24 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 171.45, 163.56, 160.23, 150.44, 145.47, 144.23, 135.55, 134.74, 131.39, 130.75, 126.30, 122.70, 121.80, 120.47, 118.56, 101.42, 24.27, 8.57; ESIMS (m/z): 482.5 (M+).

4-((4-(4-(((4-Chlorophenyl)imino)methyl)phenoxy)-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzonitrile (5b)

IR (ν_{max} cm^{-1}): 3360 (N-H, secondary), 2165 (C≡N), 834 (C_3N_3 , s-triazine); 1H NMR (400 MHz, DMSO) δ 8.72 (s, 1H), 7.50-7.36 (m, 4H), 7.30-7.15 (m, 4H), 7.11-7.02 (m, 2H), 6.96-6.71 (m, 2H), 6.20 (s, 1H), 3.52 (s, 1H), 2.45 (m, 1H), 1.64-1.42 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 172.58, 162.17, 161.23, 160.49, 150.48, 149.33, 142.27, 135.37, 134.59, 131.24, 129.54, 128.14, 120.17, 119.52, 119.04, 118.57, 101.42, 22.13, 8.85; ESIMS (m/z): 482.4 (M+).

4-((4-(Cyclopropylamino)-6-(4-(((4-fluorophenyl)imino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzonitrile (5c)

IR (ν_{max} cm^{-1}): 3372 (N-H, secondary), 2174 (C≡N), 842 (C_3N_3 , s-triazine); 1H NMR (400 MHz, DMSO) δ 8.85 (s, 1H), 7.62 (d, $J = 7.44$ Hz, 2H), 7.51 (d, $J = 7.36$ Hz, 2H), 7.51-7.34 (m, 2H), 7.30 (d, $J = 7.28$ Hz, 2H), 7.12 (t, $J = 7.7$ Hz, 2H), 6.85 (d, $J = 7.7$ Hz, 2H),

6.30 (s, 1H), 3.62 (s, 1H), 2.43-2.13 (m, 1H), 1.62-1.20 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 172.43, 162.53, 161.22, 160.37, 159.33, 158.04, 152.34, 151.13, 144.37, 135.27, 134.43, 131.14, 123.39, 120.33, 119.65, 118.24, 117.46, 116.31, 102.47, 22.03, 8.56; ESIMS (m/z): 466.3 (M+).

4-((4-(Cyclopropylamino)-6-(4-(((3-nitrophenyl)imino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (5d)

IR (vmax cm^{-1}): 3292 (N-H, secondary), 2218 (C \equiv N), 1521 (N-O stretch), 1355 (N-O stretch), 839 (C₃N₃, s-triazine); ^1H NMR (400 MHz, DMSO) δ 8.88 (s, 1H), 8.59-8.57 (m, 3H), 8.41-7.83 (m, 5H), 7.58-7.37 (m, 4H), 6.07 (s, 1H), 3.81 (s, 1H), 3.11-2.80 (m, 1H), 1.20-0.75 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 170.15, 162.60, 161.12, 153.67, 152.08, 148.43, 144.07, 135.12, 132.51, 130.30, 127.91, 126.13, 125.46, 124.17, 123.61, 122.02, 121.54, 120.65, 119.23, 101.26, 24.64, 8.57; ESIMS (m/z): 493.4 (M+).

4-((4-(Cyclopropylamino)-6-(4-(((4-nitrophenyl)imino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (5e)

IR (vmax cm^{-1}): 3385 (N-H, secondary), 2166 (C \equiv N), 1545 (N-O stretch), 1367 (N-O stretch), 845 (C₃N₃, s-triazine); ^1H NMR (400 MHz, DMSO) δ 8.75 (s, 1H), 8.20 (d, $J = 7.7$ Hz, 2H), 7.79 (d, $J = 7.42$ Hz, 2H), 7.61 (dd, $J = 17.5, 7.5$ Hz, 4H), 7.25 (d, $J = 7.1$ Hz, 2H), 6.90 (d, $J = 7.54$ Hz, 2H), 6.31 (s, 1H), 3.62 (s, 1H), 2.45-2.24 (m, 1H), 1.21-0.74 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 170.90, 163.12, 162.60, 161.15, 158.12, 151.43, 144.25, 143.62, 134.50, 133.64, 130.32, 125.25, 121.49, 120.74, 119.05, 100.26, 23.21, 8.80; ESIMS (m/z): 493.5 (M+).

4-((4-(Cyclopropylamino)-6-(4-(((3-hydroxyphenyl)imino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (5f)

IR (vmax cm^{-1}): 3427 (O-H broad band), 3314 (N-H, secondary), 2176 (C \equiv N), 1526 (N-O stretch), 1374 (N-O stretch), 856 (C₃N₃, s-triazine); ^1H NMR (400 MHz, DMSO) δ 8.84 (s, 1H), 8.25 (s, 1H), 7.46 (dd, $J = 27.1, 7.5$ Hz, 4H), 7.27 (d, $J = 7.37$ Hz, 2H), 7.12 (t, $J = 7.33$ Hz, 1H), 6.86-6.77 (m, 4H), 6.75-6.45 (m, 1H), 6.28 (s, 1H), 3.43 (s, 1H), 2.46-2.28 (m, 1H), 2.18-0.87 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 170.80, 162.54, 161.12, 158.61, 151.43, 151.10, 143.74, 134.62, 133.75, 130.94, 130.31, 121.64, 120.82, 119.10, 114.70, 113.22, 108.61, 100.24, 23.14, 8.84; ESIMS (m/z): 464.1 (M+).

4-((4-(Cyclopropylamino)-6-(4-(((4-hydroxyphenyl)imino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (5g)

IR (vmax cm^{-1}): 3456 (O-H broad band), 3327 (N-H, secondary), 2153 (C \equiv N), 1546 (N-O stretch), 1380 (N-O stretch), 844 (C₃N₃, s-triazine); ^1H NMR (400 MHz, DMSO) δ 8.73 (s, 1H), 8.42 (s, 1H), 7.46 (d, $J = 7.52$ Hz, 2H), 7.38 (d, $J = 7.41$ Hz, 2H), 7.13 (dd, $J = 12.3, 7.6$ Hz, 4H), 6.90 (d, $J = 7.33$ Hz, 2H), 6.73 (d, $J = 7.45$ Hz, 2H), 6.25 (s, 1H), 3.53 (s, 1H), 2.42-2.35 (m, 1H), 2.10-0.76 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 170.98, 163.64, 162.43, 161.34, 158.27, 151.18, 144.82, 143.74, 134.67, 133.43, 130.29, 122.56, 121.43, 120.75, 119.09, 116.76, 100.29, 23.15, 8.82; ESIMS (m/z): 464.2 (M+).

4-((4-(4-((Cyclohexylimino)methyl)phenoxy)-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzotrile (5h)

IR (vmax cm⁻¹): 3346 (N–H, secondary), 2954 (alkyl C–H stretch), 2157 (C≡N), 847 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 8.24 (s, 1H), 7.43 (d, *J* = 7.27 Hz, 2H), 7.32 (d, *J* = 7.54 Hz, 2H), 7.15 (d, *J* = 7.4 Hz, 2H), 6.90 (d, *J* = 7.6 Hz, 2H), 6.22 (s, 1H), 3.63 (s, 1H), 2.83–2.71 (m, 1H), 2.40–2.21 (m, 1H), 1.86 (dt, *J* = 7.6, 5.8 Hz, 2H), 1.81–1.40 (m, 7H), 1.30–1.17 (m, 1H), 1.05–0.22 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 170.80, 162.75, 162.23, 161.12, 150.30, 143.54, 134.40, 133.13, 130.30, 121.52, 120.90, 119.25, 100.23, 66.42, 33.73, 25.96, 25.33, 23.24, 8.65; ESIMS (m/z): 454.3 (M⁺).

4-((4-(Cyclopropylamino)-6-(4-((o-tolylimino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (5i)

IR (vmax cm⁻¹): 3348 (N–H, secondary), 2163 (C≡N), 849 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 8.77 (s, 1H), 7.64 (d, *J* = 7.5 Hz, 2H), 7.49 (d, *J* = 7.53 Hz, 2H), 7.41–6.54 (m, 8H), 6.26 (s, 1H), 3.63 (s, 1H), 2.42–2.25 (m, 4H), 1.63–1.13 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 170.96, 162.63, 161.34, 155.19, 151.27, 150.43, 143.50, 134.61, 133.73, 130.29, 129.65, 129.22, 127.70, 126.52, 121.54, 120.72, 120.17, 119.44, 100.47, 23.23, 18.46, 8.66; ESIMS (m/z): 462.6 (M⁺).

4-((4-(Cyclopropylamino)-6-(4-((p-tolylimino)methyl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (5j)

IR (vmax cm⁻¹): 3357 (N–H, secondary), 2138 (C≡N), 851 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 8.71 (s, 1H), 7.49 (dd, *J* = 14.1, 7.7 Hz, 4H), 7.32 (d, *J* = 7.43 Hz, 2H), 7.20 (dd, *J* = 13.1, 7.38 Hz, 4H), 6.95 (d, *J* = 7.58 Hz, 2H), 6.53 (s, 1H), 3.60 (s, 1H), 2.47–2.31 (m, 4H), 1.82–0.69 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 170.77, 163.13, 162.57, 161.35, 151.18, 150.43, 143.12, 134.43, 133.47, 130.58, 129.24, 121.45, 120.75, 119.25, 100.37, 23.42, 21.13, 8.52; ESIMS (m/z): 462.3 (M⁺).

General procedure for the synthesis of compounds 6a–j

A mixture of 4 (5 g, 0.0134 mol), appropriate acetophenone (0.0134 mol) and sodium hydroxide (0.51 g, 0.0147 mol) in methanol (50 mL) was refluxed for 15 hrs. After the completion of reaction, the reaction mass was cooled to room temperature, dumped into crushed ice, solid was filtered, washed with water and then dried to give the desired crude product. The crude was then purified by column chromatography to get pure title compound.

4-((4-(Cyclopropylamino)-6-(4-(3-oxo-3-phenylprop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6a)

IR (vmax cm⁻¹): 3325 (N–H, secondary), 2220 (C≡N), 1635 (alkene C=C stretch), 839 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 8.17–8.13 (m, 2H), 7.98–7.73 (m, 6H), 7.67–7.38 (m, 3H), 7.32–7.14 (m, 4H), 6.20 (s, 1H), 3.42 (s, 1H), 2.20–2.01 (m, 1H), 0.73–0.65 (m, 2H), 0.56–0.43 (m, 2H); ¹³C NMR (100 MHz, DMSO) δ 191.18, 169.33, 163.85, 161.32, 151.65, 143.36, 139.58, 131.84, 129.05, 128.83, 126.32, 125.50, 124.11, 123.36, 122.15, 121.36, 120.22, 119.53, 100.18, 22.16, 8.83; ESIMS (m/z): 475.8 (M⁺).

4-((4-(4-(3-(2-Chlorophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzotrile (6b)

IR (ν_{\max} cm^{-1}): 3337 (N–H, secondary), 2148 ($\text{C}\equiv\text{N}$), 1640 (alkene C=C stretch), 1035 (ether C–O stretch), 843 (C_3N_3 , s-triazine); ^1H NMR (400 MHz, DMSO) δ 7.81-7.63 (m, 2H), 7.54-7.45 (m, 5H), 7.40-7.26 (m, 1H), 7.16 (dd, $J = 7.3, 6.8$ Hz, 4H), 6.84 (d, $J = 7.2$ Hz, 2H), 6.21 (s, 1H), 3.65 (s, 1H), 2.46-2.32 (m, 1H), 1.98-1.25 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 189.35, 170.62, 162.57, 161.12, 151.55, 143.46, 143.73, 138.16, 135.54, 133.42, 131.47, 131.58, 130.28, 130.67, 129.86, 126.23, 122.68, 121.78, 120.38, 119.66, 100.87, 23.46, 8.28; ESIMS (m/z): 509.6 (M+).

4-((4-(4-(3-(4-Chlorophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzotrile (6c)

IR (ν_{\max} cm^{-1}): 3327 (N–H, secondary), 2141 ($\text{C}\equiv\text{N}$), 1643 (alkene C=C stretch), 1143 (ether C–O stretch), 856 (C_3N_3 , s-triazine); ^1H NMR (400 MHz, DMSO) δ 7.70 (dd, $J = 11.3, 7.2$ Hz, 3H), 7.60-7.42 (m, 5H), 7.30 (dd, $J = 7.4, 6.9$ Hz, 4H), 6.75 (d, $J = 7.37$ Hz, 2H), 6.28 (s, 1H), 3.65 (s, 1H), 2.47-2.29 (m, 1H), 2.15-1.43 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 190.58, 170.67, 162.48, 161.38, 151.57, 144.49, 143.15, 138.78, 137.49, 131.15, 131.26, 130.48, 129.67, 129.34, 122.67, 121.34, 120.21, 119.25, 100.47, 23.69, 8.58; ESIMS (m/z): 509.5 (M+).

4-((4-(Cyclopropylamino)-6-(4-(3-(2,5-dichlorophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6d)

IR (ν_{\max} cm^{-1}): 3364 (N–H, secondary), 2154 ($\text{C}\equiv\text{N}$), 1637 (alkene C=C stretch), 1143 (ether C–O stretch), 839 (C_3N_3 , s-triazine); ^1H NMR (400 MHz, DMSO) δ 7.74 (d, $J = 1.2$ Hz, 1H), 7.59 (d, $J = 14.9$ Hz, 1H), 7.52-7.35 (m, 5H), 7.28-7.14 (m, 4H), 6.75 (d, $J = 7.6$ Hz, 2H), 6.36 (s, 1H), 3.64 (s, 1H), 2.48-1.76 (m, 1H), 1.54-0.82 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 189.55, 170.82, 162.37, 161.45, 151.73, 131.54, 143.42, 143.75, 142.00, 140.27, 132.23, 131.45, 130.15, 122.43, 121.37, 120.85, 119.43, 100.18, 23.73, 8.49; ESIMS (m/z): 544.8 (M+).

4-((4-(Cyclopropylamino)-6-(4-(3-oxo-3-(o-tolyl)prop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6e)

IR (ν_{\max} cm^{-1}): 3359 (N–H, secondary), 2137 ($\text{C}\equiv\text{N}$), 1655 (alkene C=C stretch), 1059 (ether C–O stretch), 852 (C_3N_3 , s-triazine); ^1H NMR (400 MHz, DMSO) δ 7.85-7.68 (m, 2H), 7.60-7.48 (m, 4H), 7.40-7.27 (m, 2H), 7.20-7.08 (m, 4H), 6.92 (d, $J = 7.1$ Hz, 2H), 6.35 (s, 1H), 3.74 (s, 1H), 2.37-2.21 (m, 4H), 1.24-1.07 (m, 2H), 0.94-0.49 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ 193.17, 170.52, 162.73, 161.64, 151.82, 143.37, 143.49, 139.57, 137.36, 132.15, 131.46, 131.37, 131.28, 130.53, 129.42, 126.37, 122.41, 121.55, 120.76, 119.35, 100.12, 23.43, 20.75, 8.36; ESIMS (m/z): 489.3 (M+).

4-((4-(Cyclopropylamino)-6-(4-(3-(2-nitrophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6f)

IR (ν_{\max} cm^{-1}): 3349 (N–H, secondary), 2134 ($\text{C}\equiv\text{N}$), 1675 (alkene C=C stretch), 1150 (ether C–O stretch), 853 (C_3N_3 , s-triazine); ^1H NMR (400 MHz, DMSO) δ 9.10-7.42 (m, 2H), 7.75 (m, 2H), 7.46 (m, 1H), 7.40 (m, 3H), 7.26 (m, 4H), 6.73 (d, $J = 7.8$ Hz, 2H), 6.34 (s, 1H), 3.57 (s, 1H), 2.58-2.35 (m, 1H), 2.11-1.37 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ

194.15, 170.72, 162.64, 161.63, 151.58, 150.73, 143.42, 143.11, 133.37, 132.42, 131.15, 131.43, 130.85, 128.73, 122.62, 122.46, 121.75, 120.42, 119.64, 100.33, 23.42, 8.58; ESIMS (m/z): 520.4 (M⁺).

4-((4-(Cyclopropylamino)-6-(4-(3-(2-hydroxy-5-nitrophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6g)

IR (vmax cm⁻¹): 3452 (O-H broad band), 3364 (N-H, secondary), 2176 (C≡N), 1664 (alkene C=C stretch), 1556 (N-O stretch), 1360 (N-O stretch), 1184 (ether C-O stretch), 863 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 9.62 (s, 1H), 8.63 (d, *J* = 1.4 Hz, 1H), 8.40 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.82 (d, *J* = 14.9 Hz, 1H), 7.62 (t, *J* = 11.2 Hz, 3H), 7.34 (dd, *J* = 7.3, 5.4 Hz, 5H), 6.72 (d, *J* = 7.3 Hz, 2H), 6.37 (s, 1H), 3.43 (s, 1H), 2.44-2.38 (m, 1H), 2.53-1.24 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 192.53, 170.27, 169.43, 162.51, 161.34, 151.52, 143.82, 143.14, 138.30, 131.24, 131.87, 130.50, 126.42, 124.13, 122.22, 121.08, 120.63, 119.74, 119.23, 100.04, 23.37, 8.42; ESIMS (m/z): 536.7 (M⁺).

4-((4-(4-(3-(5-Chloro-2-hydroxy-3-nitrophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-6-(cyclopropylamino)-1,3,5-triazin-2-yl)amino)benzotrile (6h)

IR (vmax cm⁻¹): 3521 (O-H broad band), 3387 (N-H, secondary), 2157 (C≡N), 1678 (alkene C=C stretch), 1563 (N-O stretch), 1358 (N-O stretch), 1192 (ether C-O stretch), 860 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 13.23 (s, 1H), 8.34 (d, *J* = 1.4 Hz, 1H), 8.13 (d, *J* = 1.6 Hz, 1H), 7.54 (d, *J* = 15.1 Hz, 1H), 7.46 (dd, *J* = 12.5, 11.4 Hz, 3H), 7.31 (dd, *J* = 7.3, 6.8 Hz, 4H), 6.52 (d, *J* = 7.7 Hz, 2H), 6.37 (s, 1H), 3.40 (s, 1H), 2.37-1.92 (m, 1H), 1.73-1.24 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 192.67, 170.48, 162.29, 161.49, 155.67, 151.32, 143.45, 143.64, 136.32, 135.18, 131.43, 131.73, 130.46, 127.44, 125.75, 122.81, 121.94, 120.67, 119.78, 100.32, 23.44, 8.75; ESIMS (m/z): 570.6 (M⁺).

4-((4-(Cyclopropylamino)-6-(4-(3-(5-fluoro-2-hydroxy-3-nitrophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6i)

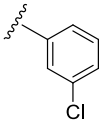
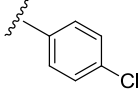
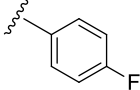
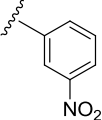
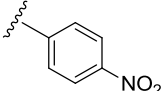
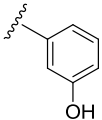
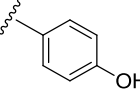
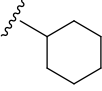
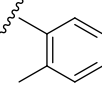
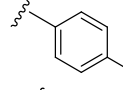
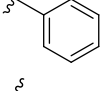
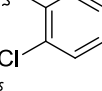
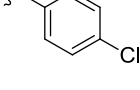
IR (vmax cm⁻¹): 3467 (O-H broad band), 3351 (N-H, secondary), 2149 (C≡N), 1674 (alkene C=C stretch), 1559 (N-O stretch), 1348 (N-O stretch), 1183 (ether C-O stretch), 854 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 13.11 (s, 1H), 8.42 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.45 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.37 (d, *J* = 15.1 Hz, 1H), 7.40 (t, *J* = 10.9 Hz, 3H), 7.75 (t, *J* = 7.7 Hz, 4H), 6.67 (d, *J* = 7.7 Hz, 2H), 6.11 (s, 1H), 3.70 (s, 1H), 2.43-1.89 (m, 1H), 1.71-1.10 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 192.40, 170.35, 162.41, 161.43, 160.12, 157.36, 154.10, 151.22, 143.43, 143.57, 136.42, 131.58, 131.10, 130.54, 126.63, 124.67, 124.28, 122.75, 121.62, 120.18, 119.61, 117.64, 117.52, 100.31, 23.48, 8.61; ESIMS (m/z): 554.9 (M⁺).

4-((4-(Cyclopropylamino)-6-(4-(3-(2,4-dihydroxy-3-methyl-5-nitrophenyl)-3-oxoprop-1-en-1-yl)phenoxy)-1,3,5-triazin-2-yl)amino)benzotrile (6j)

IR (vmax cm⁻¹): 3487 (O-H broad band), 3373 (N-H, secondary), 2168 (C≡N), 1666 (alkene C=C stretch), 1554 (N-O stretch), 1351 (N-O stretch), 1183 (ether C-O stretch), 852 (C₃N₃, s-triazine); ¹H NMR (400 MHz, DMSO) δ 9.34 (s, 1H), 9.24 (s, 1H), 8.31 (s, 1H), 7.80 (d, *J* = 15.1 Hz, 1H), 7.46-7.27 (m, 3H), 7.19-7.04 (m, 4H), 6.65 (d, *J* = 7.35 Hz, 2H), 6.37 (s, 1H), 3.37 (s, 1H), 2.43-1.84 (m, 4H), 1.60-1.36 (m, 4H); ¹³C NMR (100 MHz, DMSO) δ 192.33, 170.75, 167.43, 162.67, 161.10, 156.54, 151.63, 143.84, 143.42, 131.64,

131.35, 130.45, 125.73, 125.27, 122.95, 121.60, 120.55, 119.35, 114.67, 110.18, 100.25, 23.34, 8.93, 8.47; ESIMS (m/z): 566.4 (M⁺).

Table 1. *In-vitro* anti-bacterial activity of newly synthesized compounds **5a-j** and **6a-j**.

Entry	R/R'	Log P	Zone of Inhibition in mm (MIC in µg/mL)				
			<i>S.a</i>	<i>B.s</i>	<i>E.c</i>	<i>P.a</i>	<i>K.p</i>
5a		7.03	21 (6.25)	27 (100)	19 (200)	25 (100)	15 (50)
5b		7.03	19 (6.25)	30 (50)	13 (50)	20 (100)	11 (100)
5c		6.63	11 (50)	25 (200)	24 (6.25)	16 (25)	09 (12.5)
5d		-	15 (100)	26 (50)	17 (100)	17 (50)	14 (50)
5e		-	08 (12.5)	22 (12.5)	20 (12.5)	21 (100)	10 (200)
5f		6.08	13 (50)	31 (25)	14 (25)	19 (200)	12 (100)
5g		6.08	10 (100)	24 (100)	11 (50)	11 (50)	14 (100)
5h		6.35	11 (50)	20 (200)	13 (100)	09 (100)	09 (25)
5i		6.96	14 (200)	37 (0.78)	17 (100)	13 (25)	18 (12.5)
5j		6.96	09 (25)	23 (100)	15 (50)	33 (6.25)	07 (100)
6a		6.15	12 (100)	20 (50)	13 (12.5)	27 (50)	04 (100)
6b		6.71	17 (50)	24 (12.5)	17 (25)	24 (100)	08 (200)
6c		6.71	08 (100)	19 (50)	07 (50)	15 (100)	10 (10)

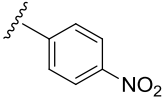
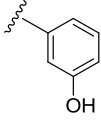
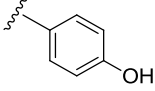
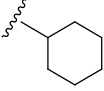
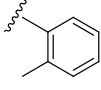
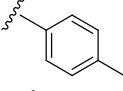
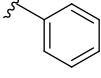
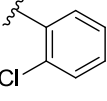
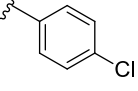
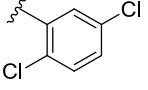
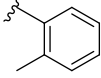
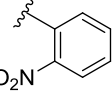
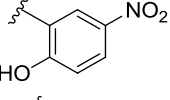
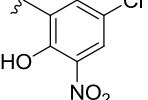
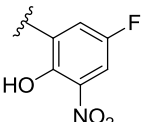
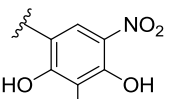
6d		7.27	23 (6.25)	39 (0.78)	10 (25)	18 (50)	04 (50)
6e		6.64	11 (200)	14 (100)	07 (12.5)	24 (100)	07 (25)
6f		-	10 (50)	22 (100)	08 (100)	27 (200)	08 (100)
6g		-	13 (12.5)	27 (200)	11 (100)	16 (25)	10 (200)
6h		-	07 (200)	14 (50)	15 (25)	10 (12.5)	13 (100)
6i		-	14 (200)	19 (100)	24 (6.25)	09 (100)	05 (50)
6j		-	11 (100)	22 (200)	16 (50)	17 (12.5)	12 (200)
Cip.	-	-	22 (6.25)	38 (0.06)	25 (6.25)	32 (6.25)	19 (12.5)
DMSO	-	-	-	-	-	-	-

Log P was calculated using the ChemDraw Ultra, version 12.0

Cip. Ciprofloxacin, S.a Staphylococcus aureus, B.c Bacillus subtilis, E.c Escherichia coli, P.a Pseudomonas aeruginosa, K.p Klebsiella pneumoniae

Table 2. In-vitro anti-fungal activity of newly synthesized compounds **5a-j** and **6a-j**.

Entry	R/R'	Log P	Zone of Inhibition in mm (MIC in $\mu\text{g/mL}$)			
			<i>A.n</i>	<i>A.f</i>	<i>A.c</i>	<i>C.a</i>
5a		7.03	12 (12.5)	20 (25)	24 (100)	21 (50)
5b		7.03	19 (25)	11 (12.5)	21 (100)	13 (12.5)
5c		6.63	30 (3.12)	15 (100)	15 (25)	20 (50)
5d		-	11 (100)	12 (50)	13 (200)	23 (200)

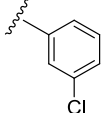
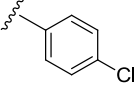
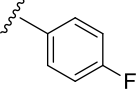
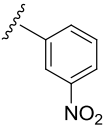
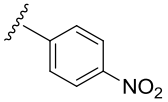
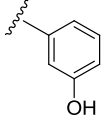
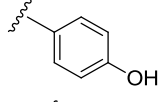
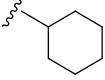
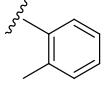
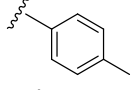
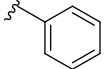
5e		-	10 (50)	21 (12.5)	20 (12.5)	17 (200)
5f		6.08	14 (100)	19 (50)	17 (200)	11 (100)
5g		6.08	18 (50)	11 (50)	24 (50)	13 (25)
5h		6.35	20 (200)	17 (100)	16 (50)	15 (50)
5i		6.96	17 (25)	13 (6.25)	22 (100)	17 (100)
5j		6.96	24 (12.5)	27 (0.78)	20 (12.5)	22 (25)
6a		6.15	21 (100)	15 (25)	17 (100)	15 (100)
6b		6.71	15 (100)	12 (50)	08 (50)	17 (12.5)
6c		6.71	11 (25)	14 (100)	06 (200)	13 (100)
6d		7.27	31 (3.12)	10 (100)	17 (50)	35 (0.78)
6e		6.64	09 (200)	07 (50)	15 (100)	24 (12.5)
6f		-	17 (200)	08 (100)	13 (200)	23 (12.5)
6g		-	16 (50)	13 (50)	14 (12.5)	17 (200)
6h		-	09 (25)	28 (0.78)	18 (25)	16 (25)
6i		-	18 (12.5)	10 (12.5)	32 (0.78)	22 (100)
6j		-	14 (6.25)	21 (6.25)	24 (100)	20 (50)

Ket.	-	-	30 (≤ 3)	29 (≤ 1)	31 (≤ 1)	33 (≤ 1)
DMSO	-	-	-	-	-	-

Log P was calculated using the ChemDraw Ultra, version 12.0

Ket. Ketoconazole, *A.n Aspergillus niger*, *A.f Aspergillus fumigates*, *A.c Aspergillus clavatus*, *C.a Candida albicans*

Table 3. *In-vitro* anti-tuberculosis activity of newly synthesized compounds **7a-j** and **9a-j**.

Entry	R/R'	Log P	L-J MIC method ^a	
			MIC ($\mu\text{g/mL}$)	% Inhibition
5a		7.03	3.12	99
5b		7.03	12.5	95
5c		6.63	100	89
5d		-	100	88
5e		-	200	80
5f		6.08	50	92
5g		6.08	50	91
5h		6.35	12.5	96
5i		6.96	25	92
5j		6.96	100	88
6a		6.15	100	89

6b		6.71	50	90
6c		6.71	12.5	93
6d		7.27	3.12	99
6e		6.64	25	90
6f		-	25	89
6g		-	12.5	93
6h		-	6.25	95
6i		-	3.12	99
6j		-	12.5	92
Isoniazid	-	-	0.25	99
Rifampicin	-	-	0.21	99
Ethambutol	-	-	3.12	99
Pyrazinamide	-	-	3.12	99

^aEach value is the mean of three independent experiment.

Table 4. Physical and analytical data of final scaffolds **5a-j** and **6a-j**.

Compound	Melting Point range (°C)	Yield (%)	Mol. Formula	Elemental analysis Found (calcd)%		
				C	H	N
5a	175-177	78	C ₂₆ H ₂₀ ClN ₇ O	64.61 (64.8)	4.19 (4.18)	20.29 (20.34)
5b	200-202	68	C ₂₆ H ₂₀ ClN ₇ O	64.90 (64.80)	4.17 (4.18)	20.29 (20.34)

5c	237-239	77	C ₂₆ H ₂₀ FN ₇ O	66.94 (67.09)	4.34 (4.33)	21.04 (21.06)
5d	269-271	76	C ₂₆ H ₂₀ N ₈ O ₃	63.58 (63.41)	4.08 (4.09)	22.70 (22.75)
5e	255-257	81	C ₂₆ H ₂₀ N ₈ O ₃	63.32 (63.41)	4.10 (4.09)	22.81 (22.75)
5f	176-178	74	C ₂₆ H ₂₁ N ₇ O ₂	67.52 (67.38)	4.56 (4.57)	21.11 (21.15)
5g	188-190	70	C ₂₆ H ₂₁ N ₇ O ₂	67.19 (67.38)	4.56 (4.57)	21.10 (21.15)
5h	117-119	68	C ₂₆ H ₂₇ N ₇ O	68.96 (68.85)	5.99 (6.00)	21.56 (21.62)
5i	247-249	65	C ₂₇ H ₂₃ N ₇ O	70.10 (70.27)	5.01 (5.02)	21.18 (21.24)
5j	222-224	73	C ₂₇ H ₂₃ N ₇ O	70.09 (70.27)	5.03 (5.02)	21.27 (21.24)
6a	167-169	69	C ₂₈ H ₂₂ N ₆ O ₂	70.80 (70.87)	4.68 (4.67)	17.67 (17.71)
6b	131-133	70	C ₂₈ H ₂₁ ClN ₆ O ₂	65.93 (66.08)	4.15 (4.16)	16.55 (16.51)
6c	141-143	77	C ₂₈ H ₂₁ ClN ₆ O ₂	66.26 (66.08)	4.17 (4.16)	16.47 (16.51)
6d	184-186	72	C ₂₈ H ₂₀ C ₁₂ N ₆ O ₂	61.78 (61.89)	3.70 (3.71)	15.45 (15.47)
6e	205-207	67	C ₂₉ H ₂₄ N ₆ O ₂	71.11 (71.30)	4.94 (4.95)	17.16 (17.20)
6f	228-230	73	C ₂₈ H ₂₁ N ₇ O ₄	64.55 (64.73)	4.07 (4.07)	18.82 (18.87)
6g	178-180	70	C ₂₈ H ₂₁ N ₇ O ₅	62.88 (62.8)	3.94 (3.95)	18.33 (18.31)
6h	150-152	69	C ₂₈ H ₂₀ ClN ₇ O ₅	58.87 (59.00)	3.55 (3.54)	17.16 (17.2)
6i	189-191	74	C ₂₈ H ₂₀ FN ₇ O ₅	60.94 (60.76)	3.63 (3.64)	17.66 (17.71)
6j	197-199	72	C ₂₉ H ₂₃ N ₇ O ₆	61.50 (61.59)	4.09 (4.10)	17.37 (17.34)

3. BIOLOGICAL EVALUATION

All newly synthesized *s*-triazinyl schiff bases and chalcone derivatives were accessed for their *in vitro* antimicrobial evaluation against five bacterial strains (*Staphylococcus aureus* MTCC 96, *Bacillus subtilis* MTCC 441, *Escherichia coli* MTCC 739, *Pseudomonas aeruginosa* MTCC 741 and *Klebsiella pneumoniae* MTCC 109) and four fungal strains (*Aspergillus niger* MTCC 282, *Aspergillus fumigates* MTCC 343, *Aspergillus clavatus* MTCC 1323, *Candida albicans* MTCC 183) using broth dilution technique.

Ciprofloxacin and ketoconazole were used as standard control drugs for antibacterial and antifungal activity, respectively. Further, all the newly synthesized derivatives were evaluated for their *in vitro* antimycobacterial activity (against *Mycobacterium tuberculosis* H37Rv) by Lowenstein-Jensen MIC method using Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide as standard control drugs.

3. 1. *In vitro* antibacterial activity

The analysis of antibacterial screening data (Table 1) reveals that some of the scaffolds were found to exhibit good to moderate efficacy against particular bacterial strain. Among them, the halogen group containing moieties **5a** and **5c** were found active against *S. aureus* MTCC 96 and *E. coli* MTCC 739, respectively, both at MIC 6.25 µg/mL. The electron donating methyl group possessing compound **5i** exhibited superior inhibition profile against *B. subtilis* MTCC 441 and *K. pneumoniae* MTCC 109 at MIC 0.78 µg/mL and MIC 12.5 µg/mL respectively. Again, the methyl group containing motif **5j** showed activity against *P. aeruginosa* MTCC 741 at MIC 6.25 µg/mL. The chalcone derivative having 2,5-dichloro phenyl residue **6d** was found to exhibit higher potential against *S. aureus* MTCC 96 and *B. subtilis* MTCC 441 at MIC 6.25 µg/mL and 0.78 µg/mL, respectively. The final chalcone compound **6i** gave significant inhibition against *E. coli* MTCC 739 at MIC 6.25 µg/mL.

3. 2. *In vitro* antifungal activity

In vitro antifungal activity (Table 2) pointed out that the final schiff base and chalcone derivatives bearing halogen group proved to be highly potent against the specific fungal strain. The final schiff base moiety **5c** having fluoro group showed inhibitory effect on *A. niger* MTCC 282 at MIC 3.12 µg/mL. The methyl group containing schiff base **5j** were found highly potent against *A. fumigates* MTCC 343 at MIC 0.78 µg/mL. The triazinyl chalcone derivatives endowed with 2,5-dichloro phenyl residue was found highly active against *A. niger* MTCC 282 and *C. albicans* MTCC 183 at MIC 3.12 µg/mL and MIC 0.78 µg/mL, respectively. The compounds **6h** and **6i** possessing chloro and fluoro group respectively, were found to possess superior inhibition profile against *A. fumigates* MTCC 343, *A. clavatus* MTCC 1323, respectively, both at MIC 0.78 µg/mL.

3. 3. *In vitro* antituberculosis activity

In vitro antituberculosis activity (Table 3) was performed for the all novel synthesized *s*-triazinyl schiff bases and chalcone derivatives against the tubercular strain *M. tuberculosis* H37Rv. All the novel congeners were evaluated for anti-TB activity using Lowenstein-Jensen MIC method. Among the all scaffolds, the chloro group possessing compounds **5a** and **6d** showed highest inhibition for tubercular strain at MIC 3.12 µg/mL. The fluoro group containing derivative **6i** also exhibited very good inhibitory effect on the mentioned tubercular strain at MIC 3.12 µg/mL.

4. CONCLUSION

The current study mainly focused on the development of novel *s*-triazinyl schiff base and chalcone derivatives in good yield and with a huge range of their pharmaceutical applications. It can be concluded from the above results that many of the synthesized derivatives exhibit good to moderate activity against specific microbial strain. Out of the all

synthesized scaffolds, the final analogues with halogen/methyl group i.e., **5a**, **5c**, **5i**, **5j**, **6d**, **6i** and **6h** were proved to be highly efficient against specific bacterial, fungal and *M. tuberculosis* H37Rv strain as well.

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