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Synthesis, Characterization and biological evaluation of novel quinoline linked 1,3,4-oxadiazoles possessing azetidin-2-one, thiazolidin-4-one and tetrazole moieties

G. Madhu[1]*, K.N.Jayaveera[1], L.K. Ravindranath[2], B. Santosh Kumar[2], P. Nagarjuna Reddy[1]

[1]Department of Chemistry, JNTUA College of Engineering, Anantapur, A.P., India.
[2]Department of Chemistry, S.K .University, Anantapur, A.P., India.

***Corres. author: madhugchem@gmail.com**

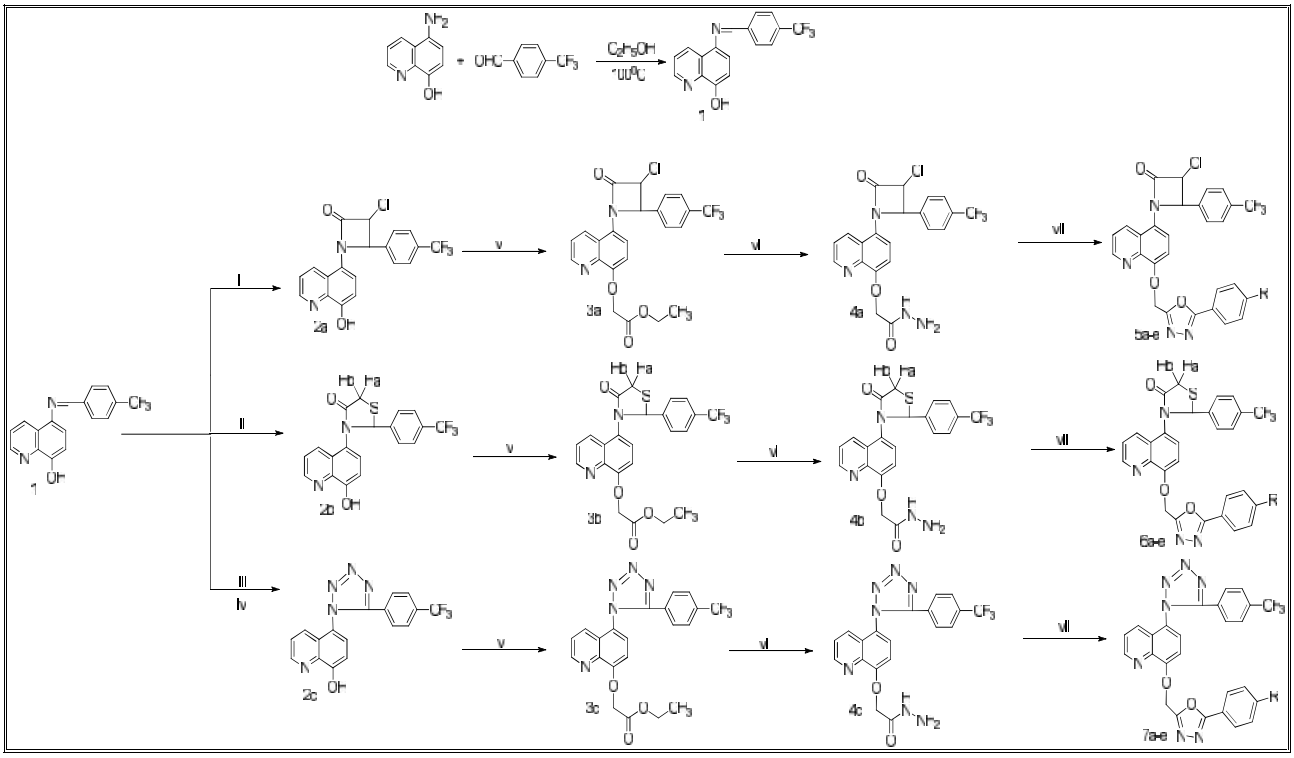
Abstract: ***Purpose***: The article is aimed to synthesize, characterize and screening the biological activity of a series of 3-chloro-1-(8-((5-(4-substitutedphenyl)-1,3,4-oxadiazol-2-yl)methoxy) quinolin-5-yl)-4-(4-trifluoro methyl) phenyl) azetidin-2-one (5a-e), 3-(8-((5-(4-substitutedphenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (6a-e) and 2-(4-substitutedphenyl)-5-(((5-(5-(4-(trifluoro methyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl)-1,3,4-oxadiazole (7a-e). ***Methods***: The newly synthesized compounds were characterized by elemental analysis and IR, ^{1}H-NMR, ^{13}C NMR and Mass spectral data. The antimicrobial activity of the novel compounds was screened by agar disc diffusion method. ***Results:*** 5d, 7a, 7d and 7e have shown better antibacterial and anti fungal activity than other compounds of the series. Quinoline linked 1,3,4-oxadiazole with tetrazole nucleus has shown good antibacterial and antifungal activities than quinoline linked 1,3,4-oxadiazole with azetidin-2-one and thiazolidin-4-one moieties.

Key Words: 1,3,4-oxadiazoles, thiazolidin-4-one, tetrazole, antibacterial and antifungal.

Introduction:

Among the five member heterocyclic compounds, 1,3,4-oxadizoles has become an important synthon for the development new therapeutic agents. Compounds with 1,3,4-oxadiazole core substantiate for broad spectrum of biological activities including antimicrobial[1], antifungal[2], antiinflammatory[3], anticonvulsant[4], antioxidant, analgesic[5] and mutagenic acctivity[6]. Compounds containing quinoline moiety are most widely used as antimalarials[7], antibacterials[8], antifungals[9], anticancer agents[10] and potential HIV-1 integrase inhibitors[11,12]. Azetidin-2-ones are very important class of compounds possessing wide range of biological activities such as antimicrobial[13,14], pesticidal[15], antitumor[16], antitubercular[17], anticancer[18], cytotoxic[19-21], enzyme inhibitors[22], elastase inhibitors[23] & cholesterol absorption inhibitors[24]. 4-thiazolidinones moiety is associated with variety of biological activities including antifungal[25], anti-inflammatory[26], anticonvulsant[27], antitubercular[28], antihistaminic[29]. Tetrazoles and its derivatives are used for biological activities such as anti-inflammatory[30], antibacterial[31], antifungal[32], analgesic[33], anticonvulsant[34], anticancer[35] and antihypertensive[36] activities.

Hence it was thought worthwhile to synthesise some new congeners 1,3,4-oxadiazole by incorporating the quinoline, azetidin-2-one, thiazolidin-4-one and tetrazole moieties in a single molecular frame work.



Comp	a	b	c	d	e
R	F	Cl	Br	NO_2	CF_3

Reagents & Conditions: (i) Chloroacetyl chloride, Triethyl amine, Dioxane, 8h. (ii) Thioglycolic acid, Zinc Chloride, Dioxane, 8h.(iii) PCl_3, 100^0C, 1h (iv) Sodium azide (ice-cold), Zinc Chloride, Sodium acetate, acetone, water RT.(v) Chloroethylacetate, DMF, K_2CO_3, RT, 8h. (vi) $N_2H_4.H_2O$, ethanol, reflux, 5h.(vii) 4-substituted benzoic acid, $POCl_3$, reflux, 5-6h.

Materials Methods:

Melting points were determined on open capillaries using a cintex melting point apparatus. T.L.C analyses were performed on precoatedsilicagel (E-Merck Kieselgel $60F_{254}$) plates and visualisation was done by exposing to iodine vapour. Solvents were purified by standard procedures before use. IR Spectra were recorded in KBr on Perkin-Elmer Spectrum BX series FT-IR spectrometer. ^{1}H-NMR spectrum were recorded on DRX 300MHz Bruker spectrometers using TMS as internal standard (chemical shifts in δ ppm). ^{13}C-NMR Spectra were recorded on a Brucker 75MHz spectrometer. Mass spectra were scanned on a varian MATCH-7 at 70ev. Elemental analyses were carried out on a carloerba 106 and Perkin-Elmer Analyser. All the chemicals used in the present investigation were purchased from Sigma-aldrich, India. The synnthon 5-amino-8-hydroxy quinoline was prepared by a reported method[37].

Results and Discussions:

The target compounds were synthesized via the route as shown in Scheme above. The synthon required for the synthesis of the target molecules 5-amino-8-hydroxy quinoline was prepared by a reported method.Filtered and recrystallized from ethanol.

Synthesis of 3-chloro-1-(8-hydroxyquinolin-5-yl)-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (2a)

5-((4-(trifluoromethyl)benzylidene)amino)quinolin-8-ol (1) was synthesized by reported procedure[38]. Monochloroacetyl chloride (0.01mol) was added drop wise to schiff's base (1) (0.01mol) and triethyl amine (0.02mol) in dioxane (25ml) at room temperature. The mixture was stirred for 8h and left at room temperature for 3 days[39,40]. The contents were poured on crushed ice. The product thus formed was filtered and washed with sodium bicarbonate solution. The dried product was recrystalised with absolute alcohol. The MP was 148-9^{0}C with a yield of 58%. ^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6 (s, 1H, -OH), 5.16 (d, 1H, -CH-$C_6H_4CF_3$), 5.44

(d, 1H, -CH–Cl), 7.3-8.8 (m, 9H, Ar-H). IR (KBr) spectra cm^{-1}: 3340 (-OH), 3048 (=C-H, aromatic), 1690 (C==O), 677 (C-Cl).

Synthesis of 3-(8-hydroxyquinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one(2b)

A mixture of schiff's base (0.01 mol) and mercaptoacetic acid (0.01 mol) dissolved in diaoxane (20 ml), anhydrous zinc chloride (0.5 mg) was added and refluxed for 8 hrs. The reaction was cooled and the resulting solid was washed with sodium bicarbonate solution and recrystalised from absolute alcohol[39,40]. The yield was 62% with MP: 162-3^{0}C. ^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6 (s, 1H, -OH), 6.44 (s, 1H, -CH-$C_6H_4CF_3$), 3.85 (d, 1H, H_a), 3.97 (d, 1H, H_b), 7.3-8.7(m, 9H, Ar-H). IR (KBr) spectra cm^{-1}: 3340 (-OH), 1690 (-C==O) and 1156 (-C-S).

Synthesis of 5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-ol (2c)

Schiff base(0.004mol) and PCl_5 (0.004mol) was heated at 100^{0}c for 1h. When the evolution of fumes of HCl ceased, excess of PCl_3 was removed under reduced pressure and the residual imidoyl chloride was treated with an ice-cold solution of sodium azide(0.0075 mol) and excess of sodium acetate in water (25ml) and acetone (30ml) with stirring[41]. Stirring was continued for overnight, thereafter acetone was removed under reduced pressure. The remaining aqueous portion was extracted with chloroform was dried. The yield was 55% with MP 174-5^{0}C. ^{1}H NMR (300MHz, DMSO-d_6): δppm 4.6 (s, 1H,-OH), 7.2-8.7 (m, 9H, Ar-H). IR (KBr) spectra cm^{-1}: 3340 (-OH), 2120 (-azide), 1157 (Tetrazole).

Synthesis of ethyl-2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl)azetidin-1-yl)quinolin-8-yl)oxy)acetate (3a)/Ethyl-2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetate(3b)/Ethyl-2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetate (3c)

A mixture of 3-chloro-1-(8-hydroxyquinolin-5-yl)-4-(4-(trifluoromethyl) phenyl) azetidin-2-one (2a) / 3-(8-hydroxyquinolin-5-yl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one(2b)/5-(5-(4-(trifluoromethyl) phenyl) -1H-tetrazol-1-yl)quinolin-8-ol (2c) (0.02M) anhydrous K_2CO_3 (0.03M) Chloro ethyl acetate (0.02M) and Dimethylformamide was stirred at room temperature for 8 hours. The progress of the reaction was monitored by TLC with acetone:ethylacetate (7:3) as eluent The reaction mixture was diluted with ice-cold water. The separated solid was identified as 3a, 3b and 3c respectively. This was collected by ***General procedure for the synthesis of acid hydrazides (4a-c)***

A solution of Ethyl-2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl)azetidin-1-yl) quinolin-8-yl)oxy)acetate (3a)/Ethyl-2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetate(3b)/Ethyl-2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl) quinolin-8-yl)oxy)acetate (3c) (0.01M) and hydrazine hydrate (0.015M) in ethanol 20 mL was refluxed for 5 hours. The reaction mixture was cooled and poured on to ice cold water with stirring. The progress of the reaction was monitored by TLC with acetone:ethyl acetate (7:3) as eluent. The separated solid was filtered, washed with water and recrystallized from ethanol to afford the compounds 4a-c.

2-((5-(3-chloro-2-oxo-4-(4-(trifluoromethyl)phenyl)azetidin-1-yl)quinolin-8-yl)oxy) acetohydrazide(4a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 2.10(s, 2H,-NH_2), 5.16 (d,1H,-CH-$C_6H_4CF_3$), 5.44 (d, 1H, -CH–Cl), 4.8 (s, 2H, -O-CH_2), 7.2-8.6 (m, 9H, Ar-H), 9.54 (s, 1H, -NH). IR (KBr) spectra cm^{-1}: 3496, 3413 (-NH_2), 3205 (-NH), 1690 (-C=O), 1620 (-C=N). Anal Calcd. for $C_{21}H_{16}ClF_3N_4O_3$ (%): C, 54.26; H, 3.47; N, 12.05; Found: C, 54.12; H, 3.41; N, 11.99; M.P: 180-181^{0}C, yield 68%.

2-((5-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy) acetohydrazide(4b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 2.05(s, 2H,-NH_2), 6.44 (s, 1H, -CH-$C_6H_4CF_3$), 3.85 (d, 1H, -H_a), 3.99 (d, 1H, -H_b), 4.58 (s, 2H, -O-CH_2), 7.25-8.7 (m, 9H of Ar-H), 10.10 (s, 1H, -NH). IR (KBr) spectra cm^{-1}: 3498, 3416 (-NH_2), 3200 (-NH), 3040 (=C-H aromatic), 1698 (-C=O), 1620 (-C=N), 1188 (C-S). Anal Calcd. for $C_{21}H_{17}F_3N_4O_3S$ (%): C, 54.54; H, 3.71; N, 12.12; Found: C, 54.43; H, 3.66; N, 12.07; M.P: 163-164^{0}C, Yield 57%.

2-((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)acetohydrazide(4c).

^{1}H NMR (300MHz, DMSO-d_6): δppm 2.05 (s, 2H, -NH_2), 4.58 (s, 2H, -O-CH_2), 7.2-8.8 (m, 9H of Ar-H), 10.10(s, 1H, -NH). IR (KBr) spectra cm^{-1}: 3498, 3416 (-NH_2), 3200 (-NH), 3040 (=C-H aromatic), 2107 (azide),

1698 (-C=O), 1620 (-C=N), 1157(tetrazole). Anal Calcd. for $C_{19}H_{14}F_3N_7O_2$ (%): C, 53.15; H, 3.29; N, 22.84; Found: C, 53.08; H, 3.21; N, 22.77; M.P: 167-168^{0}C, yield 52%.

synthesis of 1,3,4-oxadiazole ring (5a-e, 6a-e, 7a-e)

A mixture of 4-substitutedbenzoicacid (0.01mol) with compound 4a / 4b /4c (0.01mol) in phosphoryl chloride (15ml) was refluxed over a steam bath for 5-6 h. The progress of the reaction was monitored by TLC with acetone: ethyl acetate (6:4) as eluent. The reaction mixture was cooled and poured on to crushed ice (~200g) with continuous stirring. The solid mass separated was neutralized with sodium bicarbonate solution (10% w/v). The resulting solid thus obtained was collected by filtration, washed well with cold water, dried in vacuum and recrystallized from absolute ethanol (95%).

3-chloro-1-(8-((5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (5a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.21 (s, 2H, -O-CH_2), 5.16 (d, 1H, -CH-$C_6H_4CF_3$), 5.44 (d, 1H, -CH–Cl), 6.9-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 68, 72 (aliphatic -C), 107,116,120,126,129,131, 133,139,146 (Ar-C), 162(-C=O), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3040 (=C-H aromatic), 1692 (-C=O), 1617 (-C=N), 1150 (-C-O-C-), 1135 (-N-N-) 833 (-C-Cl). MS, *m/z* : (M^+, 569.12, M+2, 571.09). Anal Calcd. for $C_{28}H_{17}ClF_4N_4O_3$ (%): C, 59.11; H, 3.01; N, 9.85; Found: C, 59.08; H, 2.96; N, 9.79; M.P: 157-158^{0}C, yield 48%.

3-chloro-1-(8-((5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-4-(4-(trifluoromethyl) phenyl)azetidin-2-one (5b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.20 (s, 2H, -O-CH_2), 5.14 (d, 1H, -CH-$C_6H_4CF_3$), 5.42 (d, 1H, -CH–Cl), 6.85-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 68, 72 (aliphatic -C) 107,116, 120, 126,129, 131, 133, 134, 139, 146(Ar-C), 162(-C=O), 163(C_2 of oxadiazole), 165(C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3041(=C-H aromatic), 1698 (-C=O), 1620 (-C=N), 1157(-C-O-C-), 1137(-N-N-) 838 (-C-Cl). MS, *m/z* : (M^+, 586.16, M+2, 588.08). Anal Calcd. for $C_{28}H_{17}Cl_2F_3N_4O_3$ (%): C, 57.45; H, 2.93; N, 9.57; Found: C, 57.39; H, 2.88; N, 9.52; M.P: 168-169^{0}C, yield 51%.

1-(8-((5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-3-chloro-4-(4-(trifluoromethyl) phenyl)azetidin-2-one (5c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.22 (s, 2H, -O-CH_2), 5.15 (d, 1H,- -CH-$C_6H_4CF_3$), 5.43 (d, 1H,-CH–Cl), 6.88-8.82 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 68, 72 (aliphatic -C) 107, 116, 121, 123, 125, 129, 130, 132, 139, 146 (Ar-C), 162 (-C=O), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3045(=C-H aromatic), 1696 (-C=O), 1615 (-C=N), 1160(-C-O-C-), 1141(-N-N-) 836 (-C-Cl). MS, *m/z* : (M^+, 630.28, M+2, 632.06). Anal Calcd. for $C_{28}H_{17}BrClF_3N_4O_3$ (%): C, 53.40; H, 2.72; N, 9.05; Found: C, 53.35; H, 2.66; N, 9.01; M.P: 134-135^{0}C, yield 57%.

3-chloro-1-(8-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-4-(4-(trifluoromethyl) phenyl)azetidin-2-one (5d)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.28(s, 2H,-O-CH_2), 5.16 (d, 1H, -CH-$C_6H_4CF_3$), 5.44(d, 1H, -CH–Cl), 7.1-8.85 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 68, 72 (aliphatic -C), 107, 116, 122, 126, 129, 130, 133, 139, 146 (Ar-C), 161(-C=O), 163(C_2 of oxadiazole), 165(C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3042(=C-H aromatic), 1692 (-C=O), 1620 (-C=N), 1156(-C-O-C-), 1135(-N-N-) 832 (-C-Cl). MS, *m/z* : (M^+, 595.43, M+2, 597.32). Anal Calcd. for $C_{28}H_{17}ClF_3N_5O_5$ (%): C, 56.43; H, 2.88; N, 11.75; Found: C, 56.37; H, 2.83; N, 11.67; M.P: 177-178^{0}C, yield 45%.

3-chloro-4-(4-(trifluoromethyl)phenyl)-1-(8-((5-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-yl)methoxy) quinolin-5-yl)azetidin-2-one (5e)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.24 (s, 2H,-O-CH_2), 5.16 (d, 1H, -CH-$C_6H_4CF_3$), 5.44 (d, 1H, -CH–Cl), 6.86-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 62, 68, 72 (aliphatic -C), 107,116, 121, 126, 129, 127, 130, 131, 133, 139, 146 (Ar-C), 162 (-C=O), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3040(=C-H aromatic), 1692 (-C=O), 1617 (-C=N), 1158(-C-O-C-), 1137(-N-N-) 835 (-C-Cl). MS, *m/z* : (M^+, 618.85, M+2, 620.56). Anal Calcd. for $C_{29}H_{17}ClF_6N_4O_3$ (%): C, 56.28; H, 2.77; N, 9.05; Found: C, 56.22; H, 2.99; N, 8.99; M.P: 142-143^{0}C, yield 42%.

3-(8-((5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (6a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.87 (d, 1H, -H_a), 3.99 (d, 1H, -H_b), 4.21(s, 2H, -O-CH_2), 6.44 (s, 1H, -CH-$C_6H_4CF_3$), 6.9-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 74, 72 (aliphatic -C), 107, 116, 121, 126, 129, 130, 133, 139, 142, 146 (Ar-C), 171 (-C=O), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3048(=C-H aromatic), 1698(-C=O), 1613(-C=N), 1188 (-C-S), 1160(-C-O-C-), 1145(-N-N-). MS,*m/z*: (M^+, 566.48). Anal Calcd. for $C_{28}H_{18}F_4N_4O_3S$ (%): C, 59.31; H, 3.20; N, 9.89; Found: C, 59.31; H, 3.15; N, 9.84; M.P: 181-182^{0}C, yield 62%.

3-(8-((5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (6b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.85 (d, 1H, -H_a), 3.99 (d, 1H, -H_b), 4.20 (s, 2H,-O-CH_2), 6.44(s, 1H, -CH-$C_6H_4CF_3$), 6.8-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 74, 72 (aliphatic -C), 107, 116, 120, 125, 129, 130, 133, 135, 139, 142, 147 (Ar-C), 171(-C=O), 163(C_2 of oxadiazole), 165(C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3045(=C-H aromatic), 1696(-C=O), 1614(-C=N), 1179(-C-S), 1164(-C-O-C-), 1147(-N-N-). MS, *m/z*: (M^+, 582.26, M+2, 584.15). Anal Calcd. for $C_{28}H_{18}ClF_3N_4O_3S$ (%): C, 57.69; H, 3.11; N, 9.61; Found: C, 57.52; H, 3.04; N, 9.56; M.P: 194-195^{0}C, yield 52%.

3-(8-((5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (6c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.80 (d, 1H, -H_a), 3.92 (d, 1H, -H_b), 4.24 (s, 2H,-O-CH_2), 6.44 (s, 1H, -CH-$C_6H_4CF_3$), 6.8-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 74, 72(aliphatic -C), 107, 116, 121, 123, 126, 129, 130, 132, 133, 139, 142, 146(Ar-C), 171(-C=O), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3046(=C-H aromatic), 1697(-C=O), 1619(-C=N), 1166(-C-S), 1162(-C-O-C-), 1141(-N-N-). MS, *m/z*: (M^+, 628.35). Anal Calcd. for $C_{28}H_{18}BrF_3N_4O_3S$ (%): C, 53.60; H, 2.89; N, 8.93; Found: C, 53.56; H, 2.83; N, 8.87; M.P: 151-152^{0}C, yield 55%.

3-(8-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-2-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (6d)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.87 (d, 1H, -H_a), 3.94 (d, 1H, -H_b), 4.26 (s, 2H, -O-CH_2), 6.44(s, 1H, -CH-$C_6H_4CF_3$), 7.1-8.85 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 74, 72 (aliphatic -C), 107, 116, 120, 125, 129, 130, 133, 139, 142, 146, 147 (Ar-C), 171(-C=O), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3042(=C-H aromatic), 1692(-C=O), 1612(-C=N), 1179(-C-S), 1158(-C-O-C-), 1145(-N-N-). MS, *m/z*: (M^+, 593.09). Anal Calcd. for $C_{28}H_{18}F_3N_5O_5S$ (%): C, 56.66; H, 3.06; N, 11.80; Found: C, 56.61; H, 3.01; N, 11.80; M.P: 173-174^{0}C, yield 41%.

2-(4-(trifluoromethyl)phenyl)-3-(8-((5-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-yl) methoxy)quinolin-5-yl)thiazolidin-4-one (6e)

^{1}H NMR (300MHz, DMSO-d_6): δppm 3.87(d, 1H, -H_a), 3.95(d, 1H, -H_b), 4.22(s, 2H, -O-CH_2), 6.48(s, 1H, -CH-$C_6H_4CF_3$), 6.88-8.82(m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 33, 74, 72 (aliphatic -C), 107, 116, 120, 126, 129, 130, 133, 139, 142, 146 (Ar-C), 171(-C=O), 163(C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3040(=C-H aromatic), 1694(-C=O), 1610(-C=N), 1178(-C-S), 1166(-C-O-C-), 1147(-N-N-). MS, *m/z*: (M^+, 616.15). Anal Calcd. for $C_{29}H_{18}F_6N_4O_3S$ (%): C, 56.49; H, 2.94; N, 9.09; Found: C, 56.42; H, 2.88; N, 9.04; M.P: 134-135^{0}C, yield 44%.

2-(4-fluorophenyl)-5-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl)-1,3,4-oxadiazole (7a)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.21 (s, 2H, -O-CH_2), 7.1-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72(aliphatic -C), 107, 117, 122, 125, 126, 129, 131, 132, 134, 139, 149, 155 (Ar-C), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3045 (=C-H aromatic), 2115 (azide), 1694(-C=O), 1618 (-C=N), 1165 (-C-O-C-), 1158 (tetrazole), 1138 (-N-N-). MS, *m/z*: (M^+, 533.52). Anal Calcd. for $C_{26}H_{15}F_4N_7O_2$ (%): C, 58.54; H, 2.83; N, 18.38; Found: C, 58.49; H, 2.78; N, 18.32; M.P: 144-145^{0}C, yield 58%.

2-(4-chlorophenyl)-5-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl)-1,3,4-oxadiazole (7b)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.20 (s, 2H, -O-CH_2), 7.2-8.8 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72 (aliphatic -C), 107, 117, 122, 124, 126, 129, 131, 132, 134, 139, 149, 155 (Ar-C), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3048 (=C-H aromatic), 2108 (azide), 1692 (-C=O), 1614 (-C=N), 1160 (-C-O-C-), 1156 (tetrazole), 1132 (-N-N-). MS, *m/z*: (M^+, 549.12, M+2, 551.08). Anal Calcd. for $C_{26}H_{15}ClF_3N_7O_2$ (%): C, 56.79; H, 2.75; N, 17.83; Found: C, 56.74; H, 2.67; N, 17.78; M.P: 164-165^{0}C, yield 47%.

2-(4-bromophenyl)-5-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl)-1,3,4-oxadiazole (7c)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.24 (s, 2H, -O-CH_2), 7.1-8.82 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72 (aliphatic -C), 107, 117, 122, 125, 126, 129, 131, 132, 134, 139, 149, 155 (Ar-C), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3042 (=C-H aromatic), 2112 (azide), 1691 (-C=O), 1619 (-C=N), 1160 (-C-O-C-), 1158 (tetrazole), 1141 (-N-N-). MS, *m/z*: (M^+, 593.48). Anal Calcd. for $C_{26}H_{15}BrF_3N_7O_2$ (%): C, 52.54; H, 2.54; N, 16.50; Found: C, 52.48; H, 2.50; N, 16.43; M.P: 132-133^{0}C, yield 41%.

2-(4-nitrophenyl)-5-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy)methyl)-1,3,4-oxadiazole (7d)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.26 (s, 2H, -O-CH_2), 7.2-8.85 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72 (aliphatic -C), 107, 117, 122, 126, 129, 131, 132, 134, 139, 148, 149, 155 (Ar-C), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3052 (=C-H aromatic), 2110 (azide), 1695 (-C=O), 1612 (-C=N), 1156 (-C-O-C-), 1149 (tetrazole), 1136 (-N-N-). MS, *m/z*: (M^+, 560.36). Anal Calcd. for $C_{26}H_{15}F_3N_8O_4$ (%): C, 55.72; H, 2.70; N, 19.99; Found: C, 55.64; H, 2.67; N, 19.93; M.P: 174-175^{0}C, yield 51%.

2-(4-(trifluoromethyl)phenyl)-5-(((5-(5-(4-(trifluoromethyl)phenyl)-1H-tetrazol-1-yl)quinolin-8-yl)oxy) methyl)-1,3,4-oxadiazole (7e)

^{1}H NMR (300MHz, DMSO-d_6): δppm 4.22 (s, 2H, -O-CH_2), 7.1-8.82 (m, 13H, Ar-H). ^{13}C NMR ($CDCl_3$) (δppm) = 72 (aliphatic -C), 107, 117, 122, 126, 128, 131, 132, 134, 139, 149, 155 (Ar-C), 163 (C_2 of oxadiazole), 165 (C_5 of oxadiazole). IR (KBr) spectra cm^{-1} 3048 (=C-H aromatic), 2116 (azide), 1692 (-C=O), 1610 (-C=N), 1158 (-C-O-C-), 1155 (tetrazole), 1137 (-N-N-). MS, *m/z*: (M^+, 583.06). Anal Calcd. for $C_{27}H_{15}F_6N_7O_2$ (%): C, 55.58; H, 2.59; N, 16.80; Found: C, 55.52; H, 2.52; N, 16.80; M.P: 158-159^{0}C, yield 46%.

Anti- Bacterial Activity

The antibacterial activity of synthesised compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram-positive bacteria screened were *Staphylococcus aureus* NCCS 2079 and *Bacillus cereus* NCCS 2106. The gram negative bacteria screened were *Escherichia coli* NCCS2065 and *Pseudomonas aeruginosa* NCCS2200.

The synthesised compounds were used at the concentration of 250 µg/ml and 500 µg/ml using DMSO as a solvent. The *cefaclor* 10µg/disc was used as a standard. (Himedia Laboratories Ltd, Mumbai).

The test results presented in the table-1, suggest that 5a, 7a, 7d and 7e exhibit high activity against the tested bacteria, the rest of the compounds were found to be moderate active against the tested microorganisms.

Antifungal Activity

The antifungal activity of synthesised compounds were studied by disc diffusion method against the organisms of *Aspergillus niger* NCCS1196 and *Cadida albicans* NCCS34471.

Compounds were treated at the concentrations of 100µg/ml, 250µg/ml, 500µg/ml and 1000µg/ml using DMSO as solvent. The standard used was *Clotrimazole* 50µg/ml against both the organisms. The test results were presented in the table-2.

Table–1: Antibacterial activity by disc diffusion method of Quinoline-1,3,4-oxadiazole having azetidi-2-one(5a-e), thiazolidinone(6a-e) and tetrazole (7a-e)

Compound	Zone of Inhibition (mm)			
	Staphylococcus aureus	*Bacillus cereus*	*Escherichia coli*	*Pseudomonas aeruginosa*
5a	13	14	10	09
5b	11	10	08	07
5c	10	09	09	08
5d	15	17	13	12
5e	14	16	12	11
6a	11	12	08	07
6b	09	08	06	05
6c	08	06	07	06
6d	13	14	11	10
6e	12	13	10	09
7a	15	17	12	11
7b	14	14	11	09
7c	13	12	12	10
7d	17	19	16	15
7e	16	18	14	12
Cefaclor	19	22	19	20

Table–2: Antifungal activity by disc diffusion method for Quinoline-1,3,4-oxadiazole having azetidi-2-one (5a-e), thiazolidinone (6a-e) and tetrazole (7a-e).

Compound	Zone of Inhibition (mm)	
	Asperigillus niger	*Candida albicans*
5a	17	12
5b	15	10
5c	14	09
5d	21	17
5e	19	14
6a	15	10
6b	13	08
6c	11	06
6d	17	15
6e	16	12
7a	19	15
7b	17	13
7c	16	12
7d	23	20
7e	20	17
Clotrimazole	25-30	25-30

Conclusion:

The present investigation discovers a new class of 1,3,4-oxadizoles possessing quinoline core unit bearing azetidin-2one, thiazolidin-4-one and tetrazole moieties in a single molecular frame work, which are biologically active. These new class of oxadizoles have promising antibacterial and antifungal activities. Hence, it can be concluded that, this new class of compounds certainly holds a greater consent in the design of new potent antibacterial and antifungal agents.

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