Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(8):154-161

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, characterization and antimicrobial activity of some new 1,3,4-oxadiazoles and schiff bases bearing 5-chloroquinolin-8-ol moiety

B. Chandrashekhar. Kumar[*1], K. R. Venugopala Reddy[2] and Fasiulla[1]

[1]*Department of Chemistry, Manipal Institute of Technology, Manipal University, Udupi, Karnataka, India*
[2]*Department of Chemistry, Vijayanagara Sri Krishanadevaraya University, Bellary, Karnataka, India*

ABSTRACT

A new series of 2-(substituted phenyl)-5-(5-chloro quinolin-8-yloxy) methyl-1,3,4-oxadiazole ***(3a-j)*** *were synthesised after refluxing 2-[(5-chloro quinolin-8-yl) oxy] acetohydrazide* ***(2)*** *with different aromatic acids in presence of* $POCl_3$*. A new series of N'-(substituted benzylidene)-2-(5-chloro-8-yloxy) acetohydrazide (schiff' bases)* ***(4a-j)*** *were also synthesized from a mixture of2-[(5-chloro quinolin-8-yl) oxy] acetohydrazide* ***(2)*** *and different aromatic aldehydes in presence of glacial acetic acid. The chemical structures of these compounds were confirmed by various physic-chemical methods viz, IR,* ^{1}*HNMR, mass spectral data and elemental analysis. Newly synthesized compounds were screened in vitro for their antimicrobial activity against varieties of gram +ve and gram -ve bacterial strains such as Bacillus subtilis, Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli and fungi strains Candida albicans & Aspergillus nigar with MIC at 40 µg/mL. The newly synthesized Schiff bases and 1,3,4-Oxadiazole derivatives bearing 5-chloroquinolin-8-ol are showing moderate to highly significant antimicrobial activity. The Schiff base* ***(4i)*** *shows highly significant antimicrobial activity as compare to other synthesized Schiff bases.*

Keywords: 5-chloroquinolin-8-ol, 1,3,4-Oxadiazoles, Schiff bases, antimicrobial activity.

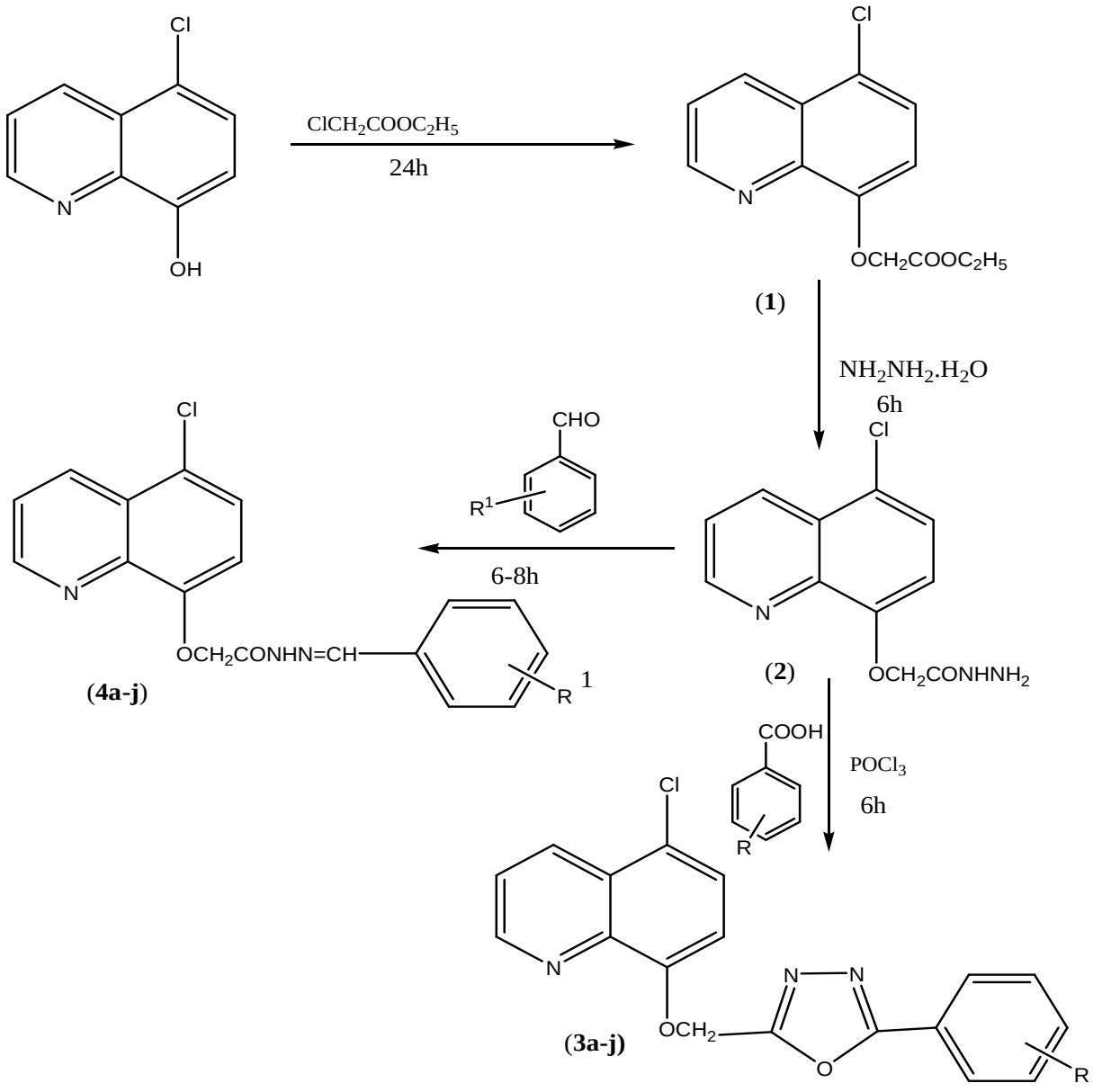
INTRODUCTION

The most popular method of synthesis 2, 5-disubstituted 1, 3, 4-oxadiazolesinvolves the cyclization of acylhydrazines with substituted carboxylic acids/acid chlorides in presence of phosphorous oxychloride. Acyl hydrazines are the keyprecursors for the synthesis 1, 3, 4oxadiazole derivatives. The hydrazine derivativescan be readily prepared from alkyl esters/ acids on treatment with hydrazine hydrate[1].1, 3, 4-oxadiazole derivatives can also be synthesized through arylidenederivatives i.e. Schiff's bases by oxidative cyclization in presence of yellow mercuricacid, acetic anhydride[2] chloramine-T[3]. Literature survey revealed that 1,3,4-oxadiazole molecule possess a number ofbiological activities like antibacterial, antifungal[4-14], antiviral[15], genotoxic[16], andanti-HIV[17], anticonvulsant activity[18-20], insecticidal activity[21-22], *Mycobacterium tuberculosis*[23-24], cytotoxic[25], tyrosinase inhibitory[26], anti-inflammatory[27], lipoxgenase inhibitory, MAOinhibitory[28], succinate dehydrogenase inhibitory[29], anti-hepatitis-B virus[30], immunosuppressive[31], activities. 1, 3, 4-oxadiazole molecules containing fluorine are reported to possess enhanced antimicrobial activity[32] and also anticancer activity[33].Some of the oxadiazoles and Schiff bases bearing quinolone moiety were reported as antimicrobial agents[34] stimulated our interest to synthesize new 1,3,4-oxadiazole and Schiff bases bearing 5-chloroquinolin-8-ol moiety.

EXPERIMENTAL SECTION

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on DR-8001 Shimadzu FT-IR spectrophotometer. ^{1}H-NMR spectra were measured using WP 400-NMR spectrometer; deuterated solvents such as dimethyl-sulphoxide (DMSO-d_6), methanol (CD_3OD) and chloroform ($CDCl_3$) were used as solvents and the chemical shifts were quoted as δ-value relative to tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on LC-MS Schimadzu 2010A using dimethyl sulfoxide as solvent. C, H, N analysis were performed at Cochin University, Sophisticated Test & Instrumentation centre, Cochin, Kerala, India. The purity of the compounds was monitored by thin layer chromatography on silica gel plates and iodine was used as a visualizing agent.

Scheme



Synthesis of ethyl 2-(5-chloroquinolin-8-yloxy)acetate (1)

A mixture of 5-chloro-8-quinolinol (0.05mol), ethylchloroacetate (0.05mol) and anhydrous potassium carbonate in dry acetone was refluxed for 24 hours on water bath at 70 ^{0}C. The resultant reaction mixture was cooled and

filtered.**IR(KBr, γmax cm^{-1}):** 3047.32(Ar C-H str), 2970.17(alkyl C-H-str), 1573.81 (Aromatic C=N str), 1195.78(C-O-C str),732.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):**8.1- 7.0(5H, m, Ar-H), 5.6(2H, s, -OCH_2), 2.3(2H, q, CH_2), 1.1(3H, t, CH_3).**MS (m/z):** 280 (M^+); Anal. Calcd (found) for $C_{14}H_{14}ClNO_3$, C, 60.00(59.75); H,5.00(4.49), N, 5.00(4.00).

Synthesis of 2-(5-chloroquinolin-8-yloxy)acetohydrazide (2)

A mixture of ethyl 2-(5-chloroquinolin-8-yloxy)acetate(0.05mol) and hydrazine hydrate 99% (0.07mol) in ethanol was refluxed for 6 hours. The excess of solvent is distilled off and the separated product was recrystallized from ethanol.**IR(KBr, γmax cm^{-1}):** 3227.35(NH str), 3000.32(Ar C-H str), 2977.17(alkyl C-H-str), 1677.98(C=O str), 1577.81(Aromatic C=N str), 1195.78(C-O-C str),732.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):**11.2(1H, s, NH),8.1- 7.0(9H, m, Ar-H), 4.2(2H, s, NH_2), 5.6(2H, s, -OCH_2), **MS(m/z):** 266 (M^+); Anal. Calcd (found) for $C_{12}H_{12}ClN_3O_2$, C, 54.13(54.10); H, 4.51(4.49); N, 15.78(15.70).

General procedure for the synthesis of 2-((5-chloroquinolin-8-yloxy) methyl)-5-(substituted phenyl)-1, 3, 4-oxadiazole(3a-j)

A mixture of ethyl 2-(5-chloroquinolin-8-yloxy)acetohydrazide**(2)** (0.01mol) and substituted benzoic acid (0.01) was heatedat 70˚C in the presence of phosphorous oxy chloride (10 ml) for 6 hours. The reaction mixture was cooled and poured onto crushed ice, stirred well and neutralized with 20% sodium carbonate. The solid thus separated was filtered and recrystallized from DMF.

2-(4-chlorophenyl)-5-((5-chloroquinolin-8-yloxy)methyl)-1,3,4-oxadiazole(3a)

IR(KBr, γmax cm^{-1}): 3092.32(Ar C-H str), 2973.17(alkyl C-H-str), 1598.09(Aromatic C=N str), 1110.92.75(C-O-C str), 750.76(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H),5.6(2H, s, -OCH_2), **MS (m/z):** 372 (M^+); Anal. Calcd (found) for $C_{18}H_{11}Cl_2N_3O_2$, C, 58.06(58.00); H, 2.95(2.90); N, 2.95(2.90).

2-((5-chloroquinolin-8-yloxy) methyl)-5-(4-nitrophenyl)-1, 3, 4-oxadiazole (3b)

IR(KBr, γmax cm^{-1}): 3008.32(Ar C-H str), 2976.17(alkyl C-H-str), 1573.81 (Aromatic C=N str), 1195.78(C-O-C str),731.17(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS (m/z):** 382 (M^+); Anal. Calcd (found) for $C_{18}H_{11}Cl_2N_4O_4$, C, 56.54(56.50); H, 2.87(2.84); N, 14.65(14.60).

2-((5-chloroquinolin-8-yloxy) methyl)-5-(4-methoxyphenyl)-1, 3, 4-oxadiazole (3c)

IR(KBr, γmax cm^{-1}): 3047.32(Ar C-H str), 2971.17(alkyl C-H-str), 1598.09 (Aromatic C=N str), 1110.92.75(C-O-C str), 763.67(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H), 5.6(2H, s, -OCH_2), 3.8(3H, S, OCH_3). **MS (m/z):** 367 (M^+); Anal. Calcd (found) for $C_{19}H_{14}ClN_3O_3$, C, 62.12(62.10); H, 3.81(3.78); N, 11.44(11.40).

4-(5-((5-chloroquinolin-8-yloxy) methyl)-1, 3, 4-oxadiazol-2-yl) phenol (3d)

IR(KBr, γmax cm^{-1}): 3048.32(Ar C-H str), 2977.17(alkyl C-H-str), 1573.09 (Aromatic C=N str), 1110.92.75(C-O-C str), 763.76(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS (m/z):** 353 (M^+); Anal. Calcd (found) for $C_{18}H_{12}ClN_3O_3$, C, 61.18(61.15); H, 11.89(11.86); N, 3.39(3.35).

2-(4-bromophenyl)-5-((5-chloroquinolin-8-yloxy) methyl)-1, 3, 4-oxadiazole (3e)

IR(KBr, γmax cm^{-1}): 3047.32(Ar C-H str), 2970.17(alkyl C-H-str), 1579.81 (Aromatic C=N str), 1195.78(C-O-C str), 836.77(C-Br str), 730.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 416 (M^+); Anal. Calcd (found) for $C_{18}H_{11}BrClN_3O_2$ C, 51.92(51.90); H, 2.64(2.60); N, 10.09(10.05).

2-(5-((5-chloroquinolin-8-yloxy)methyl)-1,3,4-oxadiazol-2-yl)-3,5-dinitrophenol(3f)

IR(KBr, γmax cm^{-1}): 3330.03(OH str), 3047.32(Ar C-H str), 2970.17(alkyl C-H-str), 1573.81 (Aromati C=N str), 1195.78(C-O-C str),750.56(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.5(1H, s, OH),8.1- 7.0(9H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 443 (M^+); Anal. Calcd (found) for $C_{18}H_{10}ClN_5O_7$, C, 48.75(48.70); H, 2.25(2.20); N, 15.80(15.80).

5-chloro-2-(5-((5-chloroquinolin-8-yloxy) methyl)-1, 3, 4-oxadiazol-2-yl) phenol (3g)

IR(KBr, γmax cm^{-1}): 3279.03 (OH str), 3047.32(Ar C-H str), 2976.17(alkyl C-H-str), 1573.81 (Aromatic C=N str), 1195.78(C-O-C str),746.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.3(1H, s, OH),8.1- 7.0(9H, m, Ar-H),

5.6(2H, s, -OCH_2), **MS (m/z):** 388 (M^+); Anal. Calcd (found) for $C_{18}H_{11}Cl_2N_3O_3$, C, 55.67(55.65); H, 2.83(2.80); N, 10.82(10.80).

2-((5-chloroquinolin-8-yloxy) methyl)-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole(3h)
IR(KBr, γmax cm^{-1}): 3047.32(Ar C-H str), 2997.17(alkyl C-H-str), 1593.82 (Aromatic C=N str), 1195.78(C-O-C str),750.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H) 5.6(2H, s, -OCH_2), **MS(m/z):** 406 (M^+); Anal. Calcd (found) for $C_{18}H_{10}Cl_3N_3O_2$, C, 53.20(53.20); H, 2.46(2.40); N, 10.34(10.37).

2-((5-chloroquinolin-8-yloxy) methyl)-5-phenyl-1,3,4-oxadiazole(3i)
IR(KBr, γmax cm^{-1}): 3041.32(Ar C-H str), 2989.17(alkyl C-H-str), 1578.71 (Aromatic C=N str), 1195.78(C-O-C str),738.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 8.1- 7.0(9H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 337 (M^+); Anal. Calcd (found) for $C_{18}H_{12}ClN_3O_2$, C, 64.09(64.05); H, 3.56(3.51); N, 12.46(12.40).

2-((5-chloroquinolin-8-yloxy) methyl)-5-(3,4-dimethoxyphenyl)-1,3,4-oxadiazole(3j)
IR(KBr, γmax cm^{-1}): 3047.32(Ar C-H str), 2937.17(alkyl C-H-str), 1573.81 (Aromatic C=N str), 1195.78(C-O-C str),732.90(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 7.9- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), 3.8(6H, s, OCH_3). **MS(m/z):** 397 (M^+); Anal. Calcd (found) for $C_{20}H_{16}ClN_3O_4$, C, 60.45(60.40); H, 4.03(4.00); N, 10.57(10.55).

General procedure for the synthesis of 2-(5-chloroquinolin-8-yloxy)-N'-(substituted benzylidene) acetohydrazide (4a-j)
A mixture of ethyl 2-(5-chloroquinolin-8-yloxy) acetohydrazide (**2)** (0.01mol) (dissolved in minimum quantity of ethanol) and different aromatic aldehydes (dissolved in minimum quantity of ethanol) was refluxed along with few drops of glacial acetic acid for 6 -8 hrs. The reaction mixture was cooled and then poured onto crushed ice and stirred well. The separated solid was filtered and recrystallized from ethanol.

2-(5-chloroquinolin-8-yloxy)-N'-(2,4-dihydroxybenzylidene)acetohydrazide(4a)
IR(KBr, γmax cm^{-1}): 3456.21(OH str), 3366.31(NH-str), 3047.32(Ar C-H str), 2930.17(alkyl C-H-str), 1618.02(C=N of imine str), 1589.23 (Aromatic C=N str), 1198.21(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 12.3(2H, s, OH), 11.8(1H, s, NH), 9.2(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 371 (M^+); Anal. Calcd (found) for $C_{18}H_{14}ClN_3O_4$, C, 58.22(58.20); H, 3.77(3.70); N, 11.32(11.30).

N'-(4-chlorobenzylidene)-2-(5-chloroquinolin-8-yloxy) acetohydrazide (4b)
IR(KBr, γmax cm^{-1}): 3366.31(NH-str), 3047.32(Ar C-H str), 2980.17(alkyl C-H-str), 1618.51(C=N of imine str), 1589.98 (Aromatic C=N str), 1178.00(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 9.3(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 374 (M^+); Anal. Calcd (found) for $C_{18}H_{13}Cl_2N_3O_2$, C, 57.75(57.70); H, 3.47(3.43); N, 11.22(11.20).

2-(5-chloroquinolin-8-yloxy)-N'-(2,4-dichlorobenzylidene)acetohydrazide(4c)
IR(KBr, γmax cm^{-1}): 3366.31(NH-str), 3047.32(Ar C-H str), 2998.17(alkyl C-H-str), 1618.47(C=N of imine str), 1589.23 (Aromatic C=N str), 1198.21(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 8.9(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 408 (M^+); Anal. Calcd (found) for $C_{18}H_{12}Cl_3N_3O_2$,C, 52.94(52.90); H, 2.94(2.90); N, 10.29(10.27).

2-(5-chloroquinolin-8-yloxy)-N'-(2-hydroxybenzylidene) acetohydrazide (4d)
IR(KBr, γmax cm^{-1}): 3540.11 (OH str), 3366.31(NH-str), 3047.32(Ar C-H str), 2977.17(alkyl C-H-str), 1638.92(C=N of imine str), 1589.23 (Aromatic C=N str), 1178.22(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 12.3(1H, s, OH), 11.8(1H, s, NH), 9.3(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 355 (M^+); Anal. Calcd (found) for $C_{18}H_{14}ClN_3O_3$C, 60.84(60.80); H, 3.94(3.90); N, 11.83(11.80) .

2-(5-chloroquinolin-8-yloxy)-N'-(4-methoxybenzylidene) acetohydrazide (4e)
IR(KBr, γmax cm^{-1}): 3395.07(NH-str), 3047.32(Ar C-H str), 2939.02 (alkyl C-H-str), 1640.00(C=N of imine str), 1589.23 (Aromatic C=N str), 1198.21(C-O-C str),763.76(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 9.4(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), 3.8(3H, s, OCH_3). **MS(m/z):** 369 (M^+); Anal. Calcd (found) for $C_{19}H_{16}ClN_3O_3$, C, 61.78(61.77); H, 4.33(4.30); N, 11.38(11.30).

N'-benzylidene-2-(5-chloroquinolin-8-yloxy) acetohydrazide (4f)
IR(KBr, γmax cm^{-1}): 3366.31(NH-str), 3007.32(Ar C-H str), 2934.17(alkyl C-H-str), 1618.92(C=N of imine str), 1589.23 (Aromatic C=N str), 1178.21(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 9.2(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 339 (M^+); Anal. Calcd (found) for $C_{18}H_{14}ClN_3O_2$, C, 63.71(63.68); H, 4.12(4.10); N, 12.38(12.35).

2-(5-chloroquinolin-8-yloxy)-N'-(4-nitrobenzylidene)acetohydrazide(4g)
IR(KBr, γmax cm^{-1}): 3366.31(NH-str), 3099.32(Ar C-H str), 2977.17(alkyl C-H-str), 1640.00(C=N of imine str), 1589.23 (Aromatic C=N str), 1188.21(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 9.0(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 384 (M^+); Anal. Calcd (found) for $C_{18}H_{13}ClN_4O_4$, C, 56.25(56.20); H, 3.38(3.35); N, 14.58(14.55).

2-(5-chloroquinolin-8-yloxy)-N'-(2-nitrobenzylidene)acetohydrazide(4h)
IR(KBr, γmax cm^{-1}): 3366.31(NH-str), 3047.32(Ar C-H str), 2974.17(alkyl C-H-str), 1620.00(C=N of imine str), 1599.23 (Aromatic C=N str), 1138.21(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 9.1(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 384 (M^+); Anal. Calcd (found) for $C_{18}H_{13}ClN_4O_4$, C, 56.25(56.20); H, 3.38(3.35); N, 14.58(14.56).

N'-(5-bromo-2-hydroxybenzylidene)-2-(5-chloroquinolin-8-yloxy)acetohydrazide(4i)
IR(KBr, γmax cm^{-1}): 3405.04(OH str), 3366.31(NH-str), 3047.32(Ar C-H str), 2971.17(alkyl C-H-str), 1618.92(C=N of imine str), 1589.23 (Aromatic C=N str), 1197.91(C-O-C str), 847.77(C-Br str), 748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 12.3(1H, s, OH), 11.8(1H, s, NH), 9.3(1H, s, CH),8.1- 7.0(8H, m, Ar-H), 5.6(2H, s, -OCH_2), **MS(m/z):** 434 (M^+); Anal. Calcd (found) for $C_{18}H_{13}BrClN_3O_3$, C, 49.76(49.74); H, 2.99(2.96); N, 9.67(9.65).

2-(5-chloroquinolin-8-yloxy)-N'-((2-methoxynaphthalen-1-yl)methylene)acetohydrazide(4j)
IR(KBr, γmax cm^{-1}): 3366.31(NH-str), 3018.98(Ar C-H str), 2970.98(alkyl C-H-str), 1649.92(C=N of imine str), 1587.23 (Aromatic C=N str), 1199.20(C-O-C str),748.33(C-Cl str). **^{1}HNMR(400 MHz, DMSO) (ppm):** 11.8(1H, s, NH), 9.2(1H, s, CH), 8.1- 7.0(10H, m, Ar-H), 5.2(2H, s, -OCH_2), 3.8(3H, s, OCH_3). **MS(m/z):** 419 (M^+); Anal. Calcd (found) for $C_{23}H_{18}ClN_3O_3$, C, 65.87(65.85); H, 4.29(4.27); N, 10.02(10.00).

Table: Ishowing physical data of 2-((5-chloroquinolin-8-yloxy)methyl)-5-(substituted phenyl)-1,3,4-oxadiazole(3a-j)

Code	R	Molecular formula	Molecular Weight	M.P (^{0}C)	Yield(%)
3a	4-Cl	$C_{18}H_{11}Cl_2N_3O_2$	372	193-195	80
3b	4-NO_2	$C_{18}H_{11}Cl_2N_4O_4$	382	132-135	65
3c	4-OCH_3	$C_{19}H_{14}ClN_3O_3$	367	122-124	62
3d	4-OH	$C_{18}H_{12}ClN_3O_3$	353	152-155	60
3e	4-Br	$C_{18}H_{11}BrClN_3O_2$	416	146-147	52
3f	3,5-NO_2, 2-OH	$C_{18}H_{10}ClN_5O_7$	443	154-158	79
3g	5-Cl,2-OH	$C_{18}H_{11}Cl_2N_3O_3$	388	116-119	54
3h	2,4-Cl	$C_{18}H_{10}Cl_3N_3O_2$	406	124-126	56
3i	H	$C_{18}H_{12}ClN_3O_2$	337	170-172	72
3j	3,4-OCH_3	$C_{20}H_{16}ClN_3O_4$	397	162-165	62

Table II: showing physical data of2-(5-chloroquinolin-8-yloxy)-N'-(substituted benzylidene)acetohydrazide (4a-j)

Code	R_1	Molecular formula	Molecular Weight	M.P(^{0}C)	Yield(%)
4a	2-OH,4-OH	$C_{18}H_{14}ClN_3O_4$	371	152-156	68
4b	4-Cl	$C_{18}H_{13}Cl_2N_3O_2$	374	164-166	72
4c	2,4-Cl	$C_{18}H_{12}Cl_3N_3O_2$	408	172-174	78
4d	2-OH	$C_{18}H_{14}ClN_3O_3$	355	150-152	70
4e	4-OCH_3	$C_{19}H_{16}ClN_3O_3$	369	148-151	65
4f	H	$C_{18}H_{14}ClN_3O_2$	339	127-129	60
4g	4-NO_2	$C_{18}H_{13}ClN_4O_4$	384	138-140	55
4h	2-NO_2	$C_{18}H_{13}ClN_4O_4$	384	136-138	53
4i	5-Br,2-OH	$C_{18}H_{13}BrClN_3O_3$	434	174-177	76
4j	2-OCH_3-H (naphthyl)	$C_{23}H_{18}ClN_3O_3$	419	186-189	67

Biological Activity

In vitro antibacterial screening

All the newly synthesized compounds **(3a-j & 4a-j)** were screened in vitro for their antibacterial activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* by disc diffusion method [35]was performed using Mueller. Hinton agar (Hi-Media) medium. Each compound was tested at a concentration at40µg/mL in DMSO. The diameter of zone of inhibition was measured in mm after 24h incubation at 37^{o}C. The known compound ciprofloxacin was used as standard drug for comparison study. The antibacterial screening data are recorded in **Table III.**

In vitro antifungal screening

The compounds **(3a-j & 4a-j)** were evaluated for their in vitro antifungal activity against *Candida albicans & Aspergillus nigar* using disc diffusion method [36] with Sabouraud's dextrose agar (Hi-Media). Each compound was tested at a concentration of 40µg/mL in DMSO. The zone of inhibition (mm) was measured. The known compound Amphotericin B was used as standard drug for comparison study. The antifungal screening data are recorded in **Table III.**

RESULTS AND DISCUSSION

Synthesis of 1, 3, 4-oxadiazole derivatives& Schiff bases by the described method resulted in products with good yield. All the reactions were carried out under prescribed laboratory conditions. The solvents and reagents used in synthetic work were of laboratory grade and were purified by distillation. Purity of the newly synthesized compounds was determined by melting point by open capillary method. Progress of the reactions was monitored by TLC.The structures of the newly synthesized compounds were established on the basis of spectral data (IR., ^{1}HNMR and Mass). (The spectral values of the compounds are given in the subsequent section). All the compounds were screened for antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus, Pseudomonas aeruginosa&Escheritia coli*using cup-plate method. Ciprofloxacin was used as standard. The compounds were also screened for antifungal activity against *Candida albicans*and *Aspergillusnigar*. Amphoterecin B was used as standard. Compounds **3e, 4i** and **4j** which have bromo, and 2-methoxy naphthyl have shown significant activity against almost all the organisms compared to that of standard drug. Compounds **4(a-j)** have shown good activity against all selected microorganismsas compare to 1,3,4-oxadiazole derivatives. Compounds having halogens have shown enhanced antimicrobial activity. From the above results it was noticed that 5-chloroquinolin-8-olderivatives are good antimicrobial agents with minimum inhibitory concentration at 40 μ/mL.

Table-III represents antimicrobial activity data of 1, 3, 4-Oxadiazoles (3a-j) & Schiff bases (4a-j)

Code	R	Antibacterial activity Zone of inhibition (in mm)				Antifungal activity Zone of inhibition (in mm)	
		B. subtilis	*P. aerugenoa*	*E. coli*	*S. aureus*	*C. albicas*	*A. nigar*
3a	4-Cl	12	12	8	12	10	8
3b	4-NO_2	13	9	8	10	9	8
3c	4-OCH_3	12	12	8	8	7	7
3d	4-OH	11	7	6	8	9	8
3e	4-Br	18	20	18	20	15	13
3f	3,5-NO_2,2-OH	10	8	7	9	9	8
3g	5-Cl,2-OH	7	8	7	6	6	6
3h	2,4-Cl	11	12	10	9	11	11
3i	H	8	9	17	18	6	6
3j	3,4-OCH_3	11	8	9	7	8	7
4a	2,4-OH	13	10	5	12	10	10
4b	4-Cl	16	9	13	12	10	10
4c	2,4-Cl	15	11	17	18	6	6
4d	2-OH	22	7	10	10	8	8
4e	4-OCH_3	15	6	6	13	7	7
4f	H(phenyl)	10	5	8	6	5	5
4g	4-NO_2	12	9	9	8	6	6
4h	2-NO_2	12	9	9	8	6	6
4i	5-Br,2-OH	32	25	30	33	20	20
4j	2-OCH_3, H (naphthyl)	17	22	23	18	18	18
Ciprofloxacin	-	38	37	37	35	-ve	-ve
Amphoterecin B	-	-ve	-ve	-ve	-ve	37	33

Control (DMSO), (– ve) – No activity

CONCLUSION

All the newly synthesized 5-chloroquinolin-8-olderivatives were resulted in good yield. The structures of the newly synthesized compounds were confirmed on the basis of ^{1}HNMR, IR and Mass spectral analysis. Compound **4i** containing 5-Br, 2-OH functional groups have shown excellent antimicrobial activity. Therefore it is evident that the substituents that are electronegative in nature can certainly potentiate the activity.

Acknowledgements
The authors wish to thank HOD, Department of chemistry, Manipal Institute of Technology, Manipal University, Manipal and Department of Biotechnology, Manipal college of pharmaceutical sciences for their support to carry out the synthesis and antimicrobial activity.

REFERENCES

[1].K IshwarBhat; KPSunil Chaitanya; D Satyanarayana;BalakrishnaKalluraya. *J SebChem Soc.*,**2007,** 72(5), 437-442.
[2].KC Ravindra; HM Vagdevi; VP Vaidya;BasavarajPadmshali. *Ind J Chem.*,**2006,** (45B), 2506-2511.
[3]. K Mogilaiah;MA Prashanthi. *Ind J Het Chem.*,**2005,** (14), 185-188.
[4]. Li Yan; Liu Jie; Zhang Hongquan; Yang ziangping; Liu Zhaojhu. *Bio Org Med ChemLett.*,**2006,** (16), 2278-2782.
[5]. Mishra Pradeep; Rajak Harish; Mehta Archana. *J Gen ApplMicrobiol.*,**2005,** (51), 133-141.
[6]. Hui Xing-Ping; Hu-Chang; Zhang Zi-Yi. *Ind J Chem.*,2002**,** (41B), 2176-2179.
[7]. V PriyaFrank;KallurayaBalakrishna. *Ind J Chem.*,**2005**, (44B), 1456-1459.
[8]. Y Jayamm; M Sarangapani; VM Reddy. *Ind J Het Chem.*,**1996,** (6), 111-114.
[9]. K Mogilaiah; K Vaidya. *Ind J Chem.*,**2006,**(45B),1905-1908.
[10]. RP Singh; CR Singh; SP Tripathi; DV Singh; S Singh;D Singh.*Ind J Het Chem.*,**2006, (**15), 345-348.
[11]. KR Agalwadi; S Suresh;SR Pattan; GV Pujar; MC. Javali. *Ind J HetChem.*,**2007**, (17), 93-94.
[12]. S Jain; N Jain;P Mishra. *Ind J Het Chem.*,**2005**, (14), 359-360.
[13]. MA Bakht; M Islam; A SIddiquiAnees. *Ind J Het Chem.*,**2006**, (15), 297-298.
[14].HRajasekhara;D Ramesh Chandrashekar; CKM Mahadevan; VPVaidya. *Ind J Het Chem.*,**2007,** (16), 353-356.
[15]. AkhtherTashfeen; HameedShahid; Al-MasaudiA.Nazim; LoddoRoberta; Colla Lao Paulo. *Acta Pharm.*,**2008,**(58),135-149.
[16]. O MaslatAhmed; Abussaud Mahmud; TashtoshHasan; Al-TalibMahmoud. *Pol J Pharmacol.*,**2002**, (54), 55-59.
[17]. HP Shah; BRShah;JJNC Bhatt Desai; PB Trivedi; NK Undavia.*Ind J Chem.*,**1998,** (37B), 180-82.
[18]. MSY Khan;RM Khan; DrabuSushma. *Ind J Het Chem.*,**2001**, (11), 119-122.
[19]. MA Mohsen; E Omar; M AboulwafaOmaima. *J Heterocyclic Chem*,**1984**,(21), 1415-1420.
[20]. ZarghiAfshin; A TabatabaiSayeed; FaiziMehrdadAhadianAvideh; NavabhiParasi;ZanganehVahideh; Shafee Abbas. *Bioorganic and Medicinal Chemistry Letters.*,**2005**, (15), 1863-1865
[21]. BS Holla; CS Prasanna; B Poojary; KSRao; K Sridhara;U.GaneshaBhat. *Ind J Chem.*,**2004,** (43B), 864-868.
[22]. T Singh;S Sharma;VKSrivastava; A Kumar. *Ind J Chem.*,**2006**, (45B), 1557-1563.
[23]. Navarette-VarquezGabriel; Molina-Salinas Gloria Maria; Daurte-FajardoZetelVahi;Vargas-Villarreal Javier; SameulEstrado-Soto; Gonzalez-SalazarFrancisco; Hernandez-Nunez; Said-Fernandez Salvador. *Bioorganic and Medicinal Chemistry.*,**2007,** (15),5502-5508.
[24].R RakeshSomani;Y PrabhakarShirodhkar; P MrunmayeeToraskar; J VilasRaoKadam.*Indian J Pharm Edu Res.*,**2008**, 42(1), 53-58.
[25]. V Padmavathi; G Sudhakar Reddy; A Padmaja;P Kondaiah Ali Shazia.*Eur J Med Chem.*,**(2008),** 4,123-7.
[26]. Tarique Hassan Khan Mahmud;IqbalChoudary Mohammed; Khan Khaleed Mohammed; Rani Mubeen; Atta-Ur-Rahaman.*Bioorganic and MedicinalChemistry.***2005,** (13), 3385-3395.
[27]. VN Sonar; SK Yazdhan;N Sreenivasulu.*Ind J Het Chem.*,**2001,** (10), 299-302.
[28].HD Boschelli; T Connor David; A BornemeierDirk; RD Dyer; J Kennedy AJhon;Kuipers Paul;GC Onokwa;DJ SChrier; D Wright Clifford.*J MedChem.*,**2000,**(36), 1802-1810.
[29]. SoniNamita; JP Barthwal; AK Saxena; KP Bhargava. *J Heterocyclic Chem.*,**1982,** (19), 29-32.
[30].AEssaway;WA Sayeed; SA Kafrawy;AS Morshedy;AH Abdel-Rahman. *Z Naturforsch [C].*,**2008,** 63(9-10), 667-674.
[31]. PB Gosh; MW Whitehouse. *J Med Chem.*,**1968,** 11, 305-310.
[32].MS Karthiketan; DJ Prasad; M Mahalinga;BS Holla; N SuchethaKumari.*Eur J Med Chem.*, **2008,** (43),25-31.
[33]. S AboriaAhmed;M Hamdy; A Rahman; M Mahfouz Nadia; MA Gendy.*Bioorg and Med ChemLett.,* **2006,** (14), 1236-1246.
[34]. P. Sunil Kumar Chaitanya; K. IshwarBhat. *Journal of chemical and pharmaceutical sciences.*, **2009**, 2 (3), 204-206.
[35] AW Bauer; WM Kirby; JC Sherris; JCM Turck.*Am .Clin.Pathol*.**1966**, 9,493.
[36]HD Joshi; PS Upadhyay; AJBaxi.*Asian J. Chem.*,**1992**, 4, 93-95.