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# Synthesis and Antimicrobial Study of Sulfonamide Derivatives of Fluoroquinolone

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**Abstract:** A new series of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-substituted piperazin-1-yl-3-quinoline carboxylic acids with amino sulfonamide and benzene sulfonamide at C-3 position have been prepared and tested against *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa* as bacterial strains, using cup plate method. All the final compounds were characterized by IR, $^{1}$H NMR spectra and elemental analysis. Compounds 4c, 4e, 4h, 5e, 5h and 6b demonstrated promising antibacterial activity against selected bacterial strains.

**Keywords:** Fluoroquinolone derivatives, sulfonamides, antibacterial activity.

## 1. Introduction:

Fluoroquinolones have been clinically applied since the mid-1980s and widely used for the treatment of various bacterial infections like lower respiratory tract, urinary tract, and skin/ soft tissue, as well as sexually transmitted diseases. Fluoroquinolones were investigated as inhibitors of DNA gyrase/topoisomerase IV enzyme [1]. Structure activity relationship of fluoroquinolones has been studied in some reviews [2, 3], which indicate that carboxylic acid group or hydrolysable carboxylic derivatives viz. ester and amide at C-3 is essential for DNA gyrase binding. Basic group at C-7 position can influence the antibacterial activity and pharmacokinetics. They are extensively investigated as antidiabetic [4], antitumor [5], antiviral [6], anti-HIV [7] and antifilarial [8] agents.

Sulfonamides were the first introduced as antimicrobial drugs. They demonstrated bacteriostatic activity by competitively inhibiting the bio-synthesis of folic acid [9]. Their derivatives act as carbonic anhydrase inhibitors [10], anticancer agent [11], anti-inflammatory agents [12], anti-HIV agents

[13], COX-2 inhibitors [14] and selective 5-HT receptor antagonist [15], antitubercular [16] and antifungal agents [17].

We have observed the structural and improved biological variation for hydrolysable carboxylic acid derivatives viz. amides and ester of fluoroquinolones [18-19], hence we have synthesized 3-sulfacaboxamide and 3-carboxamide derivatives of fluoroquinolones and studied their antibacterial activities were compared with standard drug Penicillin, Streptomycin, Tetracycline & Ciprofloxacin. The antibacterial testing was carried out by *cup-plate* method [20].

## 2. Results and Discussion:

### 2.1. Chemistry

Lead molecule converted to acid chloride on treatment with thionyl chloride, which on condensation with substituted amino sulfonamide and substituted benzene sulfonamides gave amide derivatives. Substituted piperazin-1-yl group introduced further on condensation with sulfonamide. (Scheme 1) Structure of the compounds elucidated by $^1$H NMR and IR spectroscopy. 3445 (NH), 2930 (C-H), 1642 (amide-I), 1540 (amide-II), 1268 (C-F), 1230 (amide-III), 1045 (C-N, piperazine), 1350, 1160 (S=O, asym., sym.), some additional peaks appear due to substitution in aromatic ring showing absorption band at 1356, 1550 (-$NO_2$ sym, asym). In $^1$H-NMR spectra common singlet signals appears at δ 8.18, 8.22 corresponding to $H_2$, $H_8$ and doublet at δ 8.35 corresponding to $H_5$ of quinolone ring, a multiplet at δ 3.66 corresponding to >N-CH-, a multiplet at δ 1.15 to 1.42 corresponding to cyclopropyl, a singlet at δ 9.45 corresponding to >CONH, singlet signal at δ 10.85 appeared corresponding to $SO_2$NH- and due to substitution on phenyl ring singlet single signal appeared at δ 1.95, 4.10 corresponding to –$CH_3$, -$OCH_3$, on addition of different piperazin-1-yl group multiplet at δ 2.37-3.15 observed corresponding to piperazine, multiplet at δ 2.15 due to hydroxy ethyl group, a multiplet at δ 6.24-7.50 corresponding to aromatic proton.

### 2.2. Antimicrobial activity

All the synthesized compounds were screened for their antibacterial proprieties against *S. aureus*, *B. subtilis* (Gram positive) and *E. coli*, *P. aeruginosa* (Gram negative) by cup-plate method [20] taking penicillin, streptomycin, tetracycline and ciprofloxacin as standard drugs. (Table 1) The compounds were tested at the concentration of 100 mg/ml in DMF as solvent. Compounds **4d, 5b, 5d, 5f, 5h, 6c, 6d, 6e, 6l** demonstrated comparable activity, whereas **4a, 6f** found highly active against *S. aureus*. Compounds **4a, 4g, 4i, 5a, 5b, 5d, 5k, 6c, 6d, 6h, 6i, 6k, 6j** showed promising activity, compounds **4c, 4e, 5c, 5f, 5g, 6b, 6h, 5i, 5j, 6a, 6f** found to be very active and **5e, 5h** found highest activity against *B. subtilis*. Compounds **4c, 4e, 4f, 5a, 5d, 5e,** and **5h** demonstrated comparable activity against *E. coli*. Compounds **4b, 4d, 4g, 4i, 4k, 5b, 5c, 5d, 5f, 5g, 6a, 6e, 6f, 6h** showed also comparable activity and compounds **4f, 5h, 5j, 5k, 6c, 6d** demonstrated promising activity, whereas **4h, 6b** found highest activity against *P. aeruginosa* with compared to standard drugs.

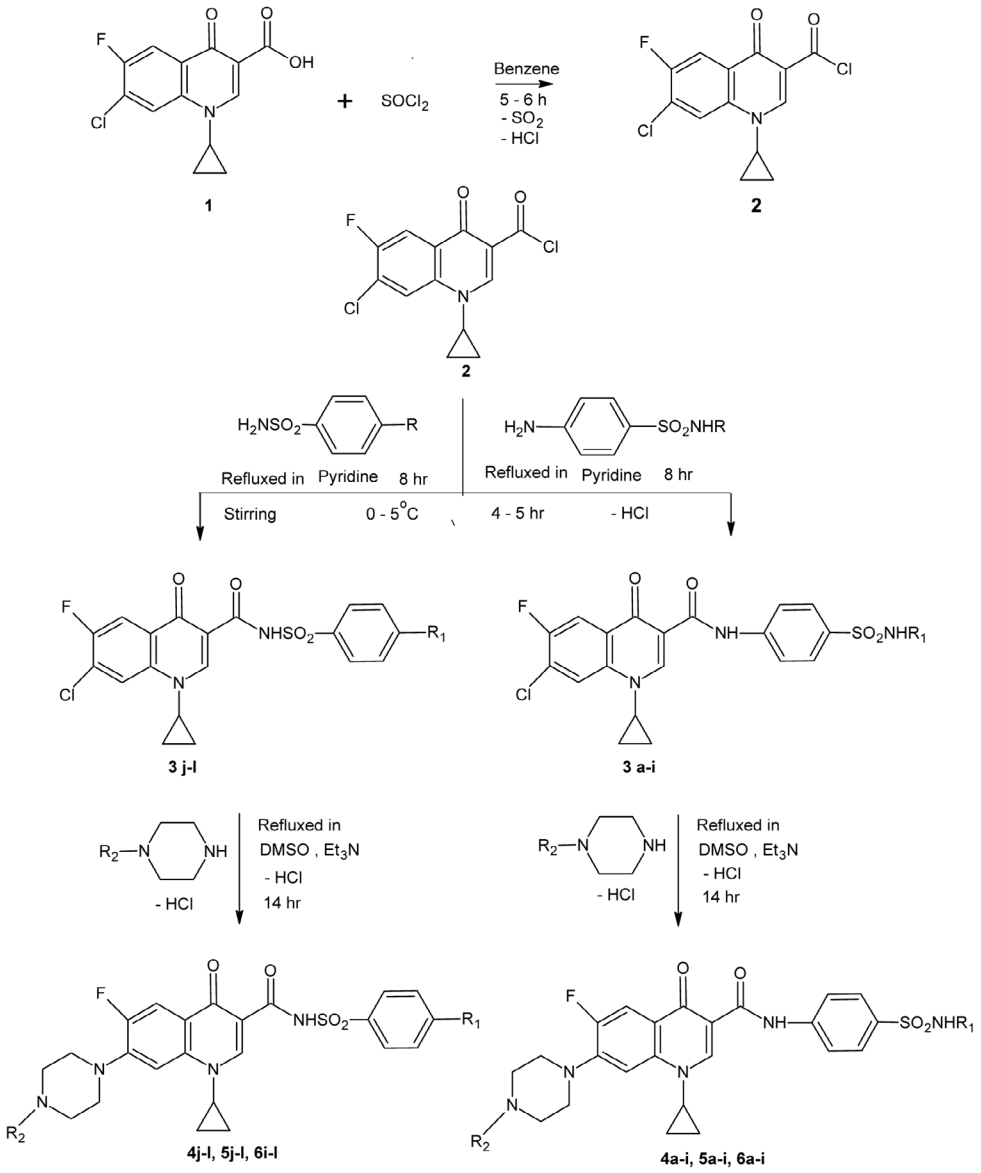
## 3. Experimental:

### 3.1. Materials, methods and instruments

All melting points were determined by using open capillary method and are uncorrected. IR spectra were recorded on Perkin-Elmer-838 FT-IR spectrophotometer using KBr pellet. $^1$H NMR spectra were recorded in $DMSOd_6$ on Bruker DRX-300 (300MHz FT NMR) instrument and chemical shifts were expressed in δ ppm against TMS as internal reference. Purity of compounds was checked by TLC using silica gel.

### 3.2 Synthesis of 1-cyclopropyl-6-fluoro-

**Scheme-1.** Synthetic protocol for final compounds **4a-l, 5a-l, 6a-l**




**$R_1$** =

a. $-C_6H_5$ b. $2\text{-}CH_3C_6H_5$ c. $4\text{-}CH_3C_6H_5$ d. $3\text{-}NO_2C_6H_5$ e. $4\text{-}NO_2C_6H_5$ f. $2\text{-}OCH_3C_6H_5$
g. $4\text{-}OCH_3C_6H_5$ h. 4,6-$(CH_3)_2$ pyridine i. 1-$(C_6H_5)$-1*H* pyrole j. $4\text{-}NHCOCH_3$ k. $4\text{-}CH_3$ l. $4\text{-}OCH_3$

**$R_2$** = H for 4a-l, **$R_2$** = $-CH_3$ for 5a-l, **$R_3$** = $-CH_2CH_2OH$ for 6a-l

**Scheme 1**

**Table 1: Antibacterial activity of synthesized compounds (4a-l, 5a-l, 6a-l)**

| Compound | *S. aureus* | | *B. subtilis* | | *E. coli* | | *P. aeruginosa* | |
|---|---|---|---|---|---|---|---|---|
| | Z.I | A.I. | Z.I. | A.I. | Z.I. | A.I. | Z.I. | A.I. |
| **4a** | 20 | 0.7 | 17 | 0.55 | 09 | 0.3 | 10 | 0.45 |
| **4b** | 09 | 0.3 | 11 | 0.35 | 11 | 0.4 | 12 | 0.5 |
| **4c** | 12 | 0.4 | 32 | 1.0 | 14 | 0.5 | 09 | 0.4 |
| **4d** | 14 | 0.5 | 14 | 0.45 | 10 | 0.4 | 12 | 0.5 |
| **4e** | 11 | 0.4 | 30 | 1.0 | 14 | 0.5 | 10 | 0.45 |
| **4f** | 09 | 0.3 | 12 | 0.4 | 13 | 0.5 | 15 | 0.7 |
| **4g** | 13 | 0.45 | 15 | 0.5 | 11 | 0.4 | 13 | 0.6 |
| **4h** | 12 | 0.4 | 13 | 0.4 | 09 | 0.3 | 24 | 1.1 |
| **4i** | 09 | 0.3 | 20 | 0.65 | 12 | 0.45 | 14 | 0.6 |
| **4j** | 10 | 0.35 | 13 | 0.4 | 10 | 0.4 | 10 | 0.45 |
| **4k** | 11 | 0.4 | 10 | 0.33 | 09 | 0.3 | 11 | 0.5 |
| **4l** | 13 | 0.45 | 13 | 0.4 | 11 | 0.4 | 09 | 0.4 |
| **5a** | 10 | 0.35 | 16 | 0.5 | 15 | 0.55 | 10 | 0.45 |
| **5b** | 14 | 0.5 | 18 | 0.6 | 09 | 0.3 | 11 | 0.5 |
| **5c** | 10 | 0.35 | 22 | 0.7 | 11 | 0.4 | 14 | 0.6 |
| **5d** | 15 | 0.5 | 17 | 0.55 | 14 | 0.5 | 15 | 0.7 |
| **5e** | 13 | 0.45 | 34 | 1.1 | 13 | 0.5 | 10 | 0.45 |
| **5f** | 14 | 0.5 | 27 | 0.9 | 09 | 0.3 | 12 | 0.5 |
| **5g** | 09 | 0.3 | 22 | 0.7 | 10 | 0.4 | 11 | 0.5 |
| **5h** | 16 | 0.55 | 35 | 1.1 | 13 | 0.5 | 16 | 0.7 |
| **5i** | 11 | 0.4 | 24 | 0.8 | 11 | 0.4 | 09 | 0.4 |
| **5j** | 13 | 0.45 | 22 | 0.7 | 10 | 0.4 | 17 | 0.75 |
| **5k** | 12 | 0.4 | 19 | 0.6 | 12 | 0.45 | 18 | 0.8 |
| **5l** | 11 | 0.4 | 14 | 0.45 | 10 | 0.4 | 10 | 0.45 |
| **6a** | 11 | 0.4 | 21 | 0.7 | 10 | 0.4 | 14 | 0.6 |
| **6b** | 09 | 0.3 | 25 | 0.8 | 09 | 0.3 | 24 | 1.1 |
| **6c** | 14 | 0.5 | 15 | 0.5 | 11 | 0.4 | 17 | 0.75 |
| **6d** | 16 | 0.55 | 17 | 0.55 | 11 | 0.4 | 19 | 0.85 |
| **6e** | 14 | 0.5 | 10 | 0.3 | 09 | 0.3 | 12 | 0.5 |
| **6f** | 22 | 0.8 | 29 | 1.0 | 09 | 0.3 | 14 | 0.6 |
| **6g** | 12 | 0.4 | 14 | 0.45 | 10 | 0.4 | 10 | 0.45 |
| **6h** | 10 | 0.35 | 19 | 0.6 | 10 | 0.4 | 12 | 0.5 |
| **6i** | 11 | 0.4 | 17 | 0.55 | 11 | 0.4 | 09 | 0.4 |
| **6j** | 09 | 0.3 | 16 | 0.5 | 09 | 0.3 | 10 | 0.45 |
| **6k** | 12 | 0.4 | 18 | 0.6 | 09 | 0.3 | 10 | 0.45 |
| **6l** | 15 | 0.5 | 14 | 0.45 | 11 | 0.4 | 09 | 0.4 |
| **Ciprofloxacin** | **28** | | **30** | | **26** | | **22** | |
| **Penicillin,** | **30** | | **28** | | **20** | | | |
| **Streptomycin,** | **28** | | **25** | | **21** | | | |
| **Tetracycline** | **26** | | **28** | | **22** | | | |

**Z.I** = Zone of inhibition in mm, **A.I.** = Activity index
**A.I.** = Zone of inhibition of compounds / Zone of inhibition of standard drug

**1,4-dihydro-4-oxo-7-chloro-3-quinoline carbonyl chloride (2)**

The mixture of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-chloro-3-quinoline carboxylic acid **1** (0.01 mol), DMF (1 ml) and thionyl chloride (0.01 mol) was refluxed using benzene as a solvent on water bath at 80 C° for 5-6 h in anhydrous condition with the help of calcium chloride guard tube, until the HCl gas evolution was ceased, then solvent and thionyl chloride were removed by distillation. The solid material of the title compound **2** obtained was cooled and used in next step.

### 3.3 General procedure for synthesis of *N*-[4-(substituted aryl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-chloro-4-oxo-1,4-dihydroquinoline-3-carboxamides (3a-i)

The respective amino sulfonamide (0.005 mol) dissolved in dry pyridine, place it in ice-bath and the solution of carbonyl chloride **2** (0.005 mol) in pyridine was added drop wise over a period of about 1.5 h with constant stirring at 0-5 °C. The reaction a mixture was stirred further for 2 h at room temperature, refluxed for 8 h and cooled to room temperature. The whole content was pour into acidic crushed ice with gentle shaking. The resultant solid was filtered and was washed thoroughly with aqueous $NaHCO_3$ (10 %) solution. All the compounds were recrystallized from ethanol: DMSO (1:2) to give **3a-i**. The purity of the compounds was checked by TLC on silica gel plate using benzene: ethyl acetate (8:2).

### 3.4. General procedure for synthesis of *N*-[(substituted phenyl) sulfonyl]-1-cyclopropyl-6-fluoro-7-chloro-4-oxo-1,4-dihydroquinoline-3-carboxamides (3j-l)

The respective substituted benzene sulfonamide (0.005 mol) dissolved in dry pyridine, place it in ice-bath and the solution of carbonyl chloride **2** (0.005 mol) in pyridine was added drop wise about 1.5 h period with constant stirring at 0-5 °C. The reaction mixture was stirred further for 2 h at room temperature, refluxed for 8 h and cooled it at room temperature. The whole content was pour into acidic crushed ice with gentle shaking. The resultant solid was filtered and was washed thoroughly with aqueous $NaHCO_3$ (10 %) solution. (1:1). All the compounds were recrystallized from ethanol: DMSO (1:2) to give **3j-l**. The purity of the compounds was checked by TLC on silica gel plate using benzene: ethyl acetate (8:2)

### 3.5 General procedure for synthesis of *N*-[4-(substituted aryl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(substituted-piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamides (4a-i, 5a-i, 6a-i)

The mixture of **3a-i** (0.001 mol), respective *N*-substituted piperazine (0.005 mol), $CH_3CN$ (10 ml), DMSO (5 ml) and $Et_3N$ was refluxed at 135C for 14 h and cool at room temperature. The resultant mass was poured in to crushed ice and neutralized with dilute HCl. The product were filtered, dried and recrystallized from absolute alcohol: DMSO (1:2) mixture to give **4a-i, 5a-i** and **6a-i**. The purities of the compounds were checked by TLC on silica gel plate using toluene: ethyl acetate (7:3).

*N-[4-(phenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7- piperazin-1-yl-4-oxo-1,4-dihydro-quinoline-3-carboxamide **(4a)***

Yield: 75%; mp: 188-189°C; IR (KBr) $cm^{-1}$: 3440 (NH), 2930 (C-H), 1645 (amide-I), 1540 (amide-II), 1350, 1160 (S=O, asym, sym), 1265 (C-F), 1230 (amide-III), 1045 (C-N piperazine);$^1$H NMR (300 MHz, $d_6$-DMSO) δ ppm: 1.15-1.52 (m, 4H, cyclopropyl), 3.77 (m, 1H, >N-CH-), 2.25-3.05 (m, 8H, piperazine), 6.24-7.50 (m, 9H, Ar-H), 8.18 (s, 1H, $H_2$), 8.37 (d, 1H, $H_5$), 8.22 (s, 1H, $H_8$), 9.45 (1H, s, -CONH-), 10.85 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.01; H, 5.03; N, 12.48. Found: C, 62.04; H, 5.04; N, 12.45.

*N-[4-(2-methylphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4b**)*
Yield: 72%; mp: 192-195˚C; IR (KBr) $cm^{-1}$: 3444 (NH), 2945 (C-H), 1652 (amide-I), 1537 (amide-II), 1360, 1165 (S=O, asym, sym), 1257 (C-F). 1212 (amide-III), 1052 (C-N piperazine); $^1H$ NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.05-1.68 (m, 4H, cyclopropyl), 3.62 (m, 1H, >N-CH-), 2.28-3.05 (m, 8H, piperazine), 6.34-7.45 (m, 8H, Ar-H), 8.16 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.35 (s, 1H, $H_8$), 2.19 (s, 3H, Ar-$CH_3$), 9.15 (s, 1H, -CONH-), 10.75 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.59; H, 5.26; N, 12.17. Found: C, 62.68; H, 5.24; N, 12.15.

*N-[4-(4-methylphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7- piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4c**)*
Yield: 69%; mp: 196-199˚C; IR (KBr) $cm^{-1}$: 3452 (NH), 2942 (C-H), 1660 (amide-I), 1540 (amide-II), 1355, 1172 (S=O, asym, sym), 1260 (C-F), 1220 (amide-III), 1047 (C-N piperazine); $^1H$ NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.15-1.70 (m, 4H, cyclopropyl), 3.67 (m, 1H, >N-CH-), 2.26-3.21 (m, 8H, piperazine), 6.24-7.35 (m, 8H, Ar-H), 8.18 (s, 1H, $H_2$), 8.47 (d, 1H, $H_5$), 8.25 (s, 1H, $H_8$), 2.21 (s, 3H, Ar-$CH_3$), 9.10 (s, 1H, -CONH-), 10.67 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.59; H, 5.26; N, 12.17. Found: C, 62.56; H, 5.23; N, 12.14.

*N-[4-(3-nitrophenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4d**)*
Yield: 68%; mp: 206-208˚C; IR (KBr) $cm^{-1}$: 3460 (NH), 2945 (C-H), 1655 (amide-I), 1535 (amide-II), 1345, 1169 (S=O, asym, sym), 1264 (C-F), 1215 (amide-III), 1035 (C-N piperazine), 1356, 1550 (-$NO_2$ sym, asym); $^1H$ NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.10-1.62 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.16-3.18 (m, 8H, piperazine), 6.10-7.25 (m, 8H, Ar-H), 8.20 (s, 1H, $H_2$), 8.48 (d, 1H, $H_5$), 8.35 (s, 1H, $H_8$), 9.10 (s, 1H, -CONH-), 10.67 (s, 1H, -$SO_2$NH-); Calcd.: C, 57.41; H, 4.49; N, 13.86. Found: C, 57.38; H, 4.46; N, 13.84.

*N-[4-(4-nitrophenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4e**)*
Yield: 69%; mp: 199-201˚C; IR (KBr) $cm^{-1}$: 3457 (NH), 2960 (C-H), 1670 (amide-I), 1540 (amide-II), 1352, 1157 (S=O, asym, sym), 1270 (C-F), 1220 (amide-III), 1040 (C-N piperazine), 1354, 1545 (-$NO_2$ sym, asym); $^1H$ NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.15-1.70 (m, 4H, cyclopropyl), 3.67 (m, 1H, >N-CH-), 2.15-3.21 (m, 8H, piperazine), 6.24-7.35 (m, 8H, Ar-H), 8.17 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.42 (s, 1H, $H_8$), 9.10 (s, 1H, -CONH-), 10.67 (s, 1H, -$SO_2$NH-); Calcd.: C, 57.41; H, 4.49; N, 13.86. Found: C, 57.39; H, 4.45; N, 13.83.

*N-[4-(2-methoxyphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4f**)*
Yield: 71%; mp: 188-190˚C; IR (KBr) $cm^{-1}$: IR: δ= 3455 (NH), 2962 (C-H), 1672 (amide-I), 1535 (amide-II), 1345, 1155 (S=O, asym, sym), 1273 (C-F), 1225 (amide-III), 1035 (C-N piperazine), 1011, 1221 (C-O-C); $^1H$ NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.18-1.62 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.17-3.05 (m, 8H, piperazine), 6.14-7.25 (m, 8H, Ar-H), 8.10 (s, 1H, $H_2$), 8.47 (d, 1H, $H_5$), 8.20 (s, 1H, $H_8$), 4.05 (s, 3H, -$OCH_3$), 9.15 (s, 1H, -CONH-), 10.68 (s, 1H, -$SO_2$NH-); Calcd.: C, 60.89; H, 5.11; N, 11.84. Found: C, 60.89; H, 5.09; N, 11.82.

*N-[4-(4-methoxyphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4g**)*
Yield: 67%; mp: 192-195˚C; IR (KBr) $cm^{-1}$: IR: δ= 3458 (NH), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276 (C-F), 1225 (amide-III), 1035 (C-N piperazine), 1015, 1219 (C-O-C); $^1H$ NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.59 (m, 4H, cyclopropyl), 3.65 (m, 1H, >N-CH-), 2.18-3.15 (m, 8H, piperazine), 6.04-7.15 (m, 8H, Ar-H),

8.07 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.15 (s, 1H, $H_8$), 4.10 (s, 3H, -$OCH_3$), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H,-$SO_2$NH-); Calcd.: C, 60.89; H, 5.11; N, 11.84. Found: C, 60.86; H, 5.09; N, 11.82.

*N-[4,6-($CH_3$)$_2$-pyridine sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4h**)*

Yield: 65%; mp: 187-190˚C; IR (KBr) $cm^{-1}$: 3458 (NH), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276 (C-F), 1225 (amide-III), 1035 (C-N piperazine), 1015, 1219 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.11-1.61 (m, 4H, cyclopropyl), 3.62 (m, 1H, >N-CH-), 2.10-3.12 (m, 8H, piperazine), 6.14-7.21 (m, 8H, Ar-H), 8.10 (s, 1H, $H_2$), 8.55 (d, 1H, $H_5$), 8.10 (s, 1H, $H_8$), 1.90 (s, 3H, -$CH_3$), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H, -$SO_2$NH-); Calcd.: C, 58.86; H, 5.11; N, 16.58. Found: C, 58.06; H, 5.09; N, 16.59.

*N-[1-phenyl-1H pyrole sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydroquinoline-3-carboxamide (**4i**)*

Yield: 70%; mp: 182-184˚C; IR (KBr) $cm^{-1}$: 3458 (NH), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276 (C-F), 1225 (amide-III), 1035 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.59 (m, 4H, cyclopropyl), 3.65 (m, 1H, >N-CH-), 2.18-3.15 (m, 8H, piperazine), 6.04-7.15 (m, 8H, Ar-H), 8.07 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.15 (s, 1H, $H_8$), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H, -$SO_2$NH-); Calcd.: C, 61.24; H, 4.51; N, 15.16. Found: C, 61.22; H, 4.48; N, 15.12.

*N-[4-(phenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5a**)*

Yield: 69%; mp: 245-247˚C; IR (KBr) $cm^{-1}$: 3437 (NH), 2945 (C-H), 1650 (amide-I), 1537 (amide-II), 1345, 1152 (S=O, asym, sym), 1262 (C-F), 1237 (amide-III), 1052 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.07-1.57 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.31-3.18 (m, 8H, piperazine), 6.14-7.43 (m, 9H, Ar-H), 8.08 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.25 (s, 1H, $H_8$), 2.22 (s, 3H, >N-CH3), 9.45 (1H, s, -CONH-), 10.72 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.59; H, 5.26; N, 12.17. Found: C, 62.54; H, 5.24; N, 12.16.

*N-[4-(2-methylphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5b**)*

Yield: 65%; mp: 253-255˚C; IR (KBr) $cm^{-1}$: 3444 (NH), 2945 (C-H), 1652 (amide-I), 1537 (amide-II), 1360, 1165 (S=O, asym, sym), 1257 (C-F). 1212 (amide-III), 1052 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.04-1.61 (m, 4H, cyclopropyl), 3.69 (m, 1H, >N-CH-), 2.22-3.18 (m, 8H, piperazine), 6.14-7.42 (m, 8H, Ar-H), 8.20 (s, 1H, $H_2$), 8.48 (d, 1H, $H_5$), 8.27 (s, 1H, $H_8$), 2.17 (s, 3H, Ar-$CH_3$), 2.21 (s, 3H, >N-$CH_3$), 9.15 (s, 1H, -CONH-), 10.75 (s, 1H, -$SO_2$NH-); Calcd.: C, 63.13; H, 5.47; N, 11.88. Found: C, 63.11; H, 5.46; N, 11.86.

*N-[4-(4-methylphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5c**)*

Yield: 63%; mp: 245-247˚C; IR (KBr) $cm^{-1}$: 3452 (NH), 2942 (C-H), 1660 (amide-I), 1540 (amide-II), 1355, 1172 (S=O, asym, sym), 1260 (C-F), 1220 (amide-III), 1047 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.15-1.70 (m, 4H, cyclopropyl), 3.67 (m, 1H, >N-CH-), 2.24-3.21 (m, 8H, piperazine), 6.24-7.35 (m, 8H, Ar-H), 8.18 (s, 1H, $H_2$), 8.47 (d, 1H, $H_5$), 8.25 (s, 1H, $H_8$), 2.21 (s, 3H, Ar-$CH_3$), 2.14 (s, 3H, >N-$CH_3$), 9.10 (s, 1H, -CONH-), 10.67 (s, 1H, -$SO_2$NH-); Calcd.: C, 63.13; H, 5.47; N, 11.88. Found: C, 63.10; H, 5.43; N, 11.87.

*N-[4-(3-nitrophenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5d**)*

Yield: 66%; mp: 208-210˚C; IR (KBr) $cm^{-1}$: 3457 (NH), 2960 (C-H), 1670 (amide-I), 1540 (amide-II), 1352, 1157 (S=O, asym, sym), 1270 (C-F), 1220 (amide-III), 1040 (C-N piperazine), 1354, 1545 (-$NO_2$ sym, asym); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.08-1.71 (m, 4H, cyclopropyl), 3.72 (m, 1H, >N-CH-), 2.21-3.15 (m, 8H, piperazine), 6.15-7.15 (m, 8H, Ar-H), 8.05 (s, 1H, $H_2$), 8.41 (d, 1H, $H_5$), 8.30 (s, 1H, $H_8$), 2.15 (s, 3H, >N-$CH_3$), 9.08 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-); Calcd.: C, 58.05; H, 4.71; N, 13.55. Found: C, 58.02; H, 4.70; N, 13.54.

*N-[4-(4-nitrophenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(5e)***

Yield: 69%; mp: 199-201˚C; IR (KBr) $cm^{-1}$: 3457 (NH), 2960 (C-H), 1670 (amide-I), 1540 (amide-II), 1352, 1157 (S=O, asym, sym), 1270 (C-F), 1220 (amide-III), 1040 (C-N piperazine), 1354, 1545 (-$NO_2$ sym, asym); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.11-1.74 (m, 4H, cyclopropyl), 3.73 (m, 1H, >N-CH-), 2.21-3.19 (m, 8H, piperazine), 6.05-7.25 (m, 8H, Ar-H), 8.07 (s, 1H, $H_2$), 8.49 (d, 1H, $H_5$), 8.29 (s, 1H, $H_8$), 2.15 (s, 3H, >N-$CH_3$), 9.15 (s, 1H, -CONH-), 10.67 (s, 1H, -$SO_2$NH-); Calcd.: C, 58.05; H, 4.71; N, 13.55. Found: C, 58.02; H, 4.70; N, 13.52.

*N-[4-(2-methoxyphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl pipera-zin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(5f)***

Yield: 62%; mp: 219-221˚C; IR (KBr) $cm^{-1}$: $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.18-1.62 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.29-3.05 (m, 8H, piperazine), 6.14-7.25 (m, 8H, Ar-H), 8.10 (s, 1H, $H_2$), 8.47 (d, 1H, $H_5$), 8.20 (s, 1H, $H_8$), 4.05 (s, 3H, -$OCH_3$), 2.18 (s, 3H, >N-$CH_3$), 9.15 (s, 1H, -CONH-), 10.68 (s, 1H, -$SO_2$NH-); IR: δ= 3455 (NH), 2967 (C-H), 1663 (amide-I), 1541 (amide-II), 1347, 1155 (S=O, asym, sym), 1265 (C-F), 1218 (amide-III), 1035 (C-N piperazine), 1020, 1210 (C-O-C); Calcd.: C, 61.47; H, 5.33; N, 11.57. Found: C, 61.45; H, 5.31; N, 11.55.

*N-[4-(4-methoxyphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperaz-in-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(5g)***

Yield: 65%; mp: 225-227˚C; IR (KBr) $cm^{-1}$: IR: δ= 3448 (NH), 2957 (C-H), 1658 (amide-I), 1537 (amide-II), 1355, 1142 (S=O, asym, sym), 1277 (C-F), 1215 (amide-III), 1037 (C-N piperazine), 1005, 1209 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.04-1.49 (m, 4H, cyclopropyl), 3.55 (m, 1H, >N-CH-), 2.26-3.15 (m, 8H, piperazine), 6.04-7.15 (m, 8H, Ar-H), 8.07 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.15 (s, 1H, $H_8$), 4.10 (s, 3H, -$OCH_3$), 2.18 (s, 3H, >N-$CH_3$) 9.05 (s, 1H,-CONH-), 10.70 (s, 1H, -$SO_2$NH-); Calcd.: C, 61.47; H, 5.33; N, 11.57. Found: C, 61.42; H, 5.30; N, 11.54.

*N-[4,6-($CH_3$)$_2$pyridine sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (****5h****)*

Yield: 69%; mp: 187-189˚C; IR (KBr) $cm^{-1}$: 3458 (NH), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276 (C-F), 1225 (amide-III), 1035 (C-N piperazine), 1015, 1219 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.11-1.61 (m, 4H, cyclopropyl), 3.62 (m, 1H, >N-CH-), 2.10-3.12 (m, 8H, piperazine), 6.14-7.21 (m, 8H, Ar-H), 8.10 (s, 1H, $H_2$), 8.55 (d, 1H, $H_5$), 8.10 (s, 1H, $H_8$), 1.90 (s, 3H, -$CH_3$), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H, -$SO_2$NH-); Calcd.: C, 59.24; H, 5.33; N, 16.20. Found: C, 59.20; H, 5.31; N, 16.18.

*N-[1-phenyl-1H pyrole sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (****5i****)*

Yield: 71%; mp: 224-226˚C; IR (KBr) $cm^{-1}$: 3458 (NH), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276

(C-F), 1225 (amide-III), 1035 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.59 (m, 4H, cyclopropyl), 3.65 (m, 1H, >N-CH-), 2.18-3.15 (m, 8H, piperazine), 6.04-7.15 (m, 8H, Ar-H), 8.07 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.15 (s, 1H, $H_8$), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.15; H, 4.43; N, 15.38. Found: C, 62.13; H, 4.41; N, 15.36.

*N-[4-(phenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl)piperazin -1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(6a)***

Yield: 67 %; mp: 286-288˚C; IR (KBr) cm$^{-1}$: 3437 (NH), 3250 (O-H), 2945 (C-H), 1650 (amide-I), 1537 (amide-II), 1345, 1152 (S=O, asym, sym), 1262 (C-F), 1237 (amide-III), 1052 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.07-1.57 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.31-3.18 (m, 8H, piperazine), 6.14-7.43 (m, 9H, Ar-H), 8.08 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.25 (s, 1H, $H_8$), 2.22 (m, 4H, -$CH_2$-$CH_2$-), 4.4 (s, 1H, -OH), 9.45 (s, 1H, -CONH-), 10.72 (s, 1H, -$SO_2$NH-); Calcd.: C, 61.47; H, 5.33; N, 11.57. Found: C, 61.45; H, 5.32; N, 11.56.

*N-[4-(2-methylphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(6b)***

Yield: 69 %; mp: 235-237˚C; IR (KBr) cm$^{-1}$: 3444 (NH), 3235 (0-H), 2945 (C-H), 1652 (amide-I), 1537 (amide-II), 1360, 1165 (S=O, asym, sym), 1257 (C-F). 1212 (amide-III), 1052 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.65 (m, 4H, cyclopropyl), 3.65 (m, 1H, >N-CH-), 2.25-3.22 (m, 8H, piperazine), 6.08-7.48 (m, 8H, Ar-H), 8.15 (s, 1H, $H_2$), 8.45 (d, 1H, $H_5$), 8.24 (s, 1H, $H_8$), 2.17 (s, 3H, Ar-$CH_3$), 1.98 (m, 4H, -$CH_2$-$CH_2$-), 4.32 (s, 1H, -OH), 9.15 (s, 1H, -CONH-), 10.75 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.01; H, 5.53; N, 11.31. Found: C, 62.00; H, 5.51; N, 11.29.

*N-[4-(4-methylphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(6c)***

Yield: 63 %; mp: 252-254˚C; IR (KBr) cm$^{-1}$: 3452 (NH), 3238 (O-H), 2942 (C-H), 1660 (amide-I), 1540 (amide-II), 1355, 1172 (S=O, asym, sym), 1260 (C-F), 1220 (amide-III), 1047 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.08-1.72 (m, 4H, cyclopropyl), 3.65 (m, 1H, >N-CH-), 2.28-3.21 (m, 8H, piperazine), 6.18-7.29 (m, 8H, Ar-H), 8.15 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.18 (s, 1H, $H_8$), 2.21 (s, 3H, Ar-$CH_3$), 1.95 (m, 3H, -$CH_2$-$CH_2$-), 4.32 (s, 1H, -OH), 9.10 (s, 1H, -CONH-), 10.67 (s, 1H, -$SO_2$NH-); Calcd.: C, 62.01; H, 5.53; N, 11.31. Found: C, 61.98; H, 5.49; N, 11.28.

*N-[4-(3-nitrophenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(6d)***

Yield: 65 %; mp: 278-280˚C; IR (KBr) cm$^{-1}$: 3452 (NH), 3234 (O-H), 2958 (C-H), 1665 (amide-I), 1535 (amide-II), 1348, 1152 (S=O, asym, sym), 1265 (C-F), 1215 (amide-III), 1035 (C-N piperazine), 1352, 1535 (-$NO_2$ sym, asym); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.05-1.62 (m, 4H, cyclopropyl), 3.61 (m, 1H, >N-CH-), 2.18-3.21 (m, 8H, piperazine), 6.06-7.09 (m, 8H, Ar-H), 8.10 (s, 1H, $H_2$), 8.41 (d, 1H, $H_5$), 8.26 (s, 1H, $H_8$), 2.08 (m, 4H, -$CH_2$-$CH_2$-), 4.28 (s, 1H, -OH), 9.18 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-); Calcd.: C, 57.21; H, 4.81; N, 12.92. Found: C, 57.19; H, 4.79; N, 12.90.

*N-[4-(4-nitrophenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide* ***(6e)***

Yield: 60 %; mp: 240-244˚C; IR (KBr) cm$^{-1}$: 3445 (NH), 3232 (O-H), 2945 (C-H), 1661 (amide-I), 1525 (amide-II), 1347, 1152 (S=O, asym, sym), 1265 (C-F), 1211 (amide-III), 1032 (C-N piperazine), 1352, 1542 (-$NO_2$ sym, asym);

$^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.12-1.62 (m, 4H, cyclopropyl), 3.55 (m, 1H, >N-CH-), 2.10-3.15 (m, 8H, piperazine), 6.20-7.18 (m, 8H, Ar-H), 8.18 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.19 (s, 1H, $H_8$), 1.95 (m, 4H, -$CH_2$-$CH_2$-), 4.28 (s, 1H, -OH), 9.05 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-); Calcd.: C, 57.21; H, 4.81; N, 12.92. Found: C, 57.20; H, 4.80; N, 12.89.

*N-[4-(2-methoxyphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxy ethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6f**)*

Yield: 68 %; mp: 275-277˚C; IR (KBr) cm$^{-1}$: 3452 (NH), 3235 (O-H), 2962 (C-H), 1651 (amide-I), 1535 (amide-II), 1352, 1160 (S=O, asym, sym), 1252 (C-F), 1220 (amide-III), 1042 (C-N piperazine), 1020, 1210 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.02-1.67 (m, 4H, cyclopropyl), 3.58 (m, 1H, >N-CH-), 2.21-3.15 (m, 8H, piperazine), 6.24-7.15 (m, 8H, Ar-H), 8.15 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.10 (s, 1H, $H_8$), 4.15 (s, 3H, -$OCH_3$), 1.97 (m, 4H, -$CH_2$-$CH_2$-), 3.98 (s, 1H, -OH), 9.10 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-); Calcd.: C, 60.45; H, 5.59; N, 11.02. Found: C, 60.42; H, 5.58; N, 11.00.

*N-[4-(4-methoxyphenyl sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxy ethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6g**)*

Yield: 64 %; mp: 232-234˚C; IR (KBr) cm$^{-1}$: 3448 (NH), 3239 (O-H), 2957 (C-H), 1658 (amide-I), 1537 (amide-II), 1355, 1142 (S=O, asym, sym), 1277 (C-F), 1215 (amide-III), 1037 (C-N piperazine), 1005, 1209 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.69 (m, 4H, cyclopropyl), 3.69 (m, 1H, >N-CH-), 2.18-3.10 (m, 8H, piperazine), 6.04-7.15 (m, 8H, Ar-H), 8.15 (s, 1H, $H_2$), 8.51 (d, 1H, $H_5$), 8.09 (s, 1H, $H_8$), 4.15 (s, 3H, -$OCH_3$), 1.95 (m, 4H, -$CH_2$-$CH_2$-), 4.15 (s, 1H, -OH), 9.15 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-); Calcd.: C, 60.45; H, 5.59; N, 11.02. Found: C, 60.41; H, 5.57; N, 11.01.

*N-[4,6-($CH_3$)$_2$pyridine sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6h**)*

Yield: 68 %; mp: 253-255˚C; IR (KBr) cm$^{-1}$: 3458 (NH), 3235 (O-H), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276 (C-F), 1225 (amide-III), 1035 (C-N piperazine), 1015, 1219 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.05-1.68 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.25-3.27 (m, 8H, piperazine), 6.15-7.38 (m, 8H, Ar-H), 8.06 (s, 1H, $H_2$), 8.49 (d, 1H, $H_5$), 8.28 (s, 1H, $H_8$), 1.90 (s, 3H, -$CH_3$), 2.05 (m, 4H, -$CH_2$-$CH_2$-), 4.05 (s, 1H, -OH), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H, -$SO_2$NH-); Calcd.: C, 58.56; H, 5.39; N, 15.43. Found: C, 58.55; H, 5.38; N, 15.41.

*N-[1-phenyl-1H pyrole sulfamoyl)phenyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6i**)*

Yield: 70 %; mp: 291-293˚C; IR (KBr) cm$^{-1}$: 3458 (NH), 3237 (O-H), 2961 (C-H), 1655 (amide-I), 1533 (amide-II), 1345, 1147 (S=O, asym, sym), 1276 (C-F), 1225 (amide-III), 1035 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.62 (m, 4H, cyclopropyl), 3.67 (m, 1H, >N-CH-), 2.08-3.25 (m, 8H, piperazine), 6.14-7.25 (m, 8H, Ar-H), 8.10 (s, 1H, $H_2$), 8.45 (d, 1H, $H_5$), 8.27 (s, 1H, $H_8$), 2.15 (m, 4H, -$CH_2$-$CH_2$-), 4.15 (s, 1H, -OH), 9.15 (s, 1H, -CONH-), 10.72 (s, 1H, -$SO_2$NH-); Calcd.: C, 61.34; H, 4.24; N, 14.74. Found: C, 61.32; H, 4.22; N, 14.71.

### 3.6 General procedure for synthesis of *N*-[(substituted phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-(substituted-piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamides (4j-l, 5j-l, 6j-l)

The mixture of **3j-l** (0.001 mol), N-substituted piperazine (0.005 mol), $CH_3CN$ (10 ml), DMSO (5 ml) and $Et_3N$ was refluxed at 135°C

for 14 h and cool at room temperature. The resultant mass was poured in to crushed ice and neutralized with dilute HCl. The product were filtered, dried and recrystallized from absolute alcohol: DMSO (1:2) mixture to give **4j-l, 5j-l** and **6j-l**. The purity of the compounds was checked by TLC on silica gel plate using toluene: ethyl acetate (7:3).

*N-[(4-acetamide phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydro quinoline-3-carboxamide (**4j**)*

Yield: 75%, mp 178-180 ˚C; IR (KBr) $cm^{-1}$: 3460 (NH), 2947 (C-H), 1655 (amide-I), 1535 (amide-II), 1347, 1160 (S=O, asym, sym), 1265 (C-F), 1225 (amide-III), 1057 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.10-1.60 (m, 4H, cyclopropyl), 3.74 (m, 1H, >N-CH-), 2.14-3.10 (m, 8H, piperazine), 6.12-7.18 (m, 4H, Ar-H), 8.10 (s, 1H, $H_2$), 8.58 (d, 1H, $H_5$), 8.18 (s, 1H, $H_8$), 9.05 (s, 1H, -CONH-), 10.70 (s, 1H, -$SO_2$NH-), (s, 1H, >$COCH_3$); Calcd.: C, 56.91; H, 4.97; N, 13.28. Found: C, 58.89; H, 4.94; N, 13.26.

*N-[(4-methyl phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydro quinoline-3-carboxamide (**4k**)*

Yield: 72%; mp: 174-176˚C; IR (KBr) $cm^{-1}$: IR: δ= 3440 (NH), 2930 (C-H), 1645 (amide-I), 1540 (amide-II), 1350, 1160 (S=O, asym, sym), 1265 (C-F), 1230 (amide-III), 1045 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.15-1.58 (m, 4H, cyclopropyl), 3.68 (m, 1H, >N-CH-), 2.27-3.15 (m, 8H, piperazine), 6.10-7.15 (m, 4H, Ar-H), 8.08 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.15 (s, 1H, $H_8$), 2.21 (s, 3H, Ar-$CH_3$), 9.15 (s, 1H, -CONH-), 10.68 (s, 1H,-$SO_2$NH-); Calcd.: C, 59.48; H, 5.20; N, 11.57. Found: C, 59.46; H, 5.18; N, 11.50.

*N-[(4-methoxy phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-piperazin-1-yl-4-oxo-1,4-dihydro quinoline-3-carboxamide (**4l**)*

Yield: 69%; mp: 172-174˚C; IR (KBr) $cm^{-1}$: IR: δ= 3452 (NH), 2955 (C-H), 1655 (amide-I), 1533 (amide-II), 1352, 1157 (S=O, asym, sym), 1270 (C-F), 1220 (amide-III), 1040 (C-N piperazine), 1011, 1221 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.11-1.69 (m, 4H, cyclopropyl), 3.62 (m, 1H, >N-CH-), 2.19-3.18 (m, 8H, piperazine), 6.24-7.18 (m, 4H, Ar-H), 8.12 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.20 (s, 1H, $H_8$), 4.15 (s, 3H, -$OCH_3$), 9.10 (s, 1H, -CONH-), 10.69 (s, 1H, -$SO_2$NH-); Calcd.: C, 57.58; H, 5.04; N, 11.20. Found: C, 57.56; H, 5.02; N, 11.18.

*N-[(4-acetamide phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5j**)*

Yield: 67%; mp: 186-188˚C; IR (KBr) $cm^{-1}$: 3454 (NH), 2942 (C-H), 1661 (amide-I), 1542 (amide-II), 1345, 1155 (S=O, asym, sym), 1268 (C-F), 1215 (amide-III), 1047 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.14-1.51 (m, 4H, cyclopropyl), 3.71 (m, 1H, >N-CH-), 2.24-3.15 (m, 8H, piperazine), 6.08-7.20 (m, 4H, Ar-H), 8.08 (s, 1H, $H_2$), 8.48 (d, 1H, $H_5$), 8.21 (s, 1H, $H_8$), 2.14 (s, 3H, >N-$CH_3$), 9.12 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-), (s, 1H, >$COCH_3$); Calcd.: C, 57.65; H, 5.21; N, 12.94. Found: C, 57.62; H, 5.19; N, 12.92.

*N-[(4-methyl phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5k**)*

Yield: 62%; mp: 177-179˚C; IR (KBr) $cm^{-1}$: 3445 (NH), 2945 (C-H), 1657 (amide-I), 1537 (amide-II), 1345, 1167 (S=O, asym, sym), 1257 (C-F), 1245 (amide-III), 1051 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.11-1.58 (m, 4H, cyclopropyl), 3.75 (m, 1H, >N-CH-), 2.29-3.05 (m, 8H, piperazine), 6.15-7.45 (m, 4H, Ar-H), 8.13 (s, 1H, $H_2$), 8.45 (d, 1H, $H_5$), 8.17 (s, 1H, $H_8$), 2.21 (s, 3H, Ar-$CH_3$), 2.08 (s, 3H, >N-$CH_3$), 9.15 (s, 1H, -CONH-), 10.68 (s, 1H, -$SO_2$NH-); Calcd.: C, 60.22; H, 5.46; N, 11.24. Found: C, 60.20; H, 5.44; N, 11.22.

*N-[(4-methoxy phenyl)sulfonyl]-1-cyclopropyl-*

*6-fluoro-7-(4-methyl piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxamide (**5l**)*
Yield: 60%; mp: 182-184˚C; IR (KBr) $cm^{-1}$: IR: δ= 3449 (NH), 2961 (C-H), 1659 (amide-I), 1539 (amide-II), 1347, 1161 (S=O, asym, sym), 1265 (C-F), 1227 (amide-III), 1055 (C-N piperazine), 1008, 1218 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.11-1.69 (m, 4H, cyclopropyl), 3.62 (m, 1H, >N-CH-), 2.24-3.18 (m, 8H, piperazine), 6.24-7.18 (m, 4H, Ar-H), 8.12 (s, 1H, $H_2$), 8.52 (d, 1H, $H_5$), 8.20 (s, 1H, $H_8$), 4.15 (s, 3H, -$OCH_3$), 2.11 (s, 3H, >N-$CH_3$), 9.10 (s, 1H, -CONH-), 10.69 (s, 1H, -$SO_2$NH-); Calcd.: C, 58.35; H, 5.29; N, 10.89. Found: C, 58.32; H, 5.28; N, 10.88.

*N-[(4-acetamide phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl) piper-azin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6j**)*
Yield: 64 %; mp: 187-189˚C; IR (KBr) $cm^{-1}$: IR: δ= 3454 (NH), 3234 (O-H), 2942 (C-H), 1661 (amide-I), 1542 (amide-II), 1345, 1155 (S=O, asym, sym), 1268 (C-F), 1215 (amide-III), 1047 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.04-1.68 (m, 4H, cyclopropyl), 3.72 (m, 1H, >N-CH-), 2.14-3.25 (m, 8H, piperazine), 6.18-7.25 (m, 4H, Ar-H), 8.10 (s, 1H, $H_2$), 8.46 (d, 1H, $H_5$), 8.28 (s, 1H, $H_8$), 2.05 (s, 3H, >N-$CH_3$), 1.92 (m, 4H, -$CH_2$-$CH_2$-), 4.05 (s, 1H, -OH), 9.08 (s, 1H, -CONH-), 10.64 (s, 1H, -$SO_2$NH-), (s, 1H, >$COCH_3$); Calcd.: C, 56.72; H, 5.29; N, 12.26. Found: C, 56.70; H, 5.27; N, 12.23.

*N-[(4-methyl phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6k**)*
Yield: 61 %; mp: 223-225˚C; IR (KBr) $cm^{-1}$: 3442 (NH), 3225 (O-H), 2935 (C-H), 1658 (amide-I), 1538 (amide-II), 1335, 1168 (S=O, asym, sym), 1267 (C-F), 1235 (amide-III), 1045 (C-N piperazine); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.18-1.68 (m, 4H, cyclopropyl), 3.68 (m, 1H, >N-CH-), 2.19-3.05 (m, 8H, piperazine), 6.05-7.35 (m, 4H, Ar-H), 8.05 (s, 1H, $H_2$), 8.42 (d, 1H, $H_5$), 8.22 (s, 1H, $H_8$), 2.05 (s, 3H, Ar-$CH_3$), 1.92 (m, 4H, -$CH_2$-$CH_2$-), 4.15 (s, 1H, -OH), 9.25 (s, 1H, -CONH-), 10.65 (s, 1H, -$SO_2$NH-); Calcd.: C, 59.07; H, 5.53; N, 10.60. Found: C, 59.03; H, 5.49; N, 10.57.

*N-[(4-methoxy phenyl)sulfonyl]-1-cyclopropyl-6-fluoro-7-[4-(2-hydroxyethyl)piperazin -1-yl]-4-oxo-1,4-dihydroquinoline-3-carboxamide (**6l**)*
Yield: 69 %; mp: 257-260˚C; IR (KBr) $cm^{-1}$: 3424 (NH), 3235 (O-H) 2955 (C-H), 1650 (amide-I), 1532 (amide-II), 1335, 1165 (S=O, asym, sym), 1262 (C-F), 1225 (amide-III), 1045 (C-N piperazine), 1010, 1205 (C-O-C); $^1$H NMR (300 MHz, $d_6$-DMSO) δ (ppm): 1.01-1.72 (m, 4H, cyclopropyl), 3.68 (m, 1H, >N-CH-), 2.04-3.28 (m, 8H, piperazine), 6.14-7.20 (m, 4H, Ar-H), 8.10 (s, 1H, $H_2$), 8.48 (d, 1H, $H_5$), 8.25 (s, 1H, $H_8$), 4.15 (s, 3H, -$OCH_3$), 1.92 (m, 4H, -$CH_2$-$CH_2$-), 4.05 (s, 1H -OH), 9.10 (s, 1H, -CONH-), 10.69 (s, 1H, -$SO_2$NH-); Calcd.: C, 57.33; H, 5.37; N, 10.29. Found: C, 57.30; H, 5.36; N, 10.26.

## 4. Conclusion:

Significant improvement in antibacterial activity was observed on the introduction of sulfonamide group for fluroquinolones. From the experimental data, it has been observed that all the compounds exhibited significant against Gram-positive bacteria. In case of Gram-negative bacterial strains, it has been concluded that, the most of the compounds showed comparable activity against *P.aeruginosa* while least activity against *E.coli.* The highest activity observed against *B. subtilis* and *P. aeruginosa*. There is no significant effect of different piperazin-1-yl group on biological activity.

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## References:


1. S. Emani, A. Shafiee, A. Foroumadi, *Iranian J Pharma Res* **2005**, *3*, 123.
2. L. A. Mitscher, *Chem Rev* **2005**, *105(2)*, 559.
3. S. K. Bhanot, M. Singh, N. R. Chatterjee, *Current Pharma Design* **2001**, *7*, 313.
4. D. Edmont, R. Rocher, C. Plisson, J. Chenault, *Bioorg Med Chem Lett* **2000**, *10*, 1831.
5. M. Shaharyar, M. A. Ali, M. M. Abdullah, *Med Chem Res* **2007**, *16*, 292.
6. B. Lucero, C. Regina, I. Frugulhetti, L. Alvarenga, M. de Souza, T. de Souzab, V. Ferreira, *Bioorg Med Chem Lett* **2006**, *16*, 1010.
7. O. Tabarrini, S. Massari, D. Daelemans, M. Stevens, G. Manfroni, S. Sabatini, J. Balzarini, V. Cecchetti, C. Pannecouque, A. Fravolini, *J Med Chem* **2008**, *51*, 5454.
8. S. K. Srivastava, P. Chauhan, A.P. Bhaduri, N. Fatima, R.K. Chatterjee, *J Med Chem* **2000**, *43*, 2275.
9. G. M. Brown, *J Bio Chem* **1962**, *237*, 536.
10. C. T. Supuran, A. Scozzafava, B. C. Jurca, M. A. Ilies, *Eur J Med Chem* **1998**, *33*, 83.
11. N. S. Reddy, M. R. Mallireddigari, C. Stephen, G. Kiranmai, B. Stanley, P. Reddy, R. Reddy, *Bioorg Med Chem Lett* **2004**, *14*, 4093.
12. J. J. Li, G. D. Anderson, E. G. Burton, J. N. Cogburn, J. T. Collins, D. J. Garland, S. A. Gregory, H. Huang, P. C. Isakson, *J Med Chem* **1995**, *38*, 4570.
13. P. Selvam, M. Chandramohan, E. De Clercq, M. Witvrouw, C. Pannecouque, *Eur J Pharma Sci* **2001**, *14*, 313.
14. G. Dannhardt, B. L. Fiebich, J. Schweppenhäuser, *Eur J Med Chem* **2002**, *37*, 147.
15. S. M. Bromidge, S. E. Clarke, F. D. King, P. J. Lovell, H. Newman, G. Riley, C. Routledge, H. T. Serafinowska, D. R. Smith, D. R. Thomas, *Bioorg Med Chem Lett* **2002**, *12*, 1357.
16. A. Kamal, S. K. Ahmed, K. S. Reddy, M. A. Khan, R. Shetty, B. Siddhardha, U.S.N. Murthy, I. A. Khan, M. Kumar, S. Sharma, A. B. Ram, *Bioorg Med Chem Lett* **2007**, *17*, 5419.
17. F. Briganti, A. Scozzafava, C. T. Supuran, *J Med Chem* **1997**, *32*, 901.
18. N. B. Patel, A. L. Patel, H. I. Chauhan, *Ind J Chem* **2007**, *46B*, 126-134.
19. P. C., Sharma, S. Jain, *Acta Pol Pharma Drug Res* **2008**, *65*, 551-556.
20. A. L. Baryy, "The Antimicrobial Susceptible Test: Principle and Practice", IIIu lea and Febiger, Philadelphia **1976**, 180p.