Research Article

Synthesis and Antibacterial, Antimycobacterial Activity of 7-[4-{5-(2-Oxo-2-*p*-substituted-phenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazinyl] Quinolone Derivatives

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Currently we screened 9 newer synthesized fluoroquinolone derivatives **5(a-i)** against two gram positive, two gram negative bacterial strains, and mycobacterium tuberculosis H₃₇Rv. These analogues were confirmed by IR, ¹H NMR, ¹³C NMR, and elemental analysis. Selected compounds were confirmed by mass spectral study. Compounds **5(b-d)** showed comparable biological activities and other analogues of the series showed moderate-to-weak activity, as compared to the reference marketed drugs.

1. Introduction

Presently some new substituted phenacyl bromide were clubbed with 1,3,4-thiadiazole and fused with piperazinyl FQ derivatives, which could be considered as hybrid compounds were synthesized. The synthesized compounds were subjected to *in vitro* antibacterial and antimycobacterial activity. Fluoroquinolones such as ciprofloxacin, gatifloxacin, and norfloxacin have shown the potential for shortening treatment duration, favourable pharmacokinetic profiles [1–3] and have been recommended in treatment of extensively drug-resistant tuberculosis (XDR-TB) [4]. In the present scenario, C-7 substitution is the most adaptable site for chemical change and is an area that determines potency and target preferences [5–8]. Hence the current work is the need for the development of novel antimicrobial agents to combat mycobacterium and bacterial infections, and providing the benefits of reduced toxicity [9].

2. Experimental

All the reagents and starting materials were purchased from Rankem, E. Merck, Himedia, and Spectrochem, India. Infrared (IR) spectra were recorded on a Nicolet MX-1 FTIR spectrophotometer, values measured in cm⁻¹. ¹H NMR were recorded at 400 MHz and ¹³C NMR were recorded at 100 MHz on a Bruker AM spectrometer, IISc Bangalore and values measured in δppm. C, H, N analysis was performed in a Heraeus CHN Rapid Analyzer. The FAB/EIMS mass spectra were recorded on Autospec Mass spectrometer, IICT, Hyderabad.

2.1. General Procedure for Synthesis of 2(a-i) [10, 11]. Equimolar quantities of substituted acetophenones **1(a-i)** and appropriate anhydrous solvents were taken in flask, the reaction condition was maintained either in cold or at room temperature, anhydrous aluminium chloride 0.1 g was

SCHEME 1

introduced and bromine (0.09 mol) was added with stirring. Compounds **2(a-i)** were obtained as brownish yellow to colourless crystals, washed twice with appropriate solvents, and recrystallized from methanol to get lachrymatory crystals (Scheme 1). Melting point ranges of **2(a-i)** were $48-50^\circ$, $90-92^\circ$, $110-112^\circ$, $96-98^\circ$, $52-58^\circ$, $72-74^\circ$, $46-48^\circ$, $64-66^\circ$, and $102-104^\circ\text{C}$, respectively; Yield: 60–65%.

2.2. General Procedure for Synthesis of 3(a-i). Add (0.1 mol) of 80% KOH to a suspension of (0.1 mol) of 2-amino-5-mercapto-1,3,4-thiadiazole, in 15 mL of water. Solution was clarified with activated charcoal and diluted with 32 mL of ethanol, 0.1 mol of **2(a-i)** was added rapidly with stirring. Thick reaction mixture was formed, stirred vigorously and cooled for 30–45 minutes, and then diluted with 200 mL of cold water. The solid was obtained by filtration, washed with water and ether. **3(a-i)** were obtained (Scheme 1), m.p. $90-98^\circ\text{C}$; Yield, 60–65%.

2.3. General Procedure for Synthesis of 4(a-i). Powder **3(a-i)** (15 mmol) with an excess of sodium nitrite (30 mmol). Introduce the mixture slowly with constant stirring, into an ice-cooled solution of 30 mL conc. hydrochloric acid and 15 mL water, maintained at $0-5^\circ\text{C}$ and heated up to 75°C for 1 hour. The reaction mixture was cooled and extracted with dry chloroform ($75\text{ mL} \times 3$). The combined

extracts were washed with sodium bicarbonate solution, and chloroform followed by evaporation under reduced pressure and finally recrystallized from ethanol to yield 2-chloro-5-benzoylmethylenethio-1,3,4-thiadiazole **4(a-i)** (Scheme 1). m.p. $108-116^\circ\text{C}$ (55–60%). Anal. Calcd.: $\text{C}_{10}\text{H}_7\text{N}_2\text{O}_2\text{S}_2\text{Cl}_2$: C, 40.00; H, 2.03; N, 9.33; Found C, 40.02; H, 2.01; N, 9.35. IR (KBr, cm^{-1}): 3100–62 (Ar. C–H Str.), 2820–60 (Ali. C–H Str.), 1635–70 (Ar. C=O Str.), 670–90 (Ali. C–S Str.). ^1H NMR(DMSO- d_6) δppm : 7.30–7.74 (m, 5H, Ar.), 4.74–5.28 (s, 2H, CH_2). ^{13}C NMR(DMSO- d_6) δppm : 194.2, 164.1, 136.1, 133.3, 40.8. MS (EIMS) m/z: 301.11 [M^+].

2.4. General Procedure for Synthesis of 5(a-i). A mixture of equimolar quantities of **4(a-i)**, and piperazinyl fluoroquinolone such as gatifloxacin, along with sodium-bicarbonate in 10 mL dimethylformamide was heated at $120-140^\circ\text{C}$ for 20–24 hrs. After cooling, 10 mL of cold water was added, and precipitate was filtered, recrystallized from DMF- H_2O to yield the titled compounds (Scheme 1).

3. Antibacterial Activity

Compounds **5b**, **5c**, and **5d** (MIC = 1, 1.5, 2.5) were found to be potent, comparable to reference, but most of the compounds did not produce enhanced gram negative activity. Reason might be the presence of tough double-layered

and excessive lipids containing cell wall of gram negative organisms. Broth microdilution method was employed for preliminary *in vitro* antibacterial activity. Two-fold serial dilutions of the test compounds and reference drugs were prepared in Mueller-Hinton agar medium. Progressive double dilutions with agar was performed to obtain the required concentrations of 0.5, 1, 2.5, 5, 7.5, 10, 12.5, 15, 17.5, and 20 $\mu\text{g/mL}$. Petri dishes were inoculated with $1-5 \times 10^4$ colonies forming units (cfu/mL) and incubated at 37°C for 18 hours [12]. The results are presented in Table 1.

4. Antimycobacterial Activity

Results indicate that 5(b, c, and d) exhibited significant activity (MIC = 1, 1.5, 1.5) as compared to first-line anti-TB drug rifampicin (MIC = 1.0 $\mu\text{g/mL}$) and comparable activity as compared to gatifloxacin (MIC = 1.0 $\mu\text{g/mL}$) and moxifloxacin (MIC = 0.5 $\mu\text{g/mL}$). Whereas moderate activity was observed in case of 5f, 5g, and 5h. *In vitro* antitubercular activity was performed using *M. tuberculosis* virulent H₃₇Rv strain. The MIC of each drug was determined by broth dilution assay, using frozen culture of Middlebrook 7H9 broth supplemented with 10% ADC (albumin dextrose catalase) and 0.2% glycerol. U-tubes were used to accommodate compounds in 20, 17.5, 15, 12.5, 10, 7.5, 05, 2.5, 1.5, 1.0, 0.5, and 0.1 $\mu\text{g/mL}$ dilutions [13–15]. The results are presented in Table 1.

5. Spectral Data

5.1. 7-[4-{5-(2-Oxo-2-phenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (5a). Yield 65%; m.p. 232°C; Anal. Calcd. for C₂₈H₂₈FN₅O₅S₂: C, 56.18; H, 4.68; N, 11.70 Found: C, 56.17; H, 4.70; N, 11.68 IR (KBr, cm⁻¹): 3420, 2850, 1730, 1680, 1620, 742, 680. ¹H NMR(DMSO-*d*₆) δ ppm: 13.50 (s, 1H, OH), 7.90 (s, 1H, H2-quinoline), 7.37–7.45 (m, 5H, Ar.), 6.70 (d, 1H, H5-quinoline), 4.24 (s, 2H, CH₂), 3.84 (s, 3H, methoxyl), 3.24–3.52 (m, 7H, piperazinyl), 3.10 (q, 2H, NCH₂CH₃), 1.34 (m, 3H, 3'-methylpiperazine), 1.14 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δ ppm: 195.4, 178.2, 166.8, 164.8, 148.2, 146.4, 145.5, 136.7, 133.2, 132.5, 129.8, 118.4, 116.5, 109.4, 108.5, 56.3, 55.4, 49.8, 38.5, 16.8 13.1. MS (FAB) m/z: 599 [M + 1].

5.2. 7-[4-{5-(2-Oxo-2-p-chlorophenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (5b). Yield 70%; m.p. 224°C; Anal. Calcd. for C₂₈H₂₇ClFN₅O₅S₂: C, 53.16; H, 4.27; N, 11.00 Found: C, 53.18; H, 4.25; N, 11.10 IR (KBr, cm⁻¹): 3448, 2825, 1720, 1690, 1622, 748, 684. ¹H NMR(DMSO-*d*₆) δ ppm: 13.68 (s, 1H, OH), 8.02 (s, 1H, H2-quinoline), 7.88 (m, 2H, Ar.), 7.40 (m, 2H, Ar.), 6.64 (d, 1H, H5-quinoline), 4.30 (s, 2H, CH₂), 3.88 (s, 3H, methoxyl), 3.20–3.46 (m, 7H, piperazinyl), 3.20 (q, 2H, NCH₂CH₃), 1.24 (m, 3H, 3'-methylpiperazine), 1.18 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δ ppm: 196.1, 178.1, 166.4, 148.2, 146.4,

138.4, 134.4, 132.0, 128.3, 119.5, 115.8, 110.8, 107.6, 56.8, 50.3, 39.7, 17.3 15.2.

5.3. 7-[4-{5-(2-Oxo-2-p-bromophenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (5c). Yield 68%; m.p. 228°C; Anal. Calcd. for C₂₈H₂₇BrFN₅O₅S₂: C, 49.70; H, 3.99; N, 10.35 Found: C, 49.68; H, 4.00; N, 10.34 IR (KBr, cm⁻¹): 3468, 2840, 1735, 1670, 1596, 752, 690. ¹H NMR(DMSO-*d*₆) δ ppm: 14.06 (br, s, 1H, OH), 7.98 (s, 1H, H2-quinoline), 7.78 (m, 2H, Ar.) 7.34 (m, 2H, Ar.), 6.66 (d, 1H, H5-quinoline), 4.24 (s, 2H, CH₂), 3.94 (s, 3H, methoxyl), 3.18–3.38 (m, 7H, piperazine), 3.10 (q, 2H, NCH₂CH₃), 1.20 (m, 3H, 3'-methylpiperazine), 1.10 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δ ppm: 197.4, 180.1, 170.4, 150.3, 145.4, 139.4, 136.4, 130.9, 126.3, 118.5, 116.8, 109.6, 105.5, 56.4, 50.4, 39.9, 16.5, 14.4. MS (FAB) m/z: 677 [M + 1].

5.4. 7-[4-{5-(2-Oxo-2-p-nitrophenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (5d). Yield 60%; m.p. 240°C; Anal. Calcd. for C₂₈H₂₇FN₆O₇S₂: C, 52.25; H, 4.19; N, 13.06 Found: C, 52.28; H, 4.20; N, 13.08 IR (KBr, cm⁻¹): 3480, 2860, 1760, 1650, 1605, 752, 692. ¹H NMR(DMSO-*d*₆) δ ppm: 14.70 (s, 1H, OH), 7.93 (s, 1H, H2-quinoline), 8.36 (m, 2H, Ar.) 8.20 (m, 2H, Ar.), 6.80 (d, 1H, H5-quinoline), 4.32 (s, 2H, CH₂), 3.96 (s, 3H, methoxyl), 3.24–3.48 (m, 7H, piperazinyl), 3.20 (q, 2H, NCH₂CH₃), 1.40 (m, 3H, 3'-methylpiperazine), 1.16 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δ ppm: 198.6, 184.2, 172.5, 152.4, 147.4, 142.3, 138.4, 133.1, 131.4, 127.4, 120.2, 117.5, 110.7, 106.7, 57.8, 51.4, 40.2, 17.2, 14.8.

5.5. 7-[4-{5-(2-Oxo-2-p-methylphenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (5e). Yield 56%, m.p. 252°C(dec.) Anal. Calcd. for C₂₉H₃₀FN₅O₅S₂: C, 56.82; H, 4.90; N, 11.43 Found C, 56.84; H, 4.88; N, 11.44. IR (KBr, cm⁻¹): 3446, 2848, 1720, 1610, 1570, 738, 670. ¹H NMR(DMSO-*d*₆) δ ppm: 14.62 (s, 1H, OH), 8.12 (m, 2H, Ar.), 7.84 (s, 1H, H2-quinoline), 7.37 (m, 2H, Ar.), 6.50 (d, 1H, H5-quinoline), 4.21 (s, 2H, CH₂), 3.84 (s, 3H, methoxyl), 3.10–3.30 (m, 7H, piperazinyl), 3.00 (q, 2H, NCH₂CH₃), 2.85 (s, 3H, Ar. methyl), 1.30 (m, 3H, 3'-methylpiperazine), 1.16 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δ ppm: 190.4, 172.3, 160.4, 158.2, 145.6, 142.8, 140.4, 135.7, 132.5, 130.4, 128.5, 126.6, 124.5, 117.6, 107.8, 56.7, 49.7, 45.4, 37.6, 24.8, 16.1, 12.9.

5.6. 7-[4-{5-(2-Oxo-2-p-methoxyphenylethylthio)-1,3,4-thiadiazol-2-yl}-3'-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (5f). Yield 60%; m.p. 228°C; Anal. Calcd. for C₂₉H₃₀FN₅O₆S₂: C, 55.41; H, 4.77; N, 11.14 Found: C, 55.43; H, 4.78; N, 11.14. IR (KBr, cm⁻¹): 3436, 2936, 2832, 1738, 1692, 1648, 1033, 742, 676. ¹H NMR(DMSO-*d*₆) δ ppm: 14.40 (s, 1H, OH), 7.82 (s, 1H, H2-quinoline), 7.75 (m, 2H, Ar.), 6.88 (m, 2H, Ar.),

TABLE 1: Antibacterial and antimycobacterial activity against the screened compounds 5(a-i).

Compound number	^b <i>Escherichiafaecelis</i>	^b <i>Staphylococcusepidermidis</i>	^b <i>Klebsiellaspecies</i>	^b <i>Citrobacterfreundi</i>	<i>MycobacteriumTuberculosis</i>
	^a MIC	^a MIC	^a MIC	^a MIC	MIC
5a	15	17.5	>20	>20	Resist
5b	1	1	2.5	>1	1
5c	2.5	2.5	5	2.5	1.5
5d	1	2.5	2.5	5	1.5
5e	≥12.5	≥12.5	15	15	Resist
5f	10	12.5	17.5	15	Resist
5g	7.5	5	10	10	5
5h	5	5	7.5	5	10
5i	10	12.5	10	12.5	15
^c CIP	≤1	1	1	1	—
^c GTZ	<1	≤1	1	1	1.0
^c RIP	—	—	—	—	1
^c MXF	—	—	—	—	0.5

^aMIC: Minimum inhibitory concentration (in µg/mL) required to inhibit 90% inhibition against *M. TB* and antibacterial.

^b*Escherichia faecelis* (Ef) MTCC 2729, *Staphylococcus epidermididis* (Se) MTCC 3382, *Klebsiella species* (Ks) MTCC 3384, and *Citrobacter freundii* (Cf) MTCC1658.

^cCIP: ciprofloxacin; GTZ: gatifloxacin; RIP: rifampicin; MXF: moxifloxacin as reference pure drug.

6.36 (d, 1H, H5-quinoline), 4.37 (s, 2H, CH₂), 4.02 (s, 3H, methoxyl), 3.75 (s, 3H, Ar. C-OCH₃), 3.20–3.40 (m, 7H, piperaziny), 3.06 (q, 2H, NCH₂CH₃), 1.18 (m, 3H, 3'-methylpiperazine), 1.14 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δppm: 192.6, 174.4, 165.2, 158.4, 145.8, 144.4, 142.3, 138.6, 132.8, 130.6, 129.8, 126.8, 125.2, 114.4, 107.4, 56.8, 49.8, 45.9, 36.5, 25.3, 16.6, 13.6.

5.7. 7-[4-{5-(2-Oxo-2-*p*-fluorophenylethylthio)-1,3,4-thiadiazol-2yl}-3'-methylpiperazin-1yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (**5g**). Yield 48%; m.p. 190°C; Anal.Calcd.for C₂₈H₂₇F₂N₅O₅S₂: C, 54.54; H, 4.38; N, 11.36 Found C, 54.56; H, 4.36; N, 11.12. IR (KBr, cm⁻¹): 3442, 2891, 2849, 1744, 1690, 1654, 764, 667. ¹H NMR(DMSO-*d*₆) δppm: 14.47 (s, 1H, OH), 7.86 (m, 2H, Ar.), 7.78 (s, 1H, H2-quinoline), 7.10 (m, 2H, Ar.), 6.50 (d, 1H, H5-quinoline), 4.35 (s, 2H, CH₂), 3.92 (s, 3H, methoxyl), 3.22–3.44 (m, 7H, piperaziny), 3.10 (q, 2H, NCH₂CH₃), 1.16 (m, 3H, 3'-methylpiperazine), 1.10 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δppm: 195.2, 176.2, 167.4, 158.6, 147.4, 145.3, 143.4, 140.2, 133.9, 132.4, 128.4, 115.6, 108.6, 56.2, 50.4, 37.4, 26.3, 17.9, 14.4.

5.8. 7-[4-{5-(2-Oxo-2-*p*-aminophenylethylthio)-1,3,4-thiadiazol-2yl}-3'-methylpiperazin-1yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (**5h**). Yield 58%; m.p. 236°C; Anal.Calcd. for C₂₈H₂₉FN₅O₅S₂: C, 54.90; H, 4.73; N, 13.72 Found C, 54.89; H, 4.74; N, 13.74. IR (KBr, cm⁻¹): 3460, 3370, 2860, 1742, 1635, 1610, 760, 690. ¹H NMR(DMSO-*d*₆) δppm: 14.90 (br, s, 1H, OH), 7.63 (m, 2H, Ar.), 7.98 (s, 1H, H2-quinoline), 6.59 (m, 2H, Ar.), 6.90 (d, 1H, H5-quinoline), 4.38 (s, 2H, CH₂), 4.10 (s, 2H, Ar.-NH₂), 3.90 (s, 3H, methoxyl), 3.30–3.54 (m, 7H, piperaziny), 3.24

(q, 2H, NCH₂CH₃), 1.46 (m, 3H, 3'-methylpiperazine), 1.21 (t, 3H, NCH₂CH₃). ¹³C NMR(DMSO-*d*₆) δppm: 200.5, 188.4, 175.6, 155.5, 145.4, 140.2, 135.4, 133.6, 128.9, 122.4, 119.7, 112.2, 108.3, 60.4, 55.7, 43.7, 19.8, 15.4. MS (FAB) m/z: 614.4 [M+2].

5.9. 7-[4-{5-(2-Oxo-2-*p*-hydroxyphenylethylthio)-1,3,4-thiadiazol-2yl}-3'-methylpiperazin-1yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic Acid (**5i**). Yield 62%; m.p. 244°C; Anal.Calcd. for C₂₈H₂₈FN₅O₆S₂: C, 54.81; H, 4.56; N, 11.41; Found C, 54.82; H, 4.56; N, 11.43. IR (KBr, cm⁻¹): 3565, 3410, 2825, 1760, 1670, 1617, 754, 680. ¹H NMR(DMSO-*d*₆) δppm: 14.60 (s, 1H, OH), 8.20 (s, 1H, H2-quinoline), 7.72 (m, 2H, Ar.), 6.86 (m, 2H, Ar.), 7.02 (d, 1H, H5-quinoline), 5.46 (s, 1H, Ar.-hydroxyl) 4.24 (s, 2H, CH₂), 3.84 (s, 3H, methoxyl), 3.28–3.49 (m, 7H, piperaziny), 3.06 (q, 2H, NCH₂CH₃), 1.22 (t, 3H, NCH₂CH₃), 1.14 (m, 3H, 3'-methylpiperazine). ¹³C NMR(DMSO-*d*₆) δppm: 196.5, 186.2, 174.3, 154.4, 149.7, 144.1, 138.2, 134.3, 127.6, 121.4, 115.3, 111.4, 107.2, 58.4, 54.3, 42.4, 17.8, 12.7.

6. Result and Discussion

6.1. *Chemistry*. The synthesis of substituted phenacyl bromide **2(a-i)** was based on free radical reaction mechanism followed by side-chain halogenations of alkyl benzene with bromide ion in presence of Lewis acid (anhydrous AlCl₃) [16]. The synthesis of 2-amino-5-benzoylmethylenethio-1,3,4-thiadiazole **3(a-i)** was carried out by reacting **2(a-i)** and 2-amino-5-mercapto-1,3,4-thiadiazole via dehydrobromination mechanisms. Compounds **3(a-i)** were directly converted to 2-chloro-5-benzoylmethylenethio-1,3,4-thiadiazole **4(a-i)** by diazotization of amines followed by

chlorination. The synthesis of 7-[4-{5-(2-oxo-2-*p*-substituted-phenylethylthio)-1,3,4-thiadiazol-2-yl}-3-methylpiperazin-1-yl]-1-ethyl-6-fluoro-8-methoxyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **5(a-i)** was based on aromatic nucleophilic substitution mechanism with FQ.

6.2. Structure Activity Relationship for **5(a-i)**

- (i) Introduction of 1,3,4-thiadiazole carrying benzoylmethylenethio moiety at N-4 position on the piperazine ring was well tolerated in terms of antibacterial and antimycobacterial activity, as exemplified by gatifloxacin and moxifloxacin analogues. Compound **5a** that is, unsubstituted analogue at R position did not produce enhanced activity.
- (ii) Halogenated analogues such as chloro, bromo and also the nitro substitution at 2-Oxo-2-*p*-phenylethylthio-1,3,4-thiadiazole linked to N-4-3' methyl piperazinyl quinolone, **5b**, **5c**, and **5d**, respectively, resulted in comparable activity with MIC = 1.0–2.5 µg/mL (gram positive and antitubercular). However the fluoro analogue **5g** showed moderate activity might be due to highly unstable behavior of fluorine atom.
- (iii) Presence of amino and hydroxyl substituent, such as **5h** and **5i**, showed moderate activity, while compounds having methyl and methoxyl substituent such as **5e** and **5f** showed weak activity.

7. Conclusions

Compounds **5(a-i)** were synthesized by conventional synthetic route and these analogues were confirmed with various spectral techniques. Titled derivatives were screened for antibacterial and antimycobacterial activity which possess similar activity for **5b**, **5c**, and **5d** compared to reference.

But less activity than moxifloxacin, whereas other derivatives of the series showed moderate to weak activity. Results indicate that further exploration in this field may lead to new synthetic derivatives and scope of other pharmacological and biological studies of the existing compounds.

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