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SYNTHESIS AND ANTI MICROBIAL STUDIES OF NOVEL 7-(N -4-SUBSTITUTED SULFONAMIDE) 6-FLUOROQUINOLONE DERIVATIVES

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ABSTRACT

A series of 1-ethyl/benzyl-6-fluoro 7-[4- (-N- 4- substituted phenyl) benzene sulfonamide)1-Piperazinyl] -1,4, dihydro -4- oxo-quinoline carboxylic acid (C_1-C_8) were synthesized and characterized by IR, MASS, NMR spectral and elemental analyses. All the compounds screened for their in vitro antibacterial and antifungal activities by paper disc diffusion method. The Minimum inhibitory concentration (MIC) of the compounds was determined by broth dilution technique. The in vivo antibacterial activity of the compounds against E.coli and Staphylococcus aureus was evaluated by mouse protection method. Compounds C_1, C_2, C_5 and C_7 exhibited very good antimicrobial activity. Compounds C_1, C_3 and C_5 showed good bactericidal and fungicidal activities.

Keywords: Fluoroquinolone, Anti – bacterial, Topoisomerases, Ciprofloxacin.

INTRODUCTION

Quinolones are synthetic antibacterial compounds based on a 4- quinolone skeleton. Quinolones have been clinically successful and more used to treat bacterial infection. Fluoroquinolones target bacterial type-II topoisomerases, generally DNA gyrase in gram negative bacteria and DNA topoisomerase in gram positive bacteria [1-3]. The synthesis and evaluation of over 10,000 quinolone derivatives resulted in thorough knowledge of the structure-activity relationship for many quinolone substituent [4]. Fluoroquinolone with 7-piperzinyl [5-12], 1-Ethyl [13-15], and 1-Benzyl [5,14,16] have been reported to posses potent antibacterial [5-16], antifungal [11], antiviral [6,11] activities. Therefore, our strategy to achieve a better antimicrobial profile has focused on introducing new functionality on the piperzine ring. From our research in C-7 piperazine modification of the quinolones, we were able to identify a series of N -substituted piperzinyl quinolones by replacement of N -4-hydrogen of piperzinyl group of quinolones by substituted sulfonamides. It was contemplate to synthesize substituted sulfonamide containing fluoroquinolone and to pursue antibacterial and antifungal screening. The results of the antibacterial and antifungal activities were discussed in this paper.

CHEMISTRY

1-Ethyl / Benzyl -6- fluoro-7-(piperazinyl)-1,4-dihydro-4-oxo-quinoline 3- carboxylic acid (7 and 8) was prepared from 3-chloro-4-fluoro aniline according to the literature method [5].

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A series of 4- chloro -N- (p-substituted phenyl) benzene sulfonamide (11a-d) were synthesized from acetanilide heated with chlorosulfonic acid to 4-acetamido bezene sulfonyl chloride (9) reacts with 4-substituted aniline to give respective amine derivatives (10). Further its convert chloro derivative compounds (11a-d) by sandmeyer reaction. Reaction of 7-piperzinyl quinolones (7,8) with compounds (11a-d) in DMF at room temperature afforded 1-Ethyl / Benzyl -6-fluoro-7 -[4- (N -4- substituted phenyl) benzene sulfonamide)1- piperazinyl] -1,4-dihydro-4- oxo-quinoline-3- carboxylic acid (C_{1-4} and C_{5-8}) in good yield based on the literature method [17]. The reaction sequences are outlined in scheme I.

RESULTS AND DISCUSSION

The IR spectrum of compound (C_2) showed an absorption band at 3095 cm^{-1} due to aromatic stretch. Another absorption band at 2872 cm^{-1} was due to aliphatic stretch. The absorption band for S=O was observe at 1352 cm^{-1}. The other prominent absorption band observed in the I.R spectrum are at 1264 (Ph-O-CH_3), 1083 (C-F), 1515 and 1342 cm^{-1} for NO_2.

The ^{1}H NMR spectrum of (**C_2**) showed a triplet at δ-1.28 attributable to CH_3 protons and the CH_2 protons resonated as a quartet at δ- 4.25. All other aromatic and aliphatic protons are observed at the expected δ region. A singlet at δ -10.35 integrating for one proton was attributable to the NH protons of sulfonamide moiety.

Further, evidence for the formation of compound (C_2) was obtained by recording its mass spectrum (The mass spectra of the compounds agreed with the proposed structure). The mass spectrum of the compounds (C_2) showed molecular ion peak observed area at *m/z* 568 in conformity with molecular formula $C_{28}H_{26}F_2N_4O_5S$. The other fragmentation peaks observed area at *m/z* 206, (10%) *m/z* 394 (22%). The characterization data of fluoroquinolones (C_1 and C_8) are given in Table 1.

PHARMACOLOGY

Antibacterial Studies

The synthesized compounds (C_1 and C_8) were screened for their in vitro antibacterial activity against *Escheria coli* (ATCC-25922), *Klebsiella pneumonia* (ATCC-11298), *Pseudomonas aeruginosa* (ATCC-2853), *Staphylococcus aureus* (ATCC-9144), *Micrococus luteus* (ATCC-4698) *Staphylococcus epidermidis* (ATCC 155) bacterial strains by disc diffusion method [18,19]. A standard inoculum (1-2 x 10 c.f.u./ml 0.5 Mc farland standard) was introduced on to the surface of sterile agar plates, and a sterile glass spreader was used for even distribution of the inoculum. The discs measuring 6.25 mm in diameter were prepared from whatman no:1 filter paper and sterilized by dry heat at 140 °C for 1 h. The sterile discs previously soaked in a known concentration of the test compounds were placed in nutrient agar medium (Hi-media laboratories, India) solvent and growth control were kept. The plates were inverted and incubated for 24h at 37 °C. Ciprofloxacin was used as a standard drug. Inhibition zones were measured and compared with the controls. The bacterial zones of inhibition values are given in Table 2.

Minimum inhibitory concentrations (MICs) were determined by broth dilution technique. The nutrient broth, which contained logarithmic serially twofold diluted amount of test compound and controls were inoculated with approximately 5x 10^5c.f.u. of actively dividing bacteria cells. The cultures were incubated for 24h at 37 °C and the growth was monitored visually and spectrophotometrically. The lowest concentration (highest dilution) required to arrest the growth of bacteria was regarded as minimum inhibitory concentration (MIC). Drug free plates were used to ensure the growth of strains.

To obtain the minimum bacterial concentration (MBC) 0.1 volume was taken from each tube and spread on agar plates. The number of c.f.u was counted after 18-24 h of incubation at 35 °C. MBC was defined as the lowest concentration at which 99.9% of the inoculum was killed. The Minimum inhibitory concentration and Minimum bactericidal concentration are given in Table 3.

The investigation of antibacterial screening data revealed that all the tested compounds showed good bacterial inhibition, Compounds C_1, C_2, C_5, C_6 and C_7 showed good inhibition against all the bacterial strains against *E.coli* and *S.aureus*. Compounds C_2, C_5 and C_7 exhibited good antibacterial activity almost equivalent to that of standard. Based on the in vitro studies all the compounds (C_1 - C_8) subjected to in vivo antibacterial activity against one gram negative (*E.coli*) and one gram positive (*S.aureus*).

Antifungal Studies

The newly prepared compounds were screened for their antifungal activity against *Candida albicans*, *Aspergillus fumigatus* in DMSO by agar diffusion method [20,21], saborauds agar medium (Hi-media laboratories, India) was prepared by dissolving peptone (1g), D-glucose(4g) and agar (2g) in distilled water (100ml) and adjusting pH to 5.7. Normal saline was used to make a suspension of spore of fungal strain for lawning. A loopful of particular fungal strain was transferred to 3ml saline to get a suspension of corresponding species. Twenty milliliters of agar media was poured into each Petri dish. Excess of suspension was decanted and the plates were dried by placing in an incubator at 37 °C for 1 h. using an agar punch, wells were made and each well was labeled. A control was also prepared in triplicate and maintained at 37 °C for 3-4 days. The fungal activity of each compound

was compared with Greseofulvin as standard drug. Inhibition zones were measured and compared with the control. The fungal zones of inhibition value are given in Table 4.

The nutrient broth, which contained logarithmic serially two fold diluted amount of test compound and control was inoculated with approximately 1.6x 10^4-6 c.f.u./ml. The cultures were incubated for 48 h at 35 °C and the growth was monitored. The lowest concentration (highest dilution) required to arrest the growth of fungus was regarded as minimum inhibitory concentration (MIC). To obtain the minimum fungicidal concentration (MFC), 0.1 ml volume was taken from each tube and spread on agar plates. The number c.f.u was counted after 48 h of incubation at 35 °C. MFC was defined as the lowest drug concentration at which 99.9% of the inoculum was killed. The minimum inhibitory concentration and minimum fungicidal concentration are given in Table 4.

The antifugal screening data showed only moderate activity. Among the screened compounds **C_3** and **C_6** showed good inhibition against all the fungal strains. The MBC of few compounds was found to be the same as MIC.

In vivo Antibacterial activity

Animals

Inbred male swiss albino mice (20-25g) were used for the in vivo antibacterial activity. They were kept in colony cages at 25 ± 2 °C, relative humidity 45-55 % under 12 h light and dark cycles. The animals were fed with standard animal feed and water ad libitum. All the animals were acclimatized for a week before use. The test compounds and the standard drugs were administered orally by gavage in the form of a suspension (1% Carboxy methyl cellulose as vehicle). Acute oral toxicity was performed for all the synthesized compounds according to organization of economic co-operation and development (OECD) guidelines. All the animal experimentation was performed as per the recommendations and the protocols of the institutional animal ethics committee.

Acute oral toxicity

Acute oral toxicity [23] was performed as per OECD-423 guidelines (acute toxic class method) swiss albino mice (*n* = 3) of either sex selected by random sampling technique was technique was used for the study. The animals were kept fasting for 3 - 4 h providing only water ad libitum. After which the test compounds (suspended in olive oil) were administered orally at the dose level of 5 mg/kg by intragastric tube and observed for 3 days. If mortality was observed in two to three animals, then the dose administered was assigned as toxic dose. If mortality was observed in one animal, then the same dose was repeated again to confirm the toxic dose. In the present study, mortality was not observed and the procedure was repeated for further higher dose such as 5, 50, 300 and 2000 mg/kg.

Mouse protection test

The in vivo antibacterial activity [11] of the compounds (C_1-C_8) against *E.coli* and *S. aureus* was determined in male swiss albino mice (*n* = 6). The mice were infected intraperitoneally with a suspension (10^5 c.f.u./ml) containing an amount of *E.coli* and *S.aureus* greater than its LD_{100}. The mice were treated orally (p.o.) with a specified amount of the synthesized compounds 1 and 4h after infection. ED_{50} values were calculated by extrapolation among survival rate in each group after a week. The ED_{50} values represent the total dose of the compound (mg/kg) required to protect 50% of the mice from an experimentally induced lethal systemic infection of *E.coli* and *S.aureus*.

Scheme I

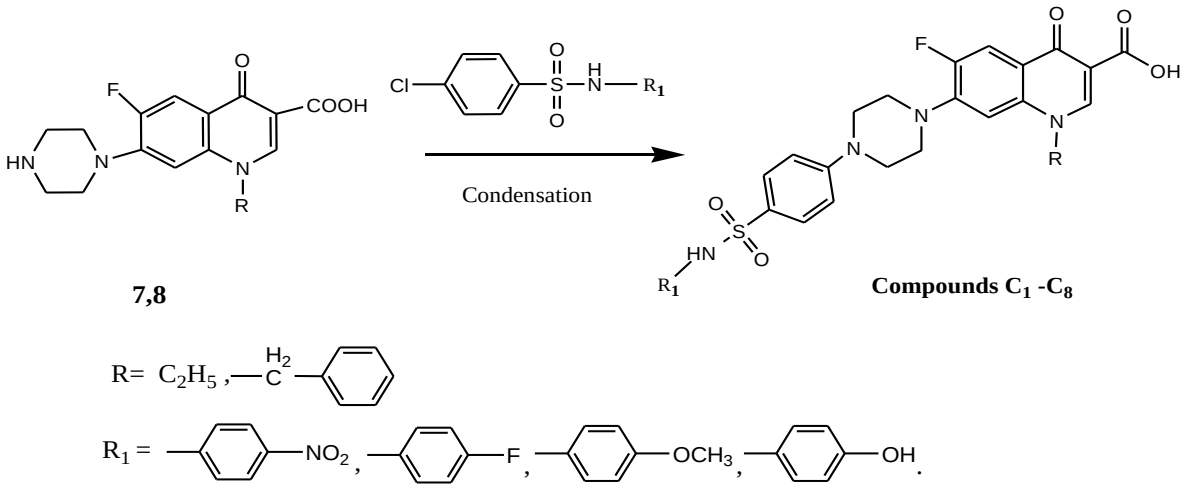

Table 1. Characterization data of synthesized compounds (C_1 - C_8)

Compounds	R	R_1	Mol. Formula	M.P [°C]	Yield [%]
C_1	$-C_2H_5$	4-Nitro phenyl	$C_{28}H_{26}FN_5O_7S$	266-268	67
C_2	$-C_2H_5$	4-Fluoro phenyl	$C_{28}H_{26}F_2N_4O_5S$	294-296	55
C_3	$-C_2H_5$	4-Methoxy phenyl	$C_{29}H_{29}FN_4O_6S$	287-289	60
C_4	$-C_2H_5$	4-Hydroxy Phenyl	$C_{28}H_{27}FN_4O_6S$	297-299	61
C_5	$-CH_2C_6H_5$	4-Nitro phenyl	$C_{33}H_{28}FN_5O_7S$	254-256	55
C_6	$-CH_2C_6H_5$	4-Fluoro phenyl	$C_{33}H_{28}F_2N_4O_5S$	297-299	56
C_7	$-CH_2C_6H_5$	4-Methoxy phenyl	$C_{34}H_{31}FN_4O_6S$	280-282	68
C_8	$-CH_2C_6H_5$	4-Hydroxy Phenyl	$C_{33}H_{29}FN_4O_6S$	276-277	52

Table 2. Zone of inhibition (mm) of the synthesized compounds (C_1 - C_8)

Compounds	Escheria coli	klebsiella pneumonia	Pseudomonas aeruginosa	Staphylococcus aureus	Micrococcus luteus	Staphylococcus epidermidis
C_1	25	17	28	25	22	24
C_2	23	15	26	22	19	22
C_3	24	15	26	24	21	20
C_4	19	17	22	22	19	18
C_5	26	18	30	26	22	25
C_6	23	16	27	22	20	20
C_7	20	17	28	24	19	18
C_8	22	17	22	22	18	16
Standard	27	19	32	29	23	24

-Indicates bacteria are resistant to the compound > 100 µg mL^{-1}. Ciprofloxacin is used as the standard.

Table 3. MBC and MIC and In vivo activity results of synthesized compounds (C_1 - C_8)

Compounds	Escheria coli		Staphylococcus aureus		In vivo activity (ED_{50}) in mg kg^{-1} Escheria coli	In vivo activity (ED_{50}) in mg kg^{-1} Staphylococcus aureus
	MIC	MBC	MIC	MBC		
C_1	6.25	12.5	6.25	6.25	100	83.3
C_2	6.25	25	12.5	12.5	66.6	100
C_3	6.25	25	6.25	12.5	83.3	66.6
C_4	-	-	12.5	100	66.6	33.3
C_5	6.25	12.5	6.25	25	83.3	100
C_6	6.25	25	6.25	6.25	100	83.3
C_7	25	50	12.5	50	66.6	66.6
C_8	50	100	25	100	66.6	66.6
Standard	6.25	12.5	6.25	12.5		

- indicates bacteria are resistant to the compounds >100 µg mL^{-1}; MIC (µg mL^{-1}) = minimum inhibitory concentration, i.e., the lowest concentration to completely inhibit bacterial concentration to completely inhibit bacterial growth ; MBC (µg mL^{-1}) = minimum bactericidal concentration, i.e., the lowest concentration to completely kill bacteria.

Table 4. Zone of Inhibition (mm) and MIC of synthesized compounds (C_1 - C_8)

- indicates bacteria are resistant to the compound > 100 µg mL^{-1}. Greseofulvin is used as the standard. MIC (µg mL^{-1}) = minimum inhibitory concentration, i.e., the lowest concentration to completely inhibit fungal growth; MFC (µg mL^{-1}) = minimum fungicidal concentration, i.e., the lowest concentration to completely kill fungus.

Compounds	Aspergillus fumigatus (mm)	Candida albicans (mm)	Aspergillus fumigatus		Candida albicans	
			MIC	MFC	MIC	MFC
C_1	23	24	12.5	25	6.25	12.5
C_2	20	25	25	50	25	50
C_3	25	24	6.25	12.5	6.25	6.25
C_4	-	22	-	-	12.5	50
C_5	25	22	6.25	12.5	6.25	6.25
C_6	22	24	12.5	25	6.25	12.5
C_7	20	22	50	25	12.5	100
C_8	16	18	25	100	12.5	25
Standard	27	30	6.25	12.5	6.25	12.5

Experimental protocols

Chemistry

The melting points were taken in open capillary tube and are uncorrected. The IR spectra (KBr pellets) of the compounds were recorded on ABB Bomem FT-IR spectrometer MB 104. The ^{1}H NMR (300MHz) spectra were recorded on a Bruker 300 NMR spectrometer using TMS as an internal standard. Mass spectra were recorded on Shimadzu GC-MS QP 5000. Microanalyses were obtained with an Elemental analyses system GmbH VarioEL V300 element analyzer. The purity of the compounds was checked by thin layer chromatography (TLC) on pre-coated SiO_2 gel (HF_{254}, 200 mesh) aluminium plates (E Merk) using n-hexane: ethyl acetate (80:20) and visualized in UV chamber. IR, ^{1}H NMR, Mass spectra and Elemental analysis were consistent with the assigned structures.

General procedure for synthesis of title compounds **(C_1-C_8).**

0.01 mol of fluoroquinolones (7,8) was suspended in pyridine (200ml). To this suspension slowly added 0.01 mol of chloro derivative of sulfonamides (11a-d) in DMF (20ml) with stirring at 120 - 130^{0}C for 5 h. After 5 h the reaction mixture was concentrated under reduced pressure. To the residue added NaOH (1N) solution to dissolve. The pH of the solution is then adjusted to 4 with acetic acid, precipitating crystals are collected by filtration washed with water and recrystallized from DMF – ethanol (completion of the reaction was monitored by TLC).

*1-ethyl -6- fluoro 7-[4- (-N -4- nitro phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (**C_1**).*

IR (KBr ; υ cm^{-1}): 1793 (C=O), 1557 (C=C), 1375 (C-N), 1445 (C-H), 3072 (C-H, Ar), 1515,1342 (NO_2), 1713 (COOH); ^{1}H NMR (DMSO- d_6): δ 1.52 (t, 3H, –CH_2CH_3), 3.25 (q, 2H, CH_2CH_3), 3.42 - 3.78 (m, 8H, piperazine), 7.11 (d, 1H, C_8-H), 8.06 (d, 1H, C_5- H), 8.85 (s, 1H, C_2-H), 7.25 - 7.95 (m, 8H, Ar-H), 13.25 (s, 1H,COOH); EI-MS (m/z): M^+ 595 (31.2%); Anal. Calcd.for $C_{28}H_{26}FN_5O_7S$: C, 56.46; H, 4.40; N, 11.76 ; Found: C, 56.44; H, 4.41; N, 11.81.

*1-ethyl -6- fluoro 7-[4- (-N -4- fluoro phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (**C_2**).*

IR (KBr ; υ cm^{-1}): 1767 (C=O), 1518 (C=C), 1389 (C-N), 1450 (C-H), 3095 (C-H, Ar), 1717 (COOH); ^{1}H NMR (DMSO- d_6): δ 1.48 (t, 3H, –CH_2CH_3); 3.26 (q, 2H, -CH_2CH_3); 3.43 - 3.82 (m, 8H, piperazine), 7.15 (d, 1H, C_8-H); 8.08 (d, 1H, C_5-H); 8.88 (s, 1H, C_2-H); 7.22-7.98 (m, 8H, Ar-H), 13.26 (s, 1H,COOH); EI-MS (m/z): M^+ 568 (30.8%); Anal. Calcd.for $C_{28}H_{26}F_2N_4O_5S$: C, 59.15; H, 4.61; N, 9.85; Found : C, 59.21; H, 4.56; N, 9.79.

1-ethyl -6- fluoro 7-[4- (-N -4- methoxy phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (C_3).

IR (KBr ; υ cm^{-1}): 1752 (C=O), 1515 (C=C), 1389 (C-N), 1447 (C-H), 3045 (C-H, Ar), 1264,1027(Ph-O-CH_3), 1735 (COOH); ^{1}H NMR (DMSO- d_6): δ 1.45 (t, 3H,–CH_2CH_3); 3.32 (q, 2H, –CH_2CH_3); 3.47 – 3.91 (m, 8H, piperazine), 7.10 (d, 1H, C_8-H); 8.08 (d, 1H, C_5-H); 8.82 (s, 1H, C_2-H); 7.25-7.89 (m, 8H, Ar-H), 13.25 (s, 1H,COOH); EI-MS (m/z): M^+ 580 (29 %); Anal. Calcd.for $C_{29}H_{29}FN_4O_6S$: C, 59.99; H, 5.03; N, 9.65; Found : C, 59.91; H, 5.06; N, 9.67.

1-ethyl -6- fluoro 7-[4- (-N -4- hydroxy phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (C_4).

IR (KBr ; υ cm^{-1}): 1695 (C=O), 1520 (C=C), 1375 (C-N), 1435 (C-H), 3110 (C-H, Ar), 3385 (OH),1735 (COOH); ^{1}H NMR (DMSO- d_6): δ 1.42 (t, 3H, –CH_2CH_3), 3.29 (q,

2H, $-CH_2CH_3$), 3.45- 4.01 (m, 8H, piperazine), 7.14 (d, 1H, C_8-H), 8.07 (d, 1H, C_5-H), 8.82 (s, 1H, C_2-H), 7.28-7.90 (m, 8H, Ar-H),13.27 (s, 1H,COOH); EI-MS (m/z): M^+ 566 (36.8%); Anal. Calcd.for $C_{28}H_{27}FN_4O_6S$: C, 59.35; H, 4.80; N, 9.89; Found : C, 59.38, H , 4.84; N, 9.88.

1-benzyl -6- fluoro 7-[4- (-N -4- nitro phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (C_5).
IR (KBr ; υ cm^{-1}): 1751 (C=O), 1589 (C=C), 1385 (C-N), 1455 (C-H), 3085 (C-H, Ar), 1520,1375 (NO_2), 1713 (COOH); ^{1}H NMR (DMSO- d_6): 3.44 - 3.97 (m, 8H, piperazine), 7.15 (d, 1H, C_8-H), 8.08 (d, 1H, C_5-H), 8.90 (s, 1H, C_2-H), 6.75 - 7.10 (m, 5H, Ar-H), 7.22 – 7.92 (m, 8H, Ar-H), 13.25 (s, 1H,COOH); EI-MS (m/z): M^+ 657 (31%); Anal. Calcd.for $C_{33}H_{28}FN_5O_7S$: C, 60.27; H, 4.29; N, 10.65; Found: C, 60.28; H, 4.26; N, 10.66.

1-benzyl -6- fluoro 7-[4- (-N -4-fluoro phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (C_6).
IR (KBr ; υ cm^{-1}): 1767 (C=O), 1518 (C=C), 1389 (C-N), 1447 (C-H), 3095 (C-H, Ar), 1717 (COOH); ^{1}H NMR (DMSO- d_6): 3.45 - 3.99 (m, 8H, piperazine), 7.18 (d, 1H, C_8-H), 8.08 (d, 1H, C_5-H), 8.85 (s, 1H, C_2-H), 6.76-7.11 (m, 5H, Ar-H), 7.26 - 7.97 (m, 8H, Ar-H), 12.28 (s, 1H,COOH); EI-MS (m/z): M^+ 630 (38%); Anal. Calcd.for $C_{33}H_{28}F_2N_4O_5S$: C, 62.85; H, 4.48; N, 8.88; Found : C, 62.86; H, 4.51; N, 8.85.

1-benzyl -6- fluoro 7-[4- (-N -4- methoxy phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (C_7).
IR (KBr ; υ cm^{-1}): 1755 (C=O), 1565 (C=C), 1368 (C-N), 1451 (C-H), 3088 (C-H, Ar), 1256,1032 (Ph-O-CH_3), 1709 (COOH); ^{1}H NMR (DMSO-d_6): 3.40 - 4.67 (m, 8H, piperazine), 7.12 (d, 1H, C_8-H), 8.06 (d, 1H, C_5-H), 8.88 (s, 1H, C_2-H), 6.76-7.08 (m, 5H, Ar-H), 7.27 - 7.96 (m, 8H, Ar-H), 13.26 (s, 1H,COOH); EI-MS (m/z): M^+ 642 (37.7 %); Anal. Calcd.for $C_{34}H_{31}FN_4O_6S$: C, 63.54; H, 4.86; N, 8.72; Found : C, 63.59; H, 4.84; N, 8.73.

1-benzyl -6- fluoro 7-[4- (-N -4- hydroxy phenyl) benzene sulfonamide) 1-Piperazinyl] -1,4, dihydro -4-oxo quinoline-3- carboxylic acid (C_8).
IR (KBr ; υ cm^{-1}): 1787 (C=O), 1522 (C=C), 1379 (C-N), 1455 (C-H), 3082 (C-H, Ar), 3392 (OH), 1722 (COOH); ^{1}H NMR (DMSO- d_6): 3.74 - 4.35 (m, 8H, piperazine), 7.15 (d, 1H, C_8-H), 8.08 (d, 1H, C_5-H), 8.89 (s, 1H, C_2-H), 6.78-7. 10 (m, 5H, Ar-H), 7.25-8.94 (m, 8H, Ar-H), 13.29 (s, 1H, COOH); EI-MS (m/z): M^+ 628 (38.2%); Anal. Calcd.for $C_{33}H_{29}FN_4O_6S$: C, 63.05; H, 4.65; N, 8.91; Found : C, 63.03; H, 4.69; N, 8.92.

CONCLUSION

In summary, we have described the genesis and synthesis of antibacterially active 1- Ethyl/Benzyl -6-fluoroquinolone bearing 4-subtituted Benzene sulfonamide derivatives. Among the synthesized fluoroquinolones, compounds with Nitro, Fluoro, Methoxy substituents in the phenyl ring at 4th position of benzene sulfonamide (-SO_2-NH-) moiety were found to increase the antimicrobial activity. Finally, according to this in vivo study the Fluoro and the nitro derivatives are the most active analogs within these series Compound with 4-fluoro phenyl moiety showed good bactericidal and fungicidal activities. The ED_{50} (in vivo antibacterial screening) of the compounds against *E. coli* and *S.aureus* was 50-150 mg/kg. The compounds (C_1-C_8) did not cause mortality upto 2000 mg/kg in acute oral toxicity (OECD-423 guidelines) and were considered as safe (x-unclassified).

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