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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis, antibacterial and anticancer evaluation of 5-substituted (1,3,4-oxadiazol-2-yl)quinoline

Salahuddin · Avijit Mazumder · Mohammad Shaharyar

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Abstract 2-Chloroquinoline-3-carbaldehyde (**2**) was synthesized via Vilsmeier–Haack method using acetanilide. Phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1*H*-benzimidazol-1-yl)acetohydrazide (**7a–c**) were synthesized using 2-[2-(phenoxy/naphthalen-1-yl/naphthalen-2-yloxy methyl)-1*H*-benzimidazol-1-yl]acetohydrazide (**6a–c**). The title compounds 2-chloro-3-{5-[(2-phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1-*H*-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}quinolone (**8a–c**) were prepared using chloramine-T. In the second series, (2-chloroquinolin-3-yl)methylidene]-substituted benzohydrazide (**11a–i**) were prepared by the reaction of 2-chloroquinoline-3-carbaldehyde (**2**) and an acid hydrazide (**10a–i**). The synthesized compounds were characterized by IR, NMR, Mass spectrometry, elemental analysis and screened for their antibacterial (serial dilution technique and disc diffusion method) and anticancer activity by NCI 60 cell screen at a single high dose (10^{-5} M) on various panel/cell lines. The synthesized compounds (**8a**, **8c**, **12a**, **12b**, **12c** and **12h**) were acting as a magic bullet against gram-positive strains of *Bacillus cereus MTCC1305*, and the compounds (**12a**, **12c** and **12h**) were also found to be extremely active against *Klebsiella pneumonia NCTC7447*. In the in vitro screen on tested cancer cell line, the compound (**12d**) showed 95.70 growth percent (GP) and highly active on SNB-75 (CNS cancer) and UO-31 (renal cancer) (GP = 53.35 and 64.35, respectively), and the compound (**8a**) showed 96.86 GP and highly active on SNB-75 (CNS cancer GP 51.27).

Keywords 1,3,4-Oxadiazole · Antibacterial · Anticancer · Quinoline

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Introduction

Heterocyclic compounds with nitrogen are considered as great interest in natural products (Jin, 2003) as they are used frequently in medicinal chemistry. Among them oxadiazoles are considered important as there is furan ring with two methane (–CH=) groups which are replaced by two pyridine types of nitrogen (–N=) atoms. Four types of isomers are observed which depend on the position of nitrogen atoms present in the ring (Somani and Shirodkar, 2009) as described in Fig. 1.

Literature survey reveals that the heterocyclic compounds containing 1,3,4-oxadiazole moiety have been used as a pi-conjugation which are used to prepare large number of donor–acceptor molecules that carry a rich pi-electron aromatic ring. Hence, compounds with 1,3,4-oxadiazole moiety are considered as a good choice for optical material or biologically active chemicals (Dabiri *et al*., 2006) with various applications like HIV-integrase inhibitor raltegravir (Steigbigel *et al*., 2008), furamizole as nitrofuran antibacterial (Ogata *et al*., 1971), antihypertensive agents tiodazosin (Vardan *et al*., 1983) and nesapidil (Schlecker and Thieme, 1988), anticancer (Sengupta *et al*., 2008; Jin *et al*., 2006; Holla *et al*., 2005), anticonvulsant (Almasirad *et al*., 2004; Aziz *et al*., 2009), antimicrobial (Shetgiri and Nayak,

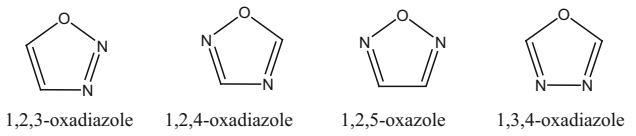


Fig. 1 Isomers of oxadiazole

2005; Manjunatha *et al*., 2010; Shailaja *et al*., 2010; Mulwad and Chaskar, 2006; Ansari and Lal, 2009), anti-inflammatory analgesic (Bhandari *et al*., 2008; Dewangan *et al*., 2010; Amir, 2007; Kumar *et al*., 2008; Jayashankar *et al*., 2009), dyes and pigments (Shui *et al*., 2010), ulcerogenic (Gilani *et al*., 2010), antitubercular (Ali and Shaharyar, 2007) etc. which are based on 1,3,4-oxadiazole moiety (Fig. 2).

A large number of antimicrobial agents show resistance to clinically significant bacteria which give rise to number of problems like local irritation, difficulty in wound healing process, hypersensitivity reactions, systemic toxicity and the emergence of resistance. So, due to this, the demand of clinical importance of drug resistant microbial pathogens has additional led to urgency in microbiological and anti-fungal research. Cancer treated as proliferation of cells which occurs in various organs of the body but does not show any certain etiopathology, so the treatment regime becomes bit difficult. Hence, different methods are employed for the treatment of cancer, i.e., immunotherapy, surgery, radiotherapy and chemotherapy. Cytotoxic agents play a very important role in the chemotherapeutics, which reduces the proliferation of malignant cells. The significant side-effects of chemotherapy are diarrhoea, nausea, vomiting, serious infections, hair loss and growth of the tumour cell population (Isikdag *et al*., 2011). Thus, our main aim was to develop a new molecule for antibacterial and anticancer drugs which can be used as a lead compound for further development.

Materials and methods

Chemistry

The chemical used for experimental work was commercially procured from various chemical units viz. E. Merck India Ltd., CDH and S.D. Fine Chem. and Qualigens. These solvent and reagents were of LR grade and purified before use. The silica gel G (160–120 mesh) used for analytical chromatography (TLC) was obtained from E. Merck India Ltd. Two solvent systems were used, i.e., benzene:acetone (9:1 and 8:2) and toluene:ethyl acetate:formic acid (5:4:1). Ashless Whatman no. 1 filter paper was used for vacuum filtration. Melting points were determined in open glass capillary using melting point apparatus and are uncorrected. The ^{1}H NMR and ^{13}C NMR were recorded on Bruker 300 MHz instrument in DMSO/$CDCl_3$ using tetramethylsilane [$(CH_3)_4Si$] as internal standard. The infrared spectra of the compound were recorded in KBr on Perkin-Elmer FTIR spectrometer, and mass spectra were recorded on API 2000 LC/MS/MS system. The iodine chamber and UV lamp were used for visualisation of TLC spots. The commercially available grades of solvents and reagents were found to be of

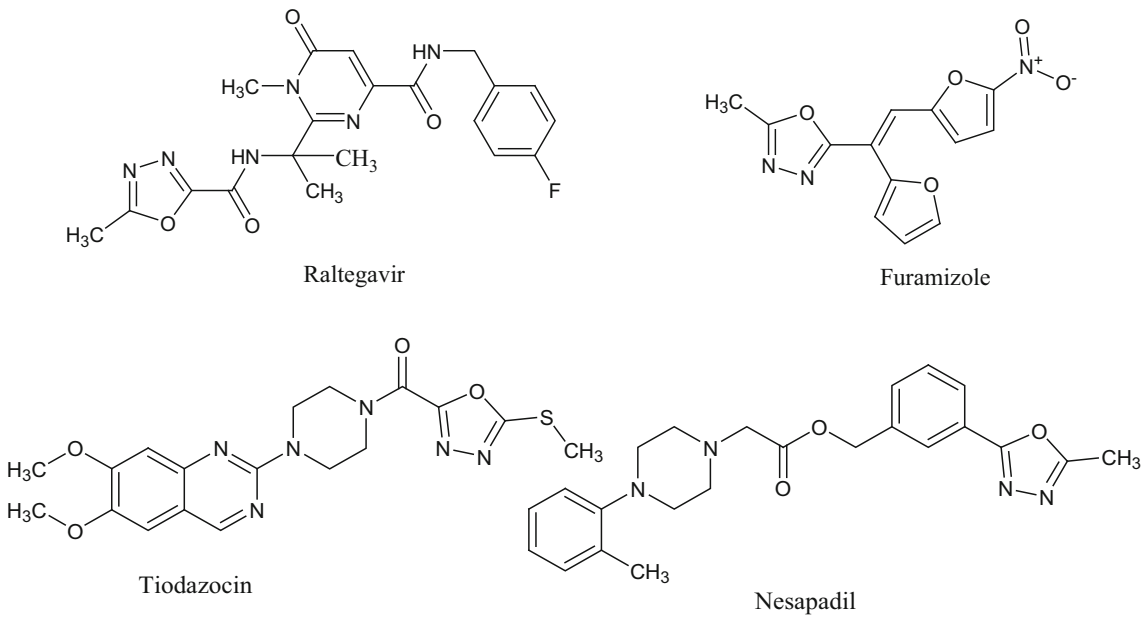


Fig. 2 Pharmacologically active compound containing 1,3,4-oxadiazole moiety

adequate purity. However, the presence of undesirable impurities and others were likely to be used for experimental work was purified/dried.

*Synthesis of 2-chloro-quinoline-3-carbaldehyde (**2**)*

2-Chloroquinoline-3-carbaldehyde was synthesized from acetanilide via Vilsmeier–Haack reaction (Srivatava and Singh, 2005). To a solution of acetanilide (0.005 mol; 0.67 g) in dry dimethylformamide (0.015 mol; 1.09 ml) at 0–5 °C with stirring, phosphorous oxychloride (0.06 mol; 5.59 ml) was added drop wise and the mixture stirred at 80–90 °C for 12 h. The mixture was poured into crushed ice and stirred for 5 min, and the resulting solid filtered was washed well with water and dried. The compound was purified by recrystallization from ethyl acetate. It was obtained as yellow solid, yield 65 %; m.p. 146–148 °C; IR (KBr) ν_{max} 2871, 1687, 749 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 10.25$ (s, 1H, CHO), 7.70 (t, 1H, $J = 6.2$, H-7), 7.25 (d, 1H, $J = 6.5$ Hz, H-6), 6.89 (d, 1H, $J = 6.3$ Hz, H-8), 6.78 (t, 1H, $J = 7.1$ Hz, H-5); ^{13}C NMR (DMSO, 75 MHz): $\delta = 190$ (CH, –CHO), 153 (C, C-2), 145.4 (CH, C-4), 134 (CH, C-8), 129.8 (C, C-3), 129.3 (CH, C-6), 128.5 (C, C-5), 128 (CH, C-9), 127.2 (CH, C-5); EIMS *m/z*: 191.01 (M^+); Anal. Calcd. for $C_{10}H_6ClNO$: C, 62.68; H, 3.16; N, 7.31. Found: C, 62.71; H, 3.18; N, 7.33.

*Synthesis of phenoxy/2-naphthalen-1-yl/naphthoxy-methyl-1H-benzimidazole (**4a–c**)*

A mixture of *o*-phenylenediamine 3 (0.05 mol; 0.54 g) and phenoxyacetic acid/naphthylacetic acid/naphthoxyacetic acid (0.05 mol) was refluxed in 4 N HCl for 4 h on a heating mantle. After completion of reaction, solution was poured onto crushed ice; ammonia solution was added drop wise to neutralize, and the resulting solid was filtered, washed with cold water, dried and recrystallized with ethanol.

*2-Phenoxymethyl-benzimidazole (**4a**)* It was obtained as yellow solid, yield 80 %; m.p. 160–164 °C. IR (KBr) ν_{max} 3450, 1540, 1240 cm^{-1}; ^1H NMR (DMSO, 300 MHz) $\delta = 12.31$ (s, 1H, NH), 7.70 (d, 1H, $J = 9.5$ Hz, H-1), 7.47 (d, 1H, $J = 9.2$ Hz, H-4), 7.29 (t, 2H, $J = 14.8$ Hz, H-2, 3), 7.19 (s, 2H, H-6, 8), 7.07 (d, 2H, $J = 8.7$, H-5, 9), 6.85 (t, 1H, $J = 12$ Hz, H-7), 5.29 (s, 2H, OCH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 154.3$ (CH_2, $–CH_2O$), 142.7 (C, C-2), 138.9 (C, C-4, 9), 130.1 (CH, C-5′), 124.8 (CH, C-3′), 124 (CH, C′-4), 123.1 (CH, C-6, 7), 115 (CH, C-5, 8), 112.3 (CH, C-2′, 6′); EIMS *m/z*: 224 (M^+); Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 75.0; H, 5.35; N, 12.45.

*2-(Naphthalene-1-ylmethyl)-1H-benzimidazole (**4b**)* It was obtained as white solid, yield 85 %; m.p. 125–126 °C; IR (KBr) ν_{max} 3,302, 1,528, 2,867 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 12.37$ (s, 1H, NH), 8.19 (d, 1H, $J = 13.2$ Hz, H-5′), 7.92 (d, 2H, $J = 9.5$ Hz, H-6, 9), 7.84 (d, 1H, $J = 7.8$ Hz, H-8′), 7.45 (d, 1H, $J = 8$ Hz, H-3′), 7.32 (d, 2H, $J = 8.3$ Hz, H-6′, 7′), 7.25 (d, 2H, $J = 8.5$ Hz, H-7, 8), 7.20 (t, 1H, $J = 12.7$ Hz, H-2′), 7.06 (d, 1H, $J = 6.7$ Hz, H-1′), 4.62 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 141.5$ (C, C-2), 138.1 (C, C-5, 9), 134.2 (C, C-5′), 133.8 (C, C-10′), 132.5 (C, C-9′), 128.6 (CH, C-6′), 127.2 (CH, C-3′), 126.9 (CH, C-2′, 4′), 125.7 (CH, C-7′, 8′), 124.3 (CH, C-9′), 123.1 (CH, C-5, 6), 115.4 (CH, C-5, 8); EIMS *m/z*: 258.1 (M^+); Anal. Calcd. for $C_{18}H_{14}N_2$: C, 83.69; H, 5.46; N, 10.84. Found: C, 83.67; H, 5.49; N, 10.82.

*2-[(Naphthalene-2-yloxy)methyl]-1H-benzimidazole (**4c**)* It was obtained as creamy-white solid, yield 84 %; m.p. 205–207 °C; IR (KBr) ν_{max} 3010, 3297, 1464, 1226 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 7.70$ (d, 2H, $J = 5.4$ Hz, H-6, 9), 7.68 (d, 1H, $J = 5.6$ Hz, H-5′), 7.64 (d, 2H, $J = 6.9$ Hz, H-3′, 8′), 7.60 (t, 1H, $J = 13.7$ Hz, H-7′), 7.30 (d, 2H, $J = 6$ Hz, H-7, 8), 7.47 (t, 1H, $J = 15.2$ Hz, H-6′), 7.30 (s, 1H, $J = 5.8$ Hz, H-13′), 7.26 (s, 1H, H′), 5.34 (s, 2H, CH_2O); ^{13}C NMR (DMSO, 75 MHz): $\delta = 155.3$ (C, C-2′), 141.7 (C, C-2), 138.2 (C, C-4, 9), 135.2 (C, C-10′), 128.2 (C, C-5′), 127.8 (CH, C-4′), 127 (CH, C-6′), 126.7 (CH, C-8′), 125.7 (CH, C-8′), 123.4 (CH, C-4′), 120.5 (CH, C-6, 7), 119.9 (CH, C-3′), 116.4 (CH, C-5, 8), 104.1 (CH, C-2′), 73.4 (CH_2, OCH_2); EIMS *m/z*: 274.1 (M^+); Anal Calcd. for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.84; H, 5.15; N, 10.25.

*Synthesis of ethyl 2-(phenoxymethyl/naphthylmethy/naphthalen-2-yloxy)methyl]-1-yl}acetate (**5a–c**)*

To a suspension of 2-[(phenoxymethyl/naphthylmethy/naphthalen-2-yloxy)methyl]-1*H*-benzimidazole (0.01 mol) and anhydrous potassium carbonate (2 g) in dry acetone, ethyl chloroacetate (0.01 mol; 1.2 ml) was added drop wise at room temperature for a period of 20–30 min. The reaction mixture was stirred at room temperature for 10–12 h. The inorganic solid was filtered off, and filtrate was concentrated under reduced pressure.

*Ethyl [2-(phenoxymethyl)-1H-benzimidazol-1-yl]acetate (**5a**)* It was obtained as white solid, yield 80 %; m.p. 160–164 °C; IR (KBr) ν_{max} 3450, 1540, 1240 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 12.31$ (s, 1H, NH), 7.59 (d, 2H, $J = 12.3$ Hz, H-6, 9), 7.30 (d, 2H, $J = 9.7$ Hz, H-7, 8), 6.97 (t, 1H, $J = 11.5$ Hz, H-4′), 6.85 (d, 2H, $J = 6.7$ Hz, H-2′, 6′), 5.29 (s, 2H, OCH_2), 4.12 (q, 2H, CH_2), 2.30

(t, 3H, $J = 12.7$ Hz, CH_3); ^{13}C NMR (DMSO, 75 MHz): $\delta = 163.4$ (C, C-1′), 142.1 (C, C-2), 138.7 (C, C-4, 9), 123. 3 (CH, C-6, 7), 120.1 (CH, C-4′), 115.7 (CH, C-5, 8), 114.6 (CH, C-2′, 6′), 66.7 (CH_2, –OCH_2), 51.5 (CH_2), 14 (CH_2, –CH_2CH_3); EIMS *m/z*: 310.1 (M^+); Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 75.0; H, 5.35; N, 12.45.

*Ethyl [2-(naphthalen-1-ylmethyl)-1H-benzimidazol-1-yl]acetate (**5b**)* It was obtained as white solid, yield 72 %; m.p. 108–112 °C; IR (KBr) ν_{max} 3010, 3206, 1436, 1229 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 7.79$ (d, 2H, $J = 7.$ 0 Hz, H-6, 9), 7.71 (d, 1H, $J = 6.3$ Hz, H-6′), 7.64 (d, 1H, $J = 4.0$ Hz, H-3′), 7.60 (d, 1H, $J = 4.8$ Hz, H-7′), 7.55 (d, 2H, $J = 7.5$ Hz, H-7, 8), 7.50 (t, 1H, $J = 9.8$ Hz, H-2′), 7. 46 (d, 2H, $J = 5.8$ Hz, H-1′6′), 5.06 (s, 2H, CH_2CO), 4.14 (q, 2H, CH_2), 2.31 (t, 3H, $J = 15.4$ Hz, CH_3); ^{13}C NMR (DMSO, 75 MHz): $\delta = 141.7$ (C, C-2), 138.5 (C, C-5, 9), 134.1 (C, C-5′), 133.5 (C, C-10′), 132.5 (C, C-9′), 128.9 (CH, C-2′, 4′), 128.6 (CH, C-6′), 127.2 (CH, C-3′), 123.2 (CH, C-7′8′), 120.5 (CH, C-9′), 116.4 (CH, C-5, 8), 50.5 (CH_2, –OCH_2), 39.4 (CH_2), 15.6 (CH_2, –CH_2CH_3); EIMS *m/z*: 344.1 (M^+); Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.70; H, 5.88; N, 8.12; O, 9. 29.

*Ethyl {2-[(naphthalen-2-yloxy)methyl]-1H-benzimidazol-1-yl}acetate (**5c**)* It was obtained as brownish solid, yield 69 %; m.p. 105–109 °C; IR (KBr) ν_{max} 2950, 1736, 1657, 1464, 1226 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 7.61$ (d, 2H, $J = 7.8$ Hz, H-6, 9), 7.46 (d, 1H, $J = 5.5$ Hz, H-5′), 7.40 (d, 2H, $J = 7.2$ Hz, H-3, 8′), 7.30 (t, 1H, $J =$ 13.5 Hz, H-7′), 7.21 (d, 2H, $J = 10.8$ Hz, H-7, 8), 7.09 (d, 1H, $J = 5.6$ Hz, H-2′), 7.09 (d, 1H, $J = 5.6$ Hz, H-2′), 6. 98 (t, 1H, $J = 11.5$ Hz, H-6′), 6.90 (s, 1H, H-10′), 5.21 (s, 2H, CH_2O), 4.72 (q, 2H, CH_2), 2.35 (t, 3H, $J = 14.4$ Hz, CH_3). ^{13}C NMR (DMSO, 75 MHz): $\delta = 171$ (C, –CO), 158.1 (C, C-1′), 142 (C, C-4, 9), 137.1 (CH, C-6′), 129.3 (CH, C-8′), 124.8 (CH, C-4′), 121.3 (CH, C-6, 7), 115.4 (CH, C-5, 8), 92.45 (CH, C-2′), 62.1 (CH_2, OCH_2), 50.7 (CH_2, –CH_2CO), 47.5 (CH_2), 13.6 (CH_2, –CH_2CH_3); EIMS *m/z* 360.1 (M^+); Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.29; H, 5.60; N, 7.80.

*Synthesis of 2-[2-(phenoxy/naphthalen-1-yl/naphthalen-2-yloxy methyl)-1H-benzimidazol-1-yl]acetohydrazide (**6a–c**)*

To an ethanolic solution of ethyl [2-phenoxymethyl/(naphthalen-1-ylmethyl)/(naphthalen-2-yloxy)methyl]-1*H*-benzimidazol-1-yl]acetate (0.01 mol), hydrazine hydrate (98 %) (0.01 mol; 0.49 ml) was added and the mixture was refluxed for 3 h. After completion of the reaction, the mixture was cooled, and the solid so obtained was filtered, washed with cold water and recrystallized from methanol.

*2-[2-(Phenoxymethyl)-1H-benzimidazol-1-yl]acetohydrazide (**6a**)* It was obtained as white solid, yield 80 %; m.p. 178–180 °C; IR (KBr): ν_{max} 3287, 3034, 1656, 1600, 1242, 1030 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 9.43$ (s, 1H, CONH), 7.69 (d, 2H, $J = 12.6$ Hz, H-6, 9), 7.31 (d, 2H, $J = 12.6$ Hz, H-7, 8), 7.18 (d, 2H, $J = 6.0$ Hz, H-3, 5′), 7.02 (t, 1H, $J = 9.5$ Hz, H-4′), 6.92 (d, 2H, $J = 6.$ 2 Hz, H-2′, 6′), 5.48 (s, 2H, CH_2O), 4.90 (s, 2H, CH_2), 2.52 (s, 1H, NH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 169.3$ (C, CONH), 165 (C, C-1′), 141.3 (C, C-2), 136.7 (C, 4, 9), 130. 5 (CH, C-3′, 122 (CH, C-6′, 7′), 120.1 (CH, C-4′), 113.4 (CH, C-5, 8), 112.1 (CH, C-2′, 6′), 67.3 (CH_2, –OCH_2), 51. 9 (CH_2, –NCH_2). EIMS *m/z*: 296.1 (M^+). Anal. Calcd. for $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.86; H, 5.42; N, 18.89.

*2-[2-(Naphthalen-1-ylmethyl)-1H-benzimidazol-1-yl]acetohydrazide (**6b**)* It was obtained as white solid, yield 82 %; m.p. 147–150 °C; IR (KBr) ν_{max} 3302, 3043, 1643, 1528, 1233 cm^{-1}; ^1HNMR (DMSO, 300 MHz): $\delta = 9.25$ (s, 1H, CONH), 8.15 (d, 2H, $J = 11.2$ Hz, H-6, 9), 7.58 (d, 1H, $J = 9.0$ Hz, H-3′), 7.64 (d, 2H, $J = 9.5$ Hz, H-5′, 8′), 7.35 (d, 2H, $J = 7.5$ Hz, H-7, 8), 7.30 (d, 2H, $J = 8.9$ Hz, H-6′, 7′), 7.18 (t, 1H, $J = 9.2$ Hz, H-2′), 7.13 (d, 1H, $J =$ 5.6 Hz, H-1′), 4.90 (s, 2H, CH_2), 2.50 (s, 1H, NH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 170.3$ (C, CONH), 140.5 (C, C-2), 138.4 (C, C-4, 9), 134.7 (C, C-10′), 133.7 (C, C-9′), 133.5 (CH, C-5′), 128.4 (CH, C-6′, 7′), 126.7 (CH, C-3′), 126.2 (CH, C-2′, 4), 123.9 (CH, C-7′, 8′), 113.7 (CH, C-5, 8), 53.1 (CH_2, –NCH_2), 32.1 (CH_2); EIMS *m/z*: 330.4 (M^+); Anal. Calcd. for $C_{22}H_{18}N_4O$: C, 72.71; H, 5.49; N, 16.96. Found: C, 72.71; H, 5.50; N, 16.94.

*2-{2-[(Naphthalen-2-yloxy)methyl]-1H-benzimidazol-1-yl}acetohydrazide (**6c**)* It was obtained as white solid, yield 82 % ; m.p. 208–210 °C; IR (KBr) ν_{max} 3292, 3056, 1668, 1466, 1254 cm^{-1}. ^1H NMR (DMSO, 300 MHz): $\delta = 9.05$ (s, 1H, CONH), 7.70 (d, 2H, $J = 5.7$ Hz, H-6, 9), 7.65 (d, 1H, $J = 5.5$ Hz, H-5′), 7.58 (d, 2H, $J = 6.5$ Hz, H-3′, 8′), 7.52 (t, 1H, $J = 11.6$ Hz, H-7′), 7.32 (d, 2H, $J = 6$ Hz, H-7, 8), 7.17 (t, 1H, $J = 12.2$ Hz, H-6′), 7.03 (s, 1H, $J = 4.7$ Hz, H-2′), 6.92 (s, 1H, H-10′), 5.35 (s, 1H, CH_2O), 4.89 (s, 2H, CH_2), 2.53 (s, 1H, NH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 170.3$ (C, CONH), 158.8 (C, C-2′), 142.6 (C, C-2), 138.9 (C, C-4, 9), 133.5 (C, C-10′), 130.7 (C, C-5′), 130.3 (CH, C-4′), 127.6 (CH, C-6′), 127.1 (CH, C-9′), 126.2 (CH, C-8′), 122.6 (CH, C-7), 120.3 (CH, C-6, 7), 117.8 (CH, C-3′), 109.4 (CH, C-5, 8), 103.8 (CH, C-1′), 66.2 (CH_2, CH_2O), 51.9 (CH_2, NCH_2). EIMS *m/z*: 346.4 (M^+); Anal.

Calcd. for $C_{22}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.17. Found: C, 69.30; H, 5.21; N, 16.21.

*Synthesis of phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1H-benzimidazol-1-yl)acetohydrazide (**7a–c**)*

A mixture of (2-phenoxy/naphthalen-1-yl/naphthalen-2-yloxy methyl)-benzoimidazol-1-yl) acetohydrazide (0.005 mol) and 2-chloroquinoline-3-carbaldehyde (0.005 mol; 0.95 g) in ethanol was refluxed for 5 h. After completion of the reaction, the reaction mixture was concentrated, cooled and poured in ice-cold water, the precipitate so formed was filtered, dried and recrystallized to give the desired compound.

*(2-Phenoxymethyl-benzoimidazol-1-yl)-acetic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**7a**)* It was obtained as yellowish solid, yield 72 %; m.p. 202–206 °C; IR (KBr) ν_{max} 3310, 3107, 1654, 1535, 1081, 723 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.94$ (s, 1H, CONH), 8.43 (s, 1H, N=CH), 8.26 (s, 1H, H-4″), 8.12 (d, 1H, $J = 8.6$ Hz, H-9″), 7.97 (d, 2H, $J = 6.9$ Hz, H-6, H-9), 7.78 (t, 1H, $J = 13.6$ Hz, H-8″), 7.66 (t, 1H, $J = 8.8$ Hz, H-7″), 7.48 (t, 1H, $J = 11.6$ Hz, H-4′), 7.20–7.34 (m, 3H, H-6″, H-7, H-8), 7.06 (d, 2H, $J = 8.7$ Hz, H-3′, H-5′), 6.96 (d, 2H, $J = 8.8$ Hz, H-2′, H-6′), 5.66 (s, 2H, CH_2O), 5.11 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 173.1$ (C, CONH), 163.7 (C, C-1′), 154.8 (CH, N=CH), 142.7 (C, C-2), 138.2 (C, C-4, C-9), 130.4 (CH, C-8″), 129.5 (CH, C-3′,C-5′), 128.3 (CH, C-9″), 126.9 (CH, C-7″), 126.7 (C, C-5″), 124.2 (C, C-3″), 123.3 (CH, C-6, C-7), 121.8 (CH, C-4′), 115.1 (CH, C-5, C-8), 110.1 (CH, C-2′, C-6′), 66 (CH_2, CH_2O), 52.2 (CH_2, NCH_2); EIMS *m/z*: 469.1 (M^+); Anal. Calcd. for $C_{26}H_{20}ClN_5O_2$: C, 66.45; H, 4.29; N, 14. 90. Found C, 66.39; H, 4.39; N, 14.87.

*(2-Naphthalen-1-ylmethyl-benzoimidazol-1-yl)-acetic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**7b**)* It was obtained as yellowish solid, yield 72 %; m.p. 232–236 °C; IR (KBr) ν_{max} 3317, 3107, 1654, 1531, 1078, 733 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 12.32$ (s, 1H, CONH), 8.33 (s, 1H, N=CH), 8.20 (s, 1H, H-4″), 8.15 (d, 1H, $J = 8.$ 1 Hz, H-9″), 8.09 (d, 1H, $J = 10.2$ Hz, H-5′), 7.92 (d, 2H, $J = 9.5$ Hz, H-6, H-9), 7.63 (t, 1H, $J = 8.8$ Hz, H-7″), 7. 41 (d, 1H, $J = 6.3$ Hz, H-3′), 7.32 (d, 2H, $J = 10.3$ Hz, H-6′, H-7′), 7.20–7.34 (m, 3H, H-6″, H-7, H-8), 7.13 (t, 1H, $J = 11.7$ Hz, H-2′), 6.91 (d, 1 H, $J = 6.7$ Hz, H-1′), 5.16 (s, 2H, CH_2), 5.13 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 173$ (C, CONH), 156.1 (C, C–Cl), 153.3 (CH, N=CH), 152.3 (C, C-10″), 142.7 (C, C-2), 137.9 (C, C-4, C-9), 137.7 (CH, C-4″), 134 (C, C-10′), 133.1 (C, C-5′), 130.2 (CH, C-8″), 128.3 (C, C-9″), 127.9 (CH, C-6′, C-9′), 126.7 (CH, C-6″), 126.4 (CH, C-2′, C-3′), 126.1 (CH, C-7″), 125.7 (C, C-5″), 124.1 (CH, C-7, C-8), 122.7 (C, C-3″), 121.7 (CH, C-6, C-7), 112.1 (CH, C-5, C-8), 52. 1 (CH_2, N-CH2), 28.1 (CH2); EIMS *m/z*: 503.1 (M^+); Anal. Calcd. for $C_{30}H_{22}ClN_5O$: C, 71.49; H, 4.40; N, 13. 90. Found: C, 69.3; H, 4.27; N, 13.49.

*[2-(Naphthalen-2-yloxymethyl)-benzoimidazol-1-yl]-acetic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**7c**)* It was obtained as brownish solid, yield 72 %; m.p. 272–276 °C; IR (KBr) ν_{max} 3307, 2967, 1667, 1555, 1079, 744 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 12.12$ (s, 1H, CONH), 8.43 (s, 1H, N=CH), 8.16 (s, 1H, H-4″), 8.08 (d, 1H, $J = 10.1$ Hz, H-9″), 7.78 (d, 1H, $J = 7.6$ Hz, H-5′), 7.62 (t, 1H, $J = 7.9$ Hz, H-7″), 7.54 (d, 2H, $J = 5.$ 4 Hz, H-3′, H-8′), 7.43 (t, 1H, $J = 10.7$ Hz, H-7′), 7.35 (d, 2H, $J = 6.7$ Hz, H-7, H-8), 7.18–7.31 (m, 3H, H-6″, H-7, H-8), 7.17 (t, 1H, $J = 15.6$ Hz, H-6′), 6.98 (d, 1H, $J = 5.$ 5 Hz, H-2′), 6.82 (s, 1H, H-10′), 5.71 (s, 2H, OCH_2), 5.40 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 173$ (C, CONH), 156.9 (C, C-2″), 154.9 (N=CH), 151.1 (C, C-10″), 142.1 (C, C-2), 137.8 (C, C-4, 9), 135.3 (C, C-5′, C-10′), 129.1 (CH, C-8″), 128.2 (CH, C-9″), 127.3 (CH, C-7″), 126.4 (CH, C-6″), 125.7 (C, C-5″), 124.9 (C, C-3″), 123.7 (CH, C-7′, C-8′), 121.9 (CH, C-6′, C-9′), 120.8 (CH, C-6, C-7), 119.7 (CH, C-3′), 112.3 (CH, C-5, C-8), 103.7 (CH, C-1′), 65.7 (CH_2, CH_2O), 52.2 (CH_2, NCH_2); EIMS *m/z*: 519.1 (M^+); Anal. Calcd. for $C_{30}H_{22}ClN_5O_2$: C, 69.3; H, 4. 26; N, 13.47. Found: C, 69.3; H, 4.27; N, 13.49.

*Procedure for the synthesis of 2-chloro-3-{5-[(2-phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1-H-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}quinoline (**8a-c**)*

To an ethanolic solution of 2-chloroquinolin-3-yl)methylidene]-2-(2-phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1*H*-benzimidazol-1-yl)acetohydrazide (0.005 mol), chloramine-T (0.01 mol; 2.27 g) was added. The solution was refluxed for 4 h, sodium chloride which separated out during the course of reaction was filtered off. Excess ethanol was completely removed from the filtrate by distillation under reduced pressure, leaving behind a solid mass which was crystallized from ethanol to give the desired compound.

*2-Chloro-3-[5-(2-phenoxymethyl-benzoimidazol-1-ylmethyl)-[1,3,4]oxadiazol-2-yl]-quinoline (**8a**)* It was obtained as yellowish solid, yield 65 %; m.p. 238–240 °C; IR (KBr) ν_{max} 2962, 1598, 1231, 1034, 743 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.08$ (s, 1H, H-4″), 8.02 (d, 1H, $J = 6.$ 6 Hz, H-9″), 7.94 (d, 2H, $J = 4.8$ Hz, H-6, H-9), 7.88 (t, 1H, $J = 13.6$ Hz, H-8″), 7.53 (t, 1H, $J = 7.8$ Hz, H-7″), 7. 55 (t, 1H, $J = 10.4$ Hz, H-4′), 7.18–7.31 (m, 3H, H-6″, H-7, H-8), 7.09 (d, 2H, $J = 8.2$ Hz, H-3′, H-5), 6.91 (d,

2H, $J = 8.4$ Hz, H-2′, H-6′), 5.64 (s, 2H, CH_2O), 5.43 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 166.7$ (C, C-5oxa), 166.2 (C, C-2oxa), 161 (C, C-1′), 155.7 (C, C-2″), 143.2 (C, C-2), 138.2 (C, C-4, C-9), 130.1 (CH, C-8″), 128.9 (CH, C-3′, C-5′), 127.8 (CH, C-9″), 127.1 (CH, C-7″), 125.6 (C, C-5″), 124.2 (C, C-3″), 122.7 (CH, C-6, C-7), 121.9 (CH, C-4′), 113.4 (CH, C-5, C-8), 112.1 (CH, C-2′, C-6′), 76.5 (CH_2, CH_2O), 46.2 (CH_2, NCH_2); EIMS *m/z*: 467.1 (M^+); Anal. Calcd. for $C_{26}H_{18}ClN_5O_2$: C, 66.74; H, 3.88; N, 14.97. Found: C, 66.70; H, 3.82; N, 14.99.

*2-Chloro-3-[5-(2-naphthalen-1-ylmethyl-benzoimidazol-1-ylmethyl)-[1,3,4]oxadiazol-2-yl]-quinoline (**8b**)* It was obtained as yellowish-white solid, yield 65 %; m.p. 197–200 °C; IR (KBr) ν_{max} 2952, 1588, 1234, 1033, 740 cm^{-1}. ^1H NMR (DMSO, 300 MHz): $\delta = 8.04$ (s, 1H, H-4″), 8.01 (d, 2H, $J = 6$ Hz, H-8″, H-9″), 7.96 (d, 1H, $J = 9.2$ Hz, H-5′), 7.74 (d, 3H, $J = 7.8$ Hz, H-8′, H-6, H-9), 7.61 (t, 1H, $J = 8.6$ Hz, H-7″), 7.39 (d, 1H, $J = 4.8$ Hz, H-3′), 7.20–7.34 (m, 5H, H-6″, H-7, H-8, H-6′, H-7′), 7.13 (t, 1H, $J = 11.2$ Hz, H-2′), 6.91 (d, 1 H, $J = 6.7$ Hz, H-1′), 5.54 (s, 2H, CH_2), 5.31 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 166.8$ (C, C-5oxa), 166.3 (C, C-2oxa), 147.7 (C, C-10″), 139.9 (C, C-2), 135.6 (C, C-4, C-9), 134 (C, C-5′, C-10′), 130.1 (CH, C-4″, C-8″), 128.6 (C, C-9″), 127.9 (CH, C-6′, C-9′), 127.1 (CH, C-6″), 126.5 (CH, C-2′, C-3′), 126.3 (CH, C-7″), 125.1 (C, C-5″), 124.4 (CH, C-7′, C-8′), 123.1 (C, C-3″), 115.3 (CH, C-6, C-7), 112.3 (CH, C-5, C-8), 45.6 (CH_2, N-CH_2), 28.4 (CH_2); EIMS *m/z*: 501.13 (M^+); Anal. Calcd. for $C_{30}H_{20}ClN_5O$: C, 71.78; H, 4.02; N, 13.95. Found: C, 71.82; H, 4.07; N, 13.94.

*2-Chloro-3-{5-[2-(naphthalen-2-yloxymethyl)-benzoimidazol-1-ylmethyl]-[1,3,4]oxadiazol-2-yl}-]-quinoline (**8c**)* It was obtained as white solid, yield 65 %; m.p. 151–156 °C; IR (KBr) ν_{max} 2952, 1588, 1238, 1023, 729 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.54$ (s, 1H, H-4″), 8.13 (d, 2H, $J = 8.1$ Hz, H-5′, H-9″), 7.94 (t, 1H, $J = 18.0$ Hz, H-7″), 7.56–7.85 (m, 5H, H-7, H-8, H-3′, H-7′, H-8′), 7.20–7.42 (m, 3H, H-6″, H-7, H-8), 6.97 (t, 1H, $J = 21$ Hz, H-6′), 6.81 (d, 1H, $J = 7.2$ Hz, H-2′), 6.13 (s, 1H, H-10′), 5.74 (s, 2H, CH_2), 5.53 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 166.6$ (C, C-5oxa), 166.1 (C, C-2oxa), 161 (C, C-2′), 155.9 (C, C-2″), 150.3 (C, C-10″), 140.5 (C, C-2), 135.8 (C, C-4, C-9), 130 (C, 5′, C-10′), 129.1 (CH, C-8), 128.4 (CH, C-8″), 126.7 (C, C-5″), 126.3 (C, C-3″), 124.9 (CH, C-7′, C-8′), 121.7 (CH, C-6′, C-9′), 120.1 (CH, C-6, 7), 116.7 (CH, C-3′), 112.8 (CH, C-5, C-8), 104.7 (CH, C-1′), 67.2 (CH_2, CH_2O), 46.2 (C'H_2, NCH_2); EIMS *m/z*: 517.3 (M^+); Anal. Calcd. for $C_{30}H_{20}ClN_5O_2$: C, 69.56; H, 3.89; N, 13.52. Found: C, 69.61; H, 3.91; N, 13.53.

*General procedure for the preparation of acid hydrazides (**10a–i**)*

The appropriate aromatic acids **9a–i** (0.01 mol) were dissolved in absolute ethanol (10 ml). Hydrazine hydrate (0.02 mol, 1 ml) and few drops of conc. sulphuric acid were added. The reaction mixture was refluxed for 6 h. The resulting solid obtained was filtered, dried and crystallized from methanol. The completion of reaction was monitored by thin-layer chromatography and infrared spectrophotometer (Jha *et al*., 2010). (10a: naphthoxy acetic acid hydrazide; 10b: phenylacetic acid hydrazide; 10c: *p*-nitrobenzoic acid hydrazide; 10d: *o*-chlorobenzoic acid hydrazide; 10e: *p*-chlorobenzoic acid hydrazide; 10f: nicotinic acid hydrazide; 10g: phenoxyacetic acid hydrazide; 10h: 3,5-dinitrobenzoic acid hydrazide; 10i: salicylic acid hydrazide.)

*Procedure for the synthesis of (2-chloroquinolin-3-yl)methylidene]-substituted benzohydrazide (**11a–i**)*

A mixture of substituted hydrazide **8a–i** (0.003 mol) and 2-chloroquinoline-3-carbaldehyde 2 (0.003 mol; 0.57 g) in ethanol was refluxed for 5 h. After completion of the reaction, the reaction mixture was concentrated, cooled and poured in ice-cold water; the precipitate so formed was filtered, dried and recrystallized to give the desired compound.

*(Naphthalen-2-yloxy)-acetic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11a**)* It was obtained as yellowish-white solid, yield 67 %; m.p. 236–239 °C; IR (KBr) ν_{max} 3311, 2921, 1605, 1693, 1605, 1500, 741 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 9.03$ (s, 1H, CONH), 8.46 (s, 1H, N=CH), 7.95 (d, 1H, $J = 9.3$ Hz, H-9′), 8.28 (s, 1H, H-4′), 8.10 (d, 1H, $J = 6$ Hz, H-6′), 7.73–7.82 (m, 4H, H-4, H-6, H-9, H-8′), 7.68 (s, 1H, H-1′), 7.17–7.34 (m, 4H, H-3, H-7, H-8, H-7′), 5.38 (s, 2H, CH_2O); ^{13}C NMR (DMSO, 75 MHz): $\delta = 173.3$ (C, CONH), 157 (C, C-2′), 155.7 (C, C-2), 153.3 (C, C-10′), 139 (CH, C-4′), 135.4 (CH, C-5, 10), 130.5 (CH, C-7′), 129.5 (CH, C-4), 128.2 (CH, C-6, C-8, C-9), 127.7 (CH, C-6′, C-9′), 127.1 (CH, C-7′), 126 (C, C-5′), 123.3 (C, C-3′), 121 (CH, C-7), 117.9 (CH, C-3), 107.4 (CH, C-1), 78.3 (CH_2, OCH_2); EIMS *m/z*: 389.0 (M^+); Anal. Calcd. for $C_{22}H_{16}ClN_3O_2$: C 67.78; H, 4.14; N, 10.78. Found: C, 67.75; H, 4.17; N, 10.81.

*Phenyl-acetic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11b**)* It was obtained as yellowish solid, yield 65 %; m.p. 212–216 °C; IR (KBr) ν_{max} 3276, 2931, 1665, 1602, 1503, 734 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.54$ (s, 1H, CONH), 8.24 (s, 1H, N=CH), 8.01 (d, 1H, $J = 10.6$ Hz, H-4′), 7.93 (d, 1H, $J = 8.7$ Hz, H-9′), 7.69 (t, 1H,

$J = 7.8$ Hz, H-8′), 7.51 (t, 1H, $J = 9.6$ Hz, H-7′), 7.18 (d, 1H, H-6′), 7.10 (t, 2H, $J = 12.3$ Hz, H-3, H-5), 7.01–7.06 (m, 3H, H-2, H-4, H-6), 4.55 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 173.5$ (C, CONH), 156 (C, C-2′), 153.2 (CH_2), 150 (C, C-10′), 139.7(CH, C-4′), 136.2 (C, C-1), 132.5 (CH, C-8′), 129.5(CH, C-2, C-6), 129 (CH, C-3, C-5), 128.3 (CH, C-6′, C-9′), 127 (CH, C-4′), 124.1 (C, C-5′), 123.2 (CH, C-7′), 120.1 (C, C-3′), 40.1 (CH_2); EIMS *m/z*: 323.08 (M^+); Anal. Calcd. for $C_{17}H_{11}Cl_2N_3O$: C, 59.32; H, 3.22; N, 12.21. Found: C, 59.30; H, 3.25; N, 12.24.

*4-Nitro-benzoic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11c**)* It was obtained as yellow solid, yield 72 %; m.p. 250–255 °C; IR (KBr) ν_{max} 3305, 2940, 1692, 1535, 1460, 756 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz): $\delta =$ 8.54 (s, 1H, CONH), 8.20 (s, 1H, N=CH), 8.03 (d, 1H, $J =$ 9.7 Hz, H-4′), 7.96 (t, 2H, $J = 12.3$ Hz, H-3, H-5), 7.88 (d, 1H, $J = 8.7$ Hz, H-9′), 7.71 (t, 1H, $J = 7.8$ Hz, H-8′), 7.51 (t, 1H, $J = 9.6$ Hz, H-7′), 7.26 (d, 2H, $J = 5.6$ Hz, H-2, H-6), 7.18 (d, 1H, H-6′); ^{13}C NMR (DMSO, 75 MHz): $\delta = 170.5$ (C, CONH), 158.5 (C, C-2′), 153.3 (CH_2), 151 (C, C-4), 148.8 (C, C-10′), 140 (C, C-1), 135.3 (CH, C-4′), 130 (CH, C-8′), 128.5 (CH, C-2, C-6), 127 (C, C-9′), 126.4 (CH, C-6′), 126 (CH, C-7′), 125.4 (C, C-5′), 122.5 (C, C-3′), 120.1 (CH, C-3, C-5); EIMS *m/z*: 354.5 (M^+); Anal. Calcd. for $C_{17}H_{11}ClN_4O_3$: C, 57.65; H, 3.13; N, 15.79. Found: C, 57.63; H, 3.11; N, 15.83.

*3,5-Dimethoxy-benzoic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11d**)* It was obtained as yellow solid, yield 63 %; m.p. 288–292 °C; IR (KBr) ν_{max} 3193, 2950, 1672, 1562, 1501, 794 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz): $\delta = 9.02$ (s, 1H, CONH), 8.56 (s, 1H, N=CH), 7.94 (d, 1H, $J = 10.2$ Hz, H-9′), 7.66 (t, 1H, $J = 7.1$ Hz, H-8), 7.52 (t, 1H, $J = 8.4$ Hz, H-7′), 7.41 (d, 1H, H-6′), 7.31–7.35 (m, 3H, H-2, H-4, H-6), 3.78 (s, 3H, 5-OCH_3), 3.67 (s, 3H, 3-OCH_3); ^{13}C NMR (DMSO, 75 MHz): $\delta = 170.2$ (C, CONH), 164 (C, C-3, C-5), 157.1 (CH, CH=N), 153.2 (C, C-10′), 136 (CH, C-4′), 132.5 (C, C-1), 130 (C, C-8′), 128.5 (C, C-9′), 127.5 (CH, C-6′), 126.6 (CH, C-7′), 125.2 (C, C-5′), 122.3 (C, C-3′), 104.6 (CH, C-2, C-6), 102 (CH, C-5), 56 (OCH_3); EIMS *m/z*: 369.08 (M^+); Anal. Calcd. for $C_{19}H_{16}ClN_3O_3$: C, 61.71; H, 4.36; N, 11.36. Found: C, 61.75; H, 4.37; N, 11.39.

*4-Chloro-benzoic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11e**)* It was obtained as yellow solid, yield 72 %; m.p. 198–202 °C; IR (KBr) ν_{max} 3312, 2945, 1675, 1534, 1464, 736 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz): $\delta =$ 8.62 (s, 1H, CONH), 8.09 (s, 1H, N=CH), 7.91 (d, 1H, $J =$ 8.7 Hz, H-4′), 7.82 (t, 2H, $J = 11.2$ Hz, H-3, H-5), 7.67 (d, 1H, $J = 9.4$ Hz, H-9′), 7.56 (t, 1H, $J = 10.6$ Hz, H-8′), 7. 43 (t, 1H, $J = 9.6$ Hz, H-7′), 7.33 (d, 1H, H-6′), 7.20 (d, 2H, $J = 7.6$ Hz, H-2, H-6); ^{13}C NMR (DMSO, 75 MHz): $\delta = 170$ (C, CONH), 158.2 (C, C-2′), 154.1 (CH, N=CH), 151 (C, C-10′), 138.1 (CH, C-4′), 137 (C, C-4), 132.2 (C, C-1), 130.5 (C, C-8′), 129.6 (CH, C-3, C-5), 128.5 (CH, C-2, C-6), 127.9 (C, C-9′), 127.8 (CH, C-6′), 125.6 (CH, C-7′), 125.3 (C, C-5′), 122.3 (C, C-3′); EIMS *m/z*: 343.02 (M^+); Anal. Calcd. for $C_{17}H_{11}Cl_2N_3O$: C, 59.32; H, 3.22; N, 12.21. Found: C, 59.35; H, 3.26; N, 12.23.

*Nicotinic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11f**)* It was obtained as brownish-yellow solid, yield 62 %; m.p. 224–228 °C; IR (KBr) ν_{max} 3192, 2927, 1633, 1502, 1454, 726 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz): $\delta =$ 8.92 (s, 1H, CONH), 8.65 (s, 1H, N=CH), 8.41 (d, 1H, $J =$ 9.7 Hz, H-4′), 7.78–7.84 (m, 4H, pyridyl), 7.63 (d, 1H, $J = 9.7$ Hz, H-9′), 7.50 (t, 1H, $J = 8.9$ Hz, H-8′), 7.41 (t, 1H, $J = 12.2$ Hz, H-7′), 7.38 (d, 1H, H-6′); ^{13}C NMR (DMSO, 75 MHz): $\delta = 171.4$ (C, CONH), 157.2 (C, C-2′), 154 (CH, N=CH), 152.3 (C, C-10′), 149.2 (CH, C-4), 138.3 (CH, C-4′), 136.6 (CH, C-6), 130.6 (CH, C-8′), 129 (CH, C-2), 127.9 (CH, C-9′), 127 (CH, C-6′), 126.5 (CH, C-7′), 125.2 (C, C-5′), 124.7 (CH, C-5), 123.3 (C, C-3′); EIMS *m/z*: 310.06 (M^+); Anal. Calcd. for $C_{16}H_{11}ClN_4O$: C, 61.84; H, 3.57; N, 18.03. Found: C, 61.80; H, 3.52; N, 18.07.

*Phenoxyacetic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11g**)* It was obtained as yellowish-brown solid, yield 67 %; m.p. 26–219 °C; IR (KBr) ν_{max} 3301, 2929, 1694, 1605, 1500, 740 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz): $\delta = 8.72$ (s, 1H, CONH), 8.45 (s, 1H, N=CH), 7.62 (d, 1H, $J = 10.3$ Hz, H-9′), 7.53 (t, 1H, $J = 9.4$ Hz, H-8′), 7.40 (t, 1H, $J = 11.2$ Hz, H-7′), 7.34 (d, 1H, $J = 6.$ 3, H-6′), 7.32 (t, 1H, $J = 7.2$, H-4), 7.06 (d, 2H, $J = 10.2$, H-3, H-5), 6.90 (d, 2H, $J = 9.2$ Hz, H-2, H-6), 5.01 (s, 1H, OCH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 172.8$ (C, CONH), 163.4 (C, C-1), 159 (C, C-2′), 154 (CH, N=CH), 150.3 (C, C-10′), 138.3(CH, C-4′), 130.3 (CH, C-8′), 128.5 (CH, C-4), 127.7 (CH, C-9′), 126 (CH, C-6′), 125.1 (CH, C-7′), 123.5 (C, C-5′), 122.6 (C, C-3′), 117.4 (CH, C-4), 110.3 (CH, C-2, 6), 78.6 (CH_2, OCH_2); EIMS *m/z*: 339.07 (M^+); Anal. Calcd. for $C_{18}H_{14}ClN_3O_2$: C, 63.63; H, 4.15; N, 12.37. Found: C, 63.60; H, 4.19; N, 12.31.

*3,5-Dinitro-benzoic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11h**)* It was obtained as brownish-yellow solid, yield 78 %; m.p. 70–72 °C; IR (KBr) ν_{max} 3305, 2924, 1670, 1504, 1461, 793 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz): $\delta = 8.87$ (s, 1H, CONH), 8.59 (s, 1H, N=CH), 8.22–8.35 (m, 3H, H-2,H-4, H-6), 7.76 (d, 1H, $J = 10.$ 5 Hz, H-9′), 7.58 (t, 1H, $J = 10.5$ Hz, H-8′), 7.43 (t, 1H, $J = 10.4$ Hz, H-7′), 7.26 (d, 1H, $J = 6.9$ Hz, H-6′); ^{13}C NMR (DMSO, 75 MHz): $\delta = 171.4$ (C, CONH), 157.6 (C, C-2′), 154.2 (CH, N=CH), 151.6 (C, C-10′), 150 (C, C-3,

C-5), 138.2 (CH, C-4′), 134.7 (C, C-1), 130.5 (CH, C-8′), 128.7 (CH, C-2, C-6), 128 (CH, C-9′), 127.8 (CH, C-6′), 126.4 (CH, C-7′), 126 (CH, C-5′), 125.5 (C, C-3′), 123 (CH, C-4); MS *m/z*: 399.0 (M^+); Anal. Calcd for $C_{17}H_{10}ClN_5O_5$: C, 51.08; H, 2.52; N, 17.52. Found: C, 51. 05; H, 2.48; N, 17.48.

*2-Hydroxy-benzoic acid (2-chloro-quinolin-3-ylmethylene)-hydrazide (**11i**)* It was obtained as yellow solid, yield 60 %; m.p. 171–173 °C; IR (KBr) ν_{max} 3307, 2965, 1664, 1500, 1473, 733 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.81$ (s, 1H, CONH), 8.50 (s, 1H, N=CH), 7.57 (d, 1H, $J = 10.5$ Hz, H-9′), 7.46 (t, 1H, $J = 10.7$ Hz, H-8′), 7.38 (t, 1H, $J = 9.2$ Hz, H-7′), 7.29 (d, 1H, $J = 7.9$, H-6′), 6.67–7.23 (m, 4H, H-2, H-3, H-5, H-6); ^{13}C NMR (DMSO, 75 MHz): $\delta = 171$ (C, CONH), 156 (C, C-2, C-2′), 154.2 (CH, N = CH), 151 (C, C-10′), 139 (CH, C-4′), 134.3 (CH, C-4), 130.7 (CH, C-8′), 129 (CH, C-6), 128.8 (CH, C-9′), 127.5 (CH, C-6′), 126.3 (CH, C-7′), 125. 2 (CH, C-5′), 123.3 (C, C-3′), 121.4 (CH, C-5), 119.2 (C, C-1), 117.7 (CH, C-3); EIMS *m/z*: 325.06 (M^+); Anal. Calcd. for $C_{17}H_{12}ClN_3O_2$: C, 62.68; H, 3.71; N, 12.90. Found: C, 62.62; H, 3.67; N, 12.94.

*Procedure for the synthesis of 2-chloro-3-(5-substituted-phenyl-1,3,4-oxadiazol-2-yl)quinoline (**12a–i**)*

To an ethanolic solution of (2-chloroquinolin-3-yl)methylidene]-substituted benzohydrazide **11a–i** (0.002 mol; 0.78 g), chloramine-T (0.004 mol; 0.90 g) was added. The solution was refluxed for 4 h, sodium chloride which separated out during the course of reaction was filtered off. Excess ethanol was completely removed from the filtrate by distillation under reduced pressure, leaving behind a solid mass which was crystallized from ethanol to give the desired compound.

*2-Chloro-3-{5-[(naphthalen-2-yloxy)methyl]-1,3,4-oxadiazol-2-yl}quinoline (**12a**)* It was obtained as brownish solid, yield 76 %; m.p. 147–150 °C; IR (KBr) ν_{max} 2916, 1597, 1297, 1045, 749 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta =$ 8.49 (s, 1H, H-9′), 8.23 (s, 1H, H-4′), 8.02 (d, 1H, $J =$ 6 Hz, H-6′), 7.67–7.80 (m, 4H, H-4, H-6, H-9, H-8′), 7.63 (s, 1H, H-1), 7.12–7.37 (m, 4H, H-3, H-7, H-8, H-7′), 4.90 (s, 2H, CH_2O); ^{13}C NMR (DMSO, 75 MHz): $\delta = 166.7$ (C, C-5oxa), 166.5 (C, C-2oxa), 157.1 (C, C-2), 154.2 (C, C-2′), 146.7 (C, C-10′), 136.6 (CH, C-4′), 135 (C, C-10), 131.9 (C, C-3′), 130.6 (CH, C-8′), 129.8 (CH and C, C-4, C-5), 127.5 (CH, C-9′), 126.9 (CH, C-6, C-9), 126.5 (CH, C-6′), 126 (CH, C-7′), 125.1 (C, C-5′), 123 (CH, C-7, C-8), 115.5 (CH, C-3), 102.5 (CH, C-1), 70.2 (CH_2); EIMS *m/z*: 387 (M^+); Anal. Calcd. for $C_{22}H_{14}ClN_3O_2$: C, 68.13; H, 3. 64; N, 10.83. Found: C, 68.10; H, 3.65; N, 10.86.

*3-(5-Benzyl-1,3,4-oxadiazol-2-yl)-2-chloroquinoline (**12b**)* It was obtained as yellowish-white solid, yield 73 %; m.p. 178–180 °C; IR (KBr) ν_{max} 2945, 1587, 1299, 1047, 728 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.05$ (d, 1H, $J = 10.9$ Hz, H-4′), 7.90 (d, 1H, $J = 9.7$ Hz, H-9′), 7.67 (t, 1H, $J = 9.7$ Hz, H-8′), 7.45 (t, 1H, $J = 13.7$ Hz, H-7), 7. 28 (d, 1H, H-6′), 7.19 (t, 2H, $J = 10.2$ Hz, H-3, H-5), 7. 08–7.16 (m, 3H, H-2, H-4, H-6), 4.56 (s, 2H, CH_2); ^{13}C NMR (DMSO, 75 MHz): $\delta = 166.4$ (C, C-5oxa), 166 (C, C-2oxa), 155.4 (C, C-2′), 146.4 (C, C-10′), 139.5 (C, C-1), 135 (CH, C-4′), 131.9 (C, C-3′), 130.7 (CH, C-8′), 129.5 (CH, C-2, C-6), 128 (CH, C-3, C-5), 127.8 (CH, C-9′), 127 (CH, C-6′), 126.5 (CH, C-7′), 126.1 (C, C-5′), 125.3 (CH, C-4), 35.8 (CH_2); EIMS *m/z*: 321.6 (M^+); Anal. Calcd. for $C_{18}H_{12}ClN_3O$: C, 67.19; H, 3.76; N, 13.06. Found: C, 67. 22; H, 3.81; N, 13.05.

*2-Chloro-3-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]quinoline (**12c**)* It was obtained as white solid, yield 66 %; m.p. 79–83 °C; IR (KBr) ν_{max} 2916, 1597, 1299, 1043, 748 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta = 8.04$ (d, 1H, $J = 9.0$ Hz, H-4′), 7.99 (t, 2H, $J = 6.3$ Hz, H-3, H-5), 7.88 (d, 1H, $J = 8.7$ Hz, H-9′), 7.63 (t, 1H, $J = 8.8$ Hz, H-8′), 7.52 (t, 1H, $J = 9.4$ Hz, H-7′), 7.28 (d, 2H, $J = 14.6$ Hz, H-2, H-6), 7.20 (d, 1H, $J = 6.6$ Hz, H-6′); ^{13}C NMR (DMSO, 75 MHz): $\delta = 166.9$ (C, C-5oxa), 166.5 (C, C-2oxa), 156 (C, C-2′), 147.5 (C, C-10′), 145.8 (C, C-4), 141 (C, C-1), 135.2 (CH, C-4′), 132.7 (C, C-3′), 131.7 (CH, C-8′), 129.3 (CH, C-9′), 128.7 (CH, C-2, C-6), 127.9 (CH, C-6′), 127 (CH, C-7′), 126.5 (C, C-5), 123.2 (CH, C-3, C-5); EIMS *m/z*: 352.02 (M^+); Anal. Calcd. for $C_{17}H_9ClN_4O_3$: C, 57.89; H, 2.57; N, 15.88. Found: C, 57. 92; H, 2.55; N, 15.90.

*2-Chloro-3-[5-(3,5-dimethoxyphenyl)-1,3,4-oxadiazol-2-yl]quinoline (**12d**)* It was obtained as brownish solid, yield 66 %; m.p. 171–175 °C; IR (KBr) ν_{max} 2926, 1527, 1280, 1092, 714 cm^{-1}; ^1H NMR (DMSO, 300 MHz): $\delta =$ 7.71 (d, 1H, $J = 12$ Hz, H-9′), 7.60 (t, 2H, $J = 8.7$ Hz, H-7′, H-8′), 7.46 (d, 1H, $J = 7.1$ Hz, H-6′), 7.26–7.36 (m, 3H, H-2, H-4, H-6), 3.43 (s, 3H, 5-OCH_3), 3.33 (s, 3H, 3-OCH_3); ^{13}C NMR (DMSO, 75 MHz): $\delta = 167.2$ (C, C-5oxa), 167 (C, C-2oxa), 163 (C, C-3, C-5), 155 (C, C-2′), 147 (C, C-10′), 141.3 (C, C-1), 135.6 (CH, C-4′), 132.4 (C, C-3′), 131 (CH, C-8′), 128.9 (CH, C-9′), 128.4 (CH, C-6′), 128 (CH, C-7′), 126.5 (C, C-5′), 104 (CH, C-2, 6), 100.7 (CH, C-4), 56 (C, 2-OCH_3); EIMS *m/z*: 367 (M^+); Anal. Calcd. for $C_{19}H_{14}ClN_3O_3$: C, 62.05; H, 3.84; N, 11.43. Found: C, 62.09; H, 3.80; N, 11.40.

*2-Chloro-3-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]quinoline (**12e**)* It was obtained as yellowish-white solid, yield 63 %; m.p. 217–221 °C; IR (KBr) ν_{max} 2906, 1531,

1289, 1108, 721 cm^{-1}; ^1H NMR (DMSO, 300 MHz): δ = 7.89 (d, 1H, J = 9.4 Hz, H-4′), 7.76 (t, 2H, J = 11.7 Hz, H-3, 5), 7.59 (d, 1H, J = 10.7 Hz, H-9′), 7.49 (t, 1H, J = 12.3 Hz, H-8′), 7.38 (t, 1H, J = 8.9 Hz, H-7′), 7.29 (d, 1H, J = 9.5 Hz, H-6′), 7.17 (d, 2H, J = 7.9 Hz, H-2, H-6); ^{13}C NMR (DMSO, 75 MHz): δ = 165.7 (C, C-5oxa), 165.4 (C, C-2oxa), 155 (C, C-2′), 147.8 (C, C-10′), 134.6 (CH, C-4′), 133.5 (C, C-1), 132.5 (C, C-4), 131.7 (C, C-3′), 130.6 (CH, C-8′), 129.8 (CH, C-3, C-5), 129 (CH, C-9′), 128.6 (CH, C-2, C-6), 127 (CH, C-6′), 126.9 (CH, C-7′), 126.3 (C, C-5′); EIMS *m/z*: 341 (M^+); Anal.Calcd. for $C_{17}H_9Cl_2N_3O$: C, 59.67; H, 2.65; N, 12.28. Found: C, 59.73; H, 2.69; N, 12.31.

2-Chloro-3-[5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl]quinoline ***(12f)*** It was obtained as white solid, yield 58 %; m.p. 135–136 °C; IR (KBr) ν_{max} 3046, 1526, 1299, 1096, 702 cm^{-1}; ^1H NMR (DMSO, 300 MHz): δ = 8.29 (d, 1H, J = 10.2 Hz, H-4′), 7.72–7.85 (m, 4H, Hpyr), 7.60 (d, 1H, J = 9.4 Hz, H-9′), 7.48 (t, 1H, J = 8.7 Hz, H-8′), 7.38 (t, 1H, J = 12 Hz, H-7′), 7.32 (d, 1H, J = 7.5 Hz, H-6′); ^{13}C NMR (DMSO, 75 MHz): δ = 166.7 (C, C-5oxa), 166.2 (C, C-2oxa), 154.5 (C, C-2′), 149.3 (CH, C-2pyr), 148.1 (CH, C-4pyr), 146.6 (C, C-10′), 136.2 (CH, C-4′), 134.2 (CH, C-6pyr), 133.2 (C, C-1pyr), 132.2 (C, C-3′), 131 (CH, C-8′), 129.6 (CH, C-9′), 128.5 (CH, C-6′), 127.1 (CH, C-7′), 126.2 (C, C-5′), 123 (CH, C-5pyr); EIMS *m/z*: 308.5 (M^+); Anal. Calcd. for $C_{16}H_9ClN_4O$: C, 62.25; H, 2.94; N, 18.15. Found: C, 62.21; H, 2.98; N, 18.14.

2-Chloro-3-[5-(phenoxymethyl)-1,3,4-oxadiazol-2-yl]quinolone ***(12g)*** It was obtained as yellowish-white solid, yield 66 %; m.p. 167–170 °C; IR (KBr) ν_{max} 2934, 1577, 1297, 1039, 739 cm^{-1}; ^1H NMR (DMSO, 300 MHz): δ = 7.58 (d, 1H, J = 8.7 Hz, H-9′), 7.53 (t, 1H, J = 9.2 Hz, H-8′), 7.47 (t, 1H, J = 10.8 Hz, H-7′), 7.42 (d, 1H, J = 7.1, H-6′), 7.37 (t, 1H, J = 11.2, H-4), 7.12 (d, 2H, J = 13.2, H-3, H-5), 6.79 (d, 2H, J = 9.8 Hz, H-2, H-6), 5.94 (s, 1H, OCH_2); ^{13}C NMR (DMSO, 75 MHz): δ = 167.7 (C, C-5oxa), 167 (C, C-2oxa), 161.6 (C, C-1), 157 (C, C-2′), 147 (C, C-10′), 137.8 (CH, C-4′), 132.4 (C, C-3′), 131.1 (CH, C-8′), 130 (CH, C-9′), 129.2 (CH, C-3, 5), 128 (CH, C-6′), 126.4 (CH, C-7′), 124.5 (C, C-5′), 120.1 (CH, C-4), 114 (CH, C-2, 6), 75.1 (OCH_2); EIMS *m/z*: 337.6 (M^+); Anal. Calcd. for $C_{18}H_{12}ClN_3O_2$: C, 64.01; H, 3.58; N, 12.44. Found: C, 64.05; H, 3.61; N, 12.47.

2-Chloro-3-[5-(3,5-dinitrophenyl)-1,3,4-oxadiazol-2-yl]quinoline ***(12h)*** It was obtained as yellow solid, yield 76 %; m.p. 134–135 °C; IR (KBr) ν_{max} 3047, 1597, 1298, 1095, 703 cm^{-1}; ^1H NMR (DMSO, 300 MHz): δ = 8.22–8.38 (m, 3H, H-2, H-4, H-6), 7.84 (d, 1H, J = 10.2 Hz, H-9′), 7.61 (t, 1H, J = 12.2 Hz, H-8′), 7.43 (t, 1H, J = 10.5 Hz, H-7′), 7.27 (d, 1H, J = 6.6, H-6′); ^{13}C NMR (DMSO, 75 MHz): δ = 166.5 (C, C-5oxa), 166.1 (C, C-2oxa), 156 (C, C-2′), 150.4 (C, C-3, C-5), 147 (C, C-10′), 137.5 (C, C-1), 133 (CH, C-4′), 130.7 (CH, C-8′), 129.4 (CH, C-9′), 128.6 (CH, C-2, C-6), 127.7 (CH, C-6′), 127 (CH, C-7′), 126.1 (C, C-5′), 115.6 (CH, C-4); EIMS m/z: 397.1 (M^+); Anal. Calcd. for $C_{17}H_8ClN_5O_5$: C, 51.34; H, 2.03; N, 17.61. Found: C, 51.37; H, 2.06; N, 17.64.

2-[5-(2-Chloroquinolin-3-yl)-1,3,4-oxadiazol-2-yl]phenol ***(12i)*** It was obtained as yellowish-white solid, yield 63 %; m.p. 141–143 °C; IR (KBr) ν_{max} 3365, 2987, 1595, 1299, 1098, 723 cm^{-1}; ^1H NMR (DMSO, 300 MHz): δ = 10.21 (s, OH, 1H), 7.51 (d, 1H, J = 7 Hz, H-9′), 7.41 (t, 1H, J = 10.3 Hz, H-8′), 7.32 (d, 1H, J = 7.0 Hz, H-7′), 7.12 (t, 1H, J = 8.4, H-6′), 6.57–6.97 (m, 4H, H-2, H-3, H-5, H-6); ^{13}C NMR (DMSO, 75 MHz): δ = 166.8 (C, C-5oxa), 166.3 (C, C-2oxa), 157 (C, C-2′), 147 (C, C-10′), 136.9 (CH, C-4′), 132.2 (C, C-3′), 131 (CH, C-8′), 130 (CH, C-9′), 129.5 (CH, C-4, C-6), 127.9 (CH, C-6′), 127.2 (CH, C-7′), 126.1 (C, C-5′), 122.7 (C, C-1), 119.5 (CH, C-5), 115 (CH, C-3); EIMS m/z: 323.4 (M^+); Anal. Calcd. for $C_{17}H_{10}ClN_3O_2$: C, 63.07; H, 3.11; N, 12.98. Found: C, 63.11; H, 3.13; N, 12.95.

Antibacterial activity

Determination of minimum inhibitory concentration by serial dilution technique

The stock solutions of synthesized compounds were reconstituted with a minimum amount of dimethyl sulfoxide (DMSO). This solvent did not possess any antimicrobial activity of its own. Calculated volume of this stock solution were dispensed in a series of McCartney bottles previously containing calculated volume of sterile cooled molten nutrient agar media (40–45 °C) to prepare final volume of 30 ml each with dilutions of 5, 12.5, 25, 50, 100, 200 and 400 μg/ml. Then these molten media containing varying concentration of compounds were poured aseptically in pre sterilized petridishes (70 mm) to give sterile nutrient agar plates with varying dilution of the compounds. These plates were then kept in the refrigerator at 4 °C for 24 h to ensure uniform diffusion of compounds. Then these plates were dried at 37 °C before spot inoculations. One loopful culture (loop diameter: 6 mm) of an overnight grown bacterial strains suspension (105 CFU/ml) was added in each quadrant as marked by checkerboard technique. The spotted plates were incubated at 37 °C for 24 h in an incubator, and MIC values were obtained (Asamenew *et al.*, 2011; Mazumder *et al.*, 2004).

Determination of zones of inhibition of disc diffusion method

A 200 μg/ml solution of both synthesized compounds and ciprofloxacin (solvent: DMSO) were prepared in sterilized McCartney bottles. Sterile molten media plates were prepared and incubated at 25 °C for 24 h to check for the presence of any sort of contamination. Then each sterilized nutrient agar plates were flooded with liquid culture of bacterial strains and dried for 30 min at 25 °C. The sterile Whatman filter paper disc (4-mm diameter) was soaked in solution of synthesized compounds and placed in appropriate position of the plates marked as quadrant at the back of petridishes. All the flooded plates with corresponding paper discs soaked with solution of synthesized compounds were incubated at 25 °C for 24 h, and diameter of zone of inhibition was measured in mm. Similar procedure was adopted for ciprofloxacin, and corresponding zone diameters were measured and compared accordingly.

Anticancer activity

Treatment of tumour cell lines

All compounds were submitted to the National Cancer Institute, and three compounds were selected for anticancer screening on NCI 60 cell lines initially at a single high dose (10^{-5} M) on leukaemia (CCRF-CEM, HL-60 (TB), K-562, MOLT-4, RPMI-8226, SR), non-small cell lung cancer (A549/ATCC, HOP-62, HOP-92, NCI-H226, NCI-H23, NCI-H322M, NCI-H460, NCI-H522), colon cancer (COLO 205, HCC-2998, HCT-116, HCT-15, HT29, KM12, SW-620), CNS cancer (SF-268,SF-295,SF-539,SNB-19, SNB-75), melanoma (LOX IMVI, MALME-3M, M14, MDA-MB-435, SK-MEL-2, SK-MEL-28, SK-MEL-5, UACC-257, UACC-62), ovarian cancer (IGROV1, OVCAR-3, OVCAR-4, OVCAR-5, OVCAR-8 NCI/ADR-RES 99.24, SK-OV-3), renal cancer (786-0, A498, ACHN, CAKI-1, SN12C, TK-10, UO-31), prostate cancer (PC-3, DU-145) and breast cancer (MCF7, MDA-MB-231/ATCC, HS 578T, BT-549, T-47D, MDA-MB-468) cell lines, nearly 60 in number. The One-dose data were reported as a mean graph of the percent growth of treated cells. The number reported for the one-dose assay is growth relative to the no-drug control, and relative to the time zero number of cells. The anticancer screening was carried out as per the NCI US protocol reported elsewhere (http://dtp.nci.nih.gov; Monks *et al.*, 1991; Boyd and Paull, 1995; Shoemaker, 2006). Using the seven absorbance measurements [time zero (T_z), control growth (C), and test growth in the presence of drug at the five concentration levels (T_i)], the percentage growth was calculated at each of the drug concentrations levels.

Percentage growth inhibition is calculated as

$[(T_i - T_z)/(C - T_z)] \times 100$ for concentrations for which $T_i \geq T_z$

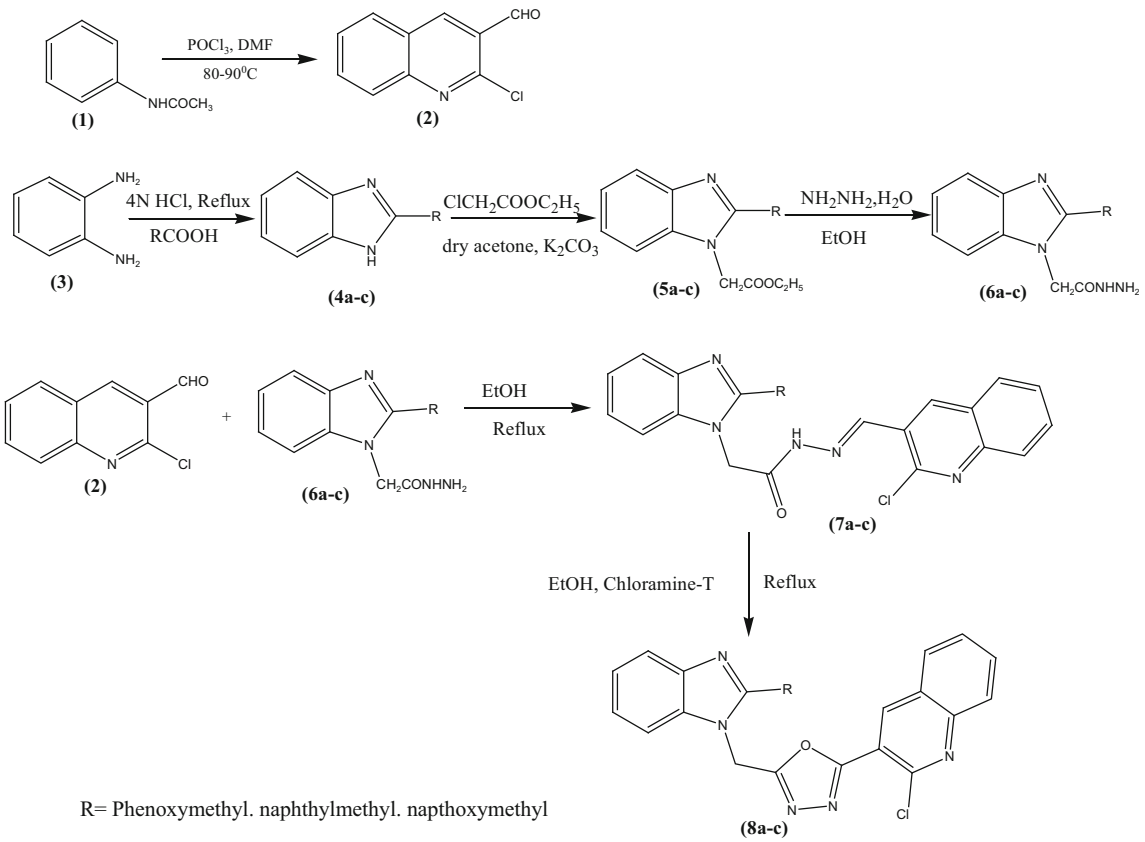
$[(T_i - T_z)/T_z] \times 100$ for concentrations for which $T_i < T_z$.

All values are statistically analysed and are expressed as mean with a range of growth for various cell lines.

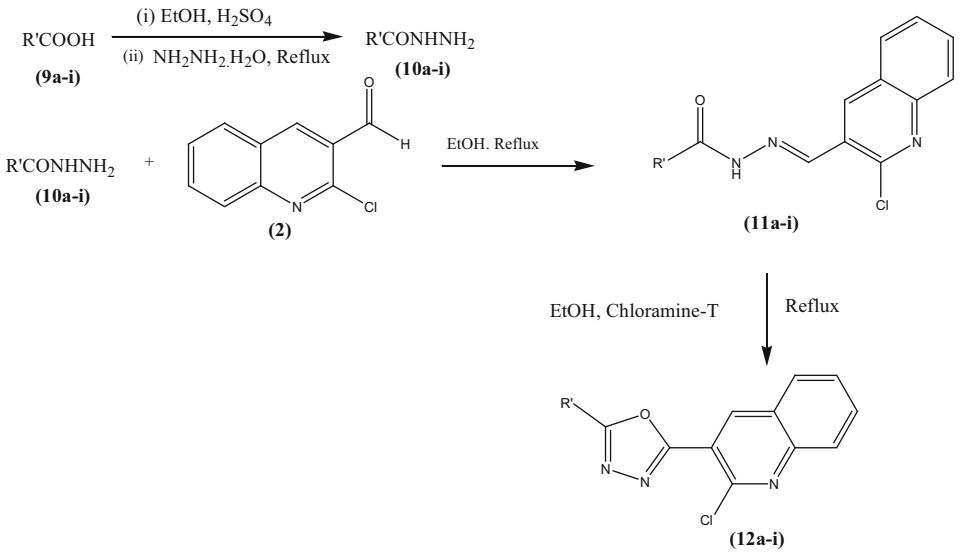
Results and discussion

Synthesis

2-Chloroquinoline-3-carbaldehyde (**2**) was prepared from acetanilide via Vilsmeier–Haack approach. In Scheme 1, the 2-[2-(phenoxy/naphthalen-1-yl/naphthalen-2-yloxy methyl)-1*H*-benzimidazol-1-yl]acetohydrazide (**6a–c**) were prepared using o-phenylenediamine and the corresponding acid by a series of step (Salahuddin *et al.*, 2014a). The phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1*H*-benzimidazol-1-yl)acetohydrazide (**7a–c**) were prepared using 2-chloroquinoline-3-carbaldehyde (**2**) and 2-[2-(phenoxy/naphthalen-1-yl/naphthalen-2-yloxymethyl)-1*H*-benzimidazol-yl]acetohydrazide (**6a–c**) in the presence of ethyl alcohol. The syntheses of 2-chloro-3-{5-[(2-phenoxy/naphthalene-1-yl/naphthalen-2-yloxy methyl-1-H-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}quinolone (**8a–c**) were prepared using chloramine-T. In Scheme 2, the different hydrazide (**10a–i**) were synthesized using different aromatic acids (Jha *et al.*, 2010). The (2-chloroquinoline-3-yl)methylidene]-substituted benzohydrazide (**11a–i**) were synthesized by reacting with 2-chloroquinoline-3-carbaldehyde (**2**) and the different hydrazide (**10a–i**). In the final step, 2-chloro-3-(5-substituted-phenyl-1,3,4-oxadiazol-2-yl)quinoline (**12a–i**) were synthesized with chloramine-T as the titled compounds. In general, the IR spectra of the compounds **7a**, **7b** and **7c** showed absorption peaks of C=O at 1654, 1654 and 1667 and NH peaks at 3310, 3317 and 3307, respectively. ^{1}H NMR spectra of the compounds **7a**, **7b** and **7c** show singlet between δ5 and δ6 of CH_2 and CH_2O respectively. The Schiff bases (**7a–c**) explained the presence of –CONH and –N=CH from the presence of two singlet between δ8 and δ9. In IR spectra of the compounds **8a–c**, disappearance of C=O and NH peaks indicates the formation of desired compounds. ^{1}H NMR spectra of the compounds **8a–c** also show two singlet between δ5 and δ6 of CH_2 and CH_2O respectively. In Scheme 2, compounds **11a–i** show two absorption peaks of C=O and –NH in IR spectra, and these two peaks were absent in the compounds **12a–i** confirm the formation of oxadiazole. The ^{13}C NMR spectra of 1,3,4-oxadiazole (**8a–c** and **12a–i**) shows two peaks between 165 and 168.



Scheme 1 Protocol for the synthesis of title compounds (**8a-c**)



R'= naphthoxymethyl, benzyl, 4-nitrophenyl, 3,5-dimethoxyphenyl, 4-chlorophenyl, nicotinyl, phenoxymethyl, 3,5-dinitrophenyl, 2-hydroxyphenyl.

Scheme 2 Protocol for the synthesis of title compounds (**12a-i**)

Antibacterial activity

It was observed that the maximum number of synthesized compounds (**8a**, **8c**, **12a**, **12b**, **12c** and **12h**) was acting as magic bullet against various gram-positive strains of *Bacillus cereus MTCC1305* as they were inhibited at very low concentration of the compounds. The compound **12c** was as potent as pure ciprofloxacin against *B. cereus*

Table 1 Preliminary antibacterial activities (MIC μg/ml) of title compounds

C8aompounds	*R*	*Shigella sonnei E08869*	*Escherichia coli 35B*	*Vibrio cholerae 765*	*Proteus vulgaris AP169*	*Bacillus subtilis MTCC441*	*Klebsella pneumoniae NCTC7447*	*Acetobacter aceti AP586*	*Pseudomonas putida MTCC2252*	*Shigella dysenteriae 9*	*Mongonella morganii ATCC25830*	*Escherichia coli Rho7/12*	*Bacillus cereus MTCC1305*
	Phenoxymethyl	–	200	–	–	25	–	–	100	>200	100	100	25
8b	Naphthylmethyl	>200	100	100	50	100	100	50	50	100	50	–	–
8c	Naphthyloxymethyl	100	25	200	100	25	50	50	100	200	100	50	25
12a	Naphthoxymethyl	100	50	–	100	100	25	100	200	>200	100	100	25
12b	Benzyl	100	100	100	50	–	200	50	–	100	50	200	25
12c	4-Nitrophenyl	–	25	200	100	25	12.5	200	100	200	200	200	12.5
12d	3,5-Dimethoxyphenyl	100	100	–	100	–	100	100	>200	–	>200	100	100
12e	4-Chlorophenyl	>200	200	–	100	100	50	100	100	–	–	100	–
12f	Nicotinyl	–	50	50	50	100	100	50	100	50	100	50	200
12g	Phenoxymethyl	50	–	100	–	100	–	–	100	100	100	100	>200
12h	3,5-Dinitrophenyl	100	50	100	100	25	12.5	100	–	200	50	–	12.5
12i	2-Hydroxyphenyl	200	200	>200	100	100	–	–	100	50	100	–	
	Ciprofloxacin	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5

– insignificant activity; MIC, minimum inhibitory concentration

Table 2 Disc diffusion study of various synthesized compounds at 200 μg/ml [mean diameter of zone of inhibition (mm) produced by synthesized compounds after tested microorganism]

Compounds	*R*	*Shigella sonnei E08869*	*Escherichia coli 35B*	*Vibrio cholerae 765*	*Proteus vulgaris AP169*	*Bacillus subtilis MTCC441*	*Klebsella pneumoniae NCTC7447*	*Acetobacter aceti AP586*	*Pseudomonas putida MTCC2252*	*Shigella dysenteriae 9*	*Mongonella morganii ATCC25830*	*Escherichia coli Rho 7/12*	*Bacillus cereus MTCC1305*
8a	Phenoxymethyl	–	7.5	–	–	10	–	–	8.0	–	7.5	8.0	9.5
8b	Naphthylmethyl	–	7.5	8.0	9.0	8.0	8.0	9.0	8.5	7.5	8.5	–	–
8c	Naphthyloxymethyl	8.0	10	6.5	7.5	10	9.0	8.5	8.0	6.0	8.0	9.0	9.5
12a	Naphthoxymethyl	8.0	9.0	–	8.0	8.5	10	7.5	7.0	5.0	7.5	7.5	10
12b	Benzyl	7.5	8.0	7.5	8.5	–	6.0	9.0	–	7.5	8.5	6.5	10
12c	4-Nitrophenyl	–	10	7.0	7.5	10	11	7.0	7.5	6.5	7.0	6.5	10.5
12d	3,5-Dimethoxyphenyl	8.0	8.0	–	7.5	–	8.0	7.5	5.0	–	6.0	8.0	7.5
12e	4-Chlorophenyl	5.0	7.0	–	6.5	7.0	9.0	8.0	7.5	–	–	7.5	–
12f	Nicotinyl	–	9.0	9.0	8.5	9.0	7.5	9.0	8.0	9.0	8.5	9.0	6.0
12g	Phenoxymethyl	9.0	–	8.0	–	7.5	–	–	8.0	7.5	8.0	8.0	5.0
12h	3,5-Dinitrophenyl	8.0	9.0	8.0	7.5	10	10.5	7.5	–	6.5	9.0	–	11
12i	2-Hydroxyphenyl	6.5	7.0	–	8.0	7.5	–	–	8.0	9.0	7.5	–	–
	Ciprofloxacin	18	17	16.5	17	15	17	14	15	18	17	17.5	15.5

MTCC1305. The synthesized compounds (**12a**, **12c** and **12h**) were also found to be extremely active against *Klebsiella pneumonia NCTC7447*, and hence they may be regarded as potent-promising agent for controlling pneumonia. It was also noted that **8c** and **12f** were very instrumental in inhibiting most of the pathogenic multidrug resistant of various gram-negative species including *E. coli 35B*, *Vibrio cholera 765* and *Proteus vulgaris AP169*. Compounds **8b** and **12b** were having a MIC of 50 μg/ml against *Acetobacter aceti AP586* and *Mongonella morganii ATCC 25830* when tested. *Shigella sonnei E08869*, *Pseudomonas putida MTCC 2252* and *Shigella dysenteriae 9* found to show significant degree of resistance against majority of synthesized compounds; however, both the strains of *S. dysenteriae 9* and *S. sonnei E08869* were effectively controlled by the synthesized compound (**12f**) at a concentration as low as 50 μg/ml (Table 1). Thus, we observe from our study that these compounds have a fairly broad spectrum of antibacterial efficacy and hence may be regarded as a potent candidate to control the global thread of drug resistant in future.

The disc diffusion study reveals that the diameter of zone of inhibition was in coherence with the study of MIC conducted on various synthesized compounds against the selected microorganisms. It was observed that compound with lower MIC showed a great zone of inhibition against all the test microorganisms. Compounds (**8a**, **8c**, **12a**, **12b**, **12c** and **12h**) was found to be most active against gram-positive bacteria particularly *B. cereus MTCC1305* showing zone of inhibition 9.5–11 mm. Compounds **12a**, **12c** and **12h** were found to be most active against *K. pneumonia NCTC7447* and it shows zone of inhibition MIC of 12.5 μg/ml and maximum zone of inhibition 10.5, 10 and 11 mm, respectively (Table 2).

Anticancer activity (Salahuddin *et al*., 2014b)

The synthesized compounds displayed moderate to low activity in the in vitro screen on all tested cancer cell lines and are given in Table 3. The compounds **8a** and **12d** were found to be the most active compound of the series and much better growth interaction as compared to **12f** against SNB-75. The compound **12d** showed 95.70 growth percent (GP) and highly active on SNB-75 (CNS cancer), UO-31 and CAKI-1 (renal cancer) (GP = 53.35, 64.35, and 77.71, respectively), and the compound **8a** showed 96.86 GP and highly active on SNB-75 (CNS cancer), UO-31 (renal cancer) and IGROV1 (ovarian cancer) with GP of 51.27, 67.58 and 77.85, while compound **12f** showed maximum sensitivity on SNB-75 (CNS cancer) with GP of 60.89. The compounds **8a**, **12d** and **12f** were found to be highly sensitive on SNB-75 and UO-31. The GP and percent growth inhibition (GI) of these compounds are shown in Fig. 3. The maximum percent growth inhibition was recorded for SNB-75 with GP of 51.27 and percent GI of 48.73.

Structure activity relationship (SAR)

On the basis of our findings, we could analyse the following points for antibacterial and anticancer activities:

- The compounds having 1,3,4-oxadiazole carrying benzimidazole moiety have better antibacterial activity (**8a** and **8c**) and anticancer activity (**8a**) than those of the compounds having only 1,3,4-oxadiazole moiety.
- Groups like 2-phenoxy-methyl/2-naphthoxymethyl and naphthoxymethyl benzimidazole shown good antibacterial activity.
- The antibacterial activity was improved due to the presence of electron withdrawing groups viz. 4-nitro,

Table 3 Anticancer activities of selected compound by NCI

Compounds	Sixty cell lines assay in one dose 10^{-5} M conc.				
	NSC code	Mean growth %	Range of growth %	The most sensitive cell line	Growth % of the most sensitive cell line
8a	772520	96.86	51.27–123.33	SNB-75 (CNS Cancer)	51.27
				UO-31 (renal cancer)	67.58
				IGROV1 (ovarian cancer)	77.85
12d	772522	95.70	53.35–104.73	SNB-75 (CNS cancer)	53.35
				UO-31 (renal cancer)	64.35
				CAKI-1(renal cancer)	77.71
12f	772521	101.07	60.89–119.03	SNB-75 (CNS cancer)	60.89
				NCI-H522 (non-small cell lung cancer)	81.23
				UO-31 (renal cancer)	82.81

The growth percentage depicted in Table 2 reveals the mean values of triplicate readings. All the values are statistically analysed and are expressed as mean with a range of growth for various cell lines

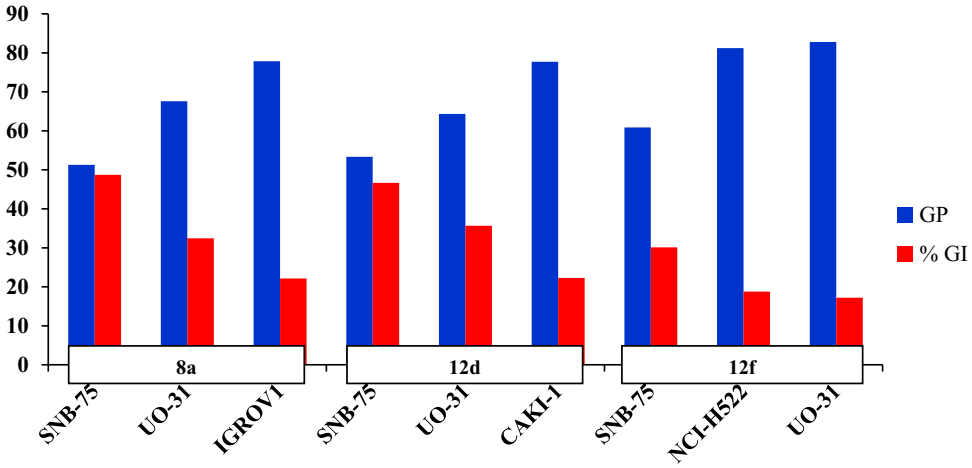


Fig. 3 The growth percent (GP) and percent growth inhibition (GI) of the compounds **8a**, **12d**, and **12f** on most sensitive cell lines

3,5-dinitro and 4-chloro (**12a**, **12c** and **12h**)-substituted phenyl on 1,3,4-oxadiazole ring against *B. cereus MTCC1305* and *K. pneumonia NCTC7447*.

- The compound having electron-releasing substituent like 3,5-dimethoxy and nicotinyl (**12d** and **12f**) has better anticancer activity, i.e. GP of the most sensitive cell lines.

Conclusion

Two series of 2,5-disubstitutedoxadiazole (**8a–c** and **12a–i**) were synthesized successfully by the Schiff base (**7a–c** and **11a–i**) with chloramine-T. Among the synthesized compound mainly 1,3,4-oxadiazole derivatives (**8a**, **8c**, **12a**, **12b**, **12c** and **12h**) emerged as lead compounds, these compounds showed good antibacterial activity with MIC 12.5 and 25 μg/ml. The compounds **8a**, **12d** and **12f** showed significant anticancer activity which can be further modified to exhibit better potency.

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