



## Synthesis, Antioxidant and Cytotoxic Activity Studies of 2-Chlorobenzo[h]quinoline containing 2,4,5-Trisubstituted Imidazole Derivatives

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A series of 2-chlorobenzo[h]quinoline containing 2,4,5-trisubstituted imidazole derivatives (**4a-h**) were synthesized and characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, FT-IR and mass spectral analysis. All the synthesized compounds were evaluated for their *in vitro* antioxidant activity by DPPH method and cytotoxicity study against Colo-205, HeLa and A549 human cancer cell lines by MTT assay method. Among the synthesized compounds, compound **4a** has showed significant cytotoxicity against all the three tested cancer cell lines, compound **4f** showed good cytotoxic activity against Colo-205 and HeLa cell lines, while compound **4c** has showed good cytotoxicity against HeLa cell line. With respect to antioxidant activity, the synthesized compounds **4a**, **4d** and **4e** found to exhibit good activity as compared to other compounds of the series.

**Keywords:** 2-Chlorobenzo[h]quinoline, MTT assay, Cytotoxicity, DPPH assay, Antioxidant activity.

### INTRODUCTION

Benzo[h]quinoline is a crucial heterocyclic compound that contains a fused ring structure and nitrogen. Several benzo[h]quinoline derivatives have identified as bioactive molecules and possess various biological activities like antioxidant [1], G-quadruplex binding agents [2], antimalarial [3,4], anticancer [5-9], vesicular glutamate transporter (VGLUT) inhibitors [10], anti-inflammatory [11] antiviral [12] and antimicrobial [13,14]. On the other hand, 2,4,5-trisubstituted imidazoles also exhibited variety of biological activities such as antioxidant agents [15], antibacterial agents [16], anti-inflammatory agents [17], anti-HIV agents [18], antidiabetic agents [19], cardiovascular agents [20], anticancer agents [21,22], angiotensin II receptor antagonists [23] and non-toxic modulators of P-glycoprotein mediated multidrug resistance [24] and inhibitors of enzyme *M. tuberculosis* glutamine synthetase [25].

Among heterocycles, quinoline and imidazole derivatives are preferable scaffolds for the development of novel therapeutic molecules. Thus, considering the bioprofiles of the benzo[h]quinoline and imidazoles, we reported the synthesis of new hybrid

molecules 2-chlorobenzo[h]quinoline containing imidazole analogs and screened for their cytotoxicity activity on three human cell lines (Colo-205, HeLa and A549). In addition to the anticancer activity, the synthesized molecules were screened for their antioxidant activity.

### EXPERIMENTAL

The chemicals utilized were procured from Sigma-Aldrich, USA, while the solvents were obtained from S.D. Fine Chemicals, India. The reaction progress and sample purity were assessed using thin layer chromatography (TLC) with a mobile phase consisting of petroleum ether and ethyl acetate mixture at a ratio of 8:2. The TLC stationary phase consisted of silica gel coated aluminum sheets (silica gel 60 F<sub>254</sub>) obtained from Merck, India. The UV radiation was employed to detect the spots of the compounds present on the TLC plates. The FT-IR spectra were acquired using a JASCO FTIR-4100 spectrophotometer, employing the KBr pellet method. The Agilent 400 MHz NMR apparatus was used to record the <sup>1</sup>H & <sup>13</sup>C NMR spectra. TMS was used as the internal standard and the chemical shift values

are reported in  $\delta$  (ppm) scale. The melting points of the synthesized compounds were determined using the Mvtec melting point apparatus and recorded using the open capillary method. These values are uncorrected.

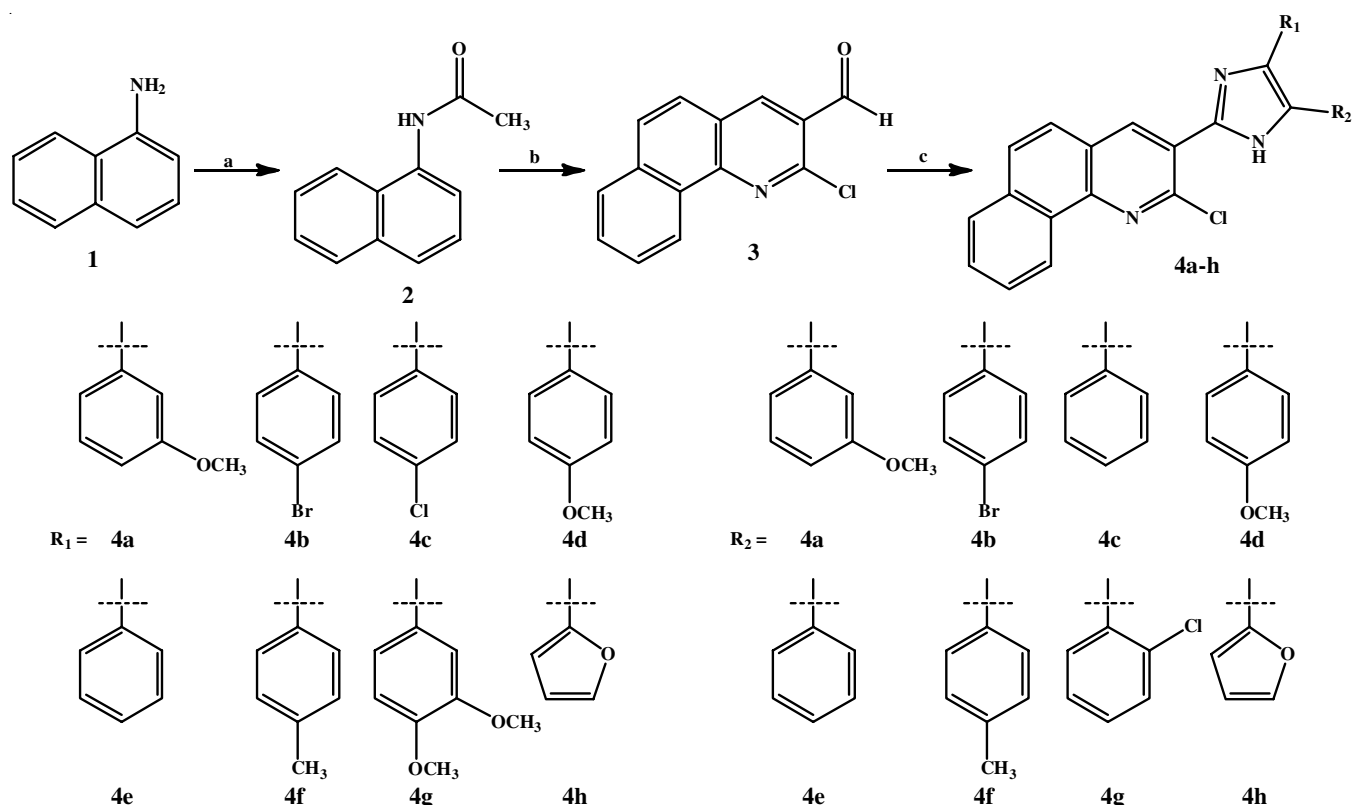
**Synthesis of *N*-(naphthalene-1-yl)acetamide (2):** In a round bottom flask, a solution consisting of naphthalen-1-amine (25 g, 175 mmol), acetic anhydride (21.4 g, 20 mL, 210 mmol) and 250 mL of methanol with catalytic amount of acetic acid was refluxed for 4 h. TLC was used to monitor the reaction progress using petroleum ether-ethyl acetate (8:2). The mixture was poured into ice cold water after the completion of the reaction. Solid product obtained was filtered, washed with water, dried and re-crystallized from ethanol. Off white solid; yield: 91%; m.p.: 131-132 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3271 (N-H), 3049 (Ar-H), 1654 (C=O);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 1.89 (s, 1H, N-H), 3.33 (s, 3H, -CH<sub>3</sub>), 7.41-7.90 (m, 7H, Ar-H); MS ( $m/z$ ): calcd. 185.22, found 186.22 [M+1].

**Synthesis of 2-chlorobenzo[*h*]quinoline-3-carbaldehyde (3):** Freshly distilled  $\text{POCl}_3$  (82.8 g, 51 mL, 540 mmol) was added dropwise to DMF (39.5 g, 42 mL, 540 mmol) at 0 °C and the mixture was left for 20 min. To the above mixture, compound 2 (20 g, 108 mmol) was added and refluxed for 6 h. TLC was used to check the completion of the reaction using petroleum ether-ethyl acetate (8:2). After completion of the reaction, mixture was poured into crushed ice, neutralized with  $\text{NaHCO}_3$  and solid obtained was filtered, washed with water, dried and recrystallized using ethanol. Yellow solid; yield: 76%; m.p.: 178-180 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3054 (Ar-H), 1685 (C=O), 1605 (C=C), 1577 (C=N), 756 (C-Cl);  $^1\text{H}$  NMR (400 MHz,

$\text{CDCl}_3$ )  $\delta$  ppm: 7.73 (m, 3H, Ar-H), 7.85 (d,  $J = 9.2$  Hz, 1H, Ar-H), 7.90 (d,  $J = 5.6$  Hz, 1H, Ar-H), 8.69 (s, 1H, Ar-H), 9.20 (d,  $J = 6.0$  Hz, 1H, Ar-H), 10.58 (s, 1H, CHO);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 119.70, 120.35, 121.29, 122.46, 122.62, 123.97, 124.57, 124.88, 129.66, 133.44, 143.89, 144.69, 184.01.

**2-Chlorobenzo[*h*]quinoline containing 2,4,5-trisubstituted imidazoles (4a-h):** A reaction mixture containing 2-chlorobenzo[*h*]quinoline-3-carbaldehyde (10 mmol), substituted benzil (10 mmol), ammonium acetate (50 mmol), acetic acid (20 mol%) and ethanol as solvent was taken in a three necked round bottom flask and refluxed for 9-12 h. TLC was used to monitor the reaction progress with petroleum ether and ethyl acetate (8:2) as a mobile phase. After completion of the reaction, the mixture was poured into ice cold water. The solid compound precipitated was filtered and dried (Scheme-I). The crude product was purified by column chromatography.

**3-[4,5-Bis(3-methoxyphenyl)-1*H*-imidazol-2-yl]-2-chlorobenzo[*h*]quinoline (4a):** Pale yellow; yield 91%; m.p.: 140-141 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3383 (N-H), 3053 (Ar-H), 2850 (-OCH<sub>3</sub>), 1601 (C=C), 1581 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 3.76 (s, 6H, -CH<sub>3</sub>), 6.84 (s, 1H, Ar-H), 6.89 (d,  $J = 6.8$  Hz, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 7.09 (d,  $J = 6.4$  Hz, 1H, Ar-H), 7.26 (d,  $J = 6.0$  Hz, 3H, Ar-H), 7.30 (m, 1H, Ar-H), 7.68 (m, 3H, Ar-H), 7.80 (d,  $J = 8.8$  Hz, 1H, Ar-H), 7.87 (d,  $J = 7.2$  Hz, 1H, Ar-H), 9.14 (d,  $J = 8.0$  Hz, 1H, Ar-H), 9.18 (s, 1H, Ar-H), 10.50 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 55.24, 112.95, 113.35, 113.53, 113.93, 120.14, 120.43, 122.80, 124.73, 125.60, 127.49, 127.91, 128.31, 128.93, 129.04, 129.38, 130.10, 131.71, 134.08, 135.59, 138.59, 141.15,



**Scheme-I:** Reagents and reaction conditions: (a)  $(\text{CH}_3\text{CO})_2\text{O}/\text{CH}_3\text{COOH}/\text{reflux}$ , (b)  $\text{POCl}_3/\text{DMF}/\text{reflux}$ , (c) substituted benzil,  $\text{CH}_3\text{COONH}_4$ ,  $\text{CH}_3\text{COOH}/\text{reflux}$

143.95, 145.61, 159.65, 159.87; MS (*m/z*): calcd. 491.13, found 492.01 [M+1].

**3-[4,5-Bis(4-bromophenyl)-1*H*-imidazol-2-yl]-2-chlorobenzo[*h*]quinoline (4b):** Brown solid; yield: 78%; m.p.: 243-244 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3389 (N-H), 3053 (Ar-H), 1600 (C=C), 1584 (C=N), 826 (C-Br);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 7.34 (d,  $J = 8.4$  Hz, 2H, Ar-H), 7.46 (d,  $J = 8.8$  Hz, 2H, Ar-H), 7.53 (m, 4H, Ar-H), 7.71 (m, 3H, Ar-H), 7.84 (d,  $J = 8.8$  Hz, 1H, Ar-H), 7.89 (dd,  $J = 2.8$  Hz, 3.6 Hz, 1H, Ar-H), 9.15 (dd,  $J = 2.8$  Hz, 3.6 Hz, 1H, Ar-H), 9.19 (s, 1H, Ar-H), 10.45 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 121.53, 122.49, 122.61, 124.64, 124.78, 125.62, 127.36, 127.59, 127.95, 129.12, 129.18, 129.29, 129.34, 130.09, 131.68, 132.44, 133.00, 134.15, 137.98, 138.67, 141.85, 143.82, 145.85; MS (*m/z*): calcd. 586.93, found 587.79 [M+1].

**2-Chloro-3-[4-(4-chlorophenyl)-5-phenyl-1*H*-imidazol-2-yl]benzo[*h*]quinoline (4c):** Off white solid; yield: 75%; m.p.: 188-190 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3404 (N-H), 3052 (Ar-H), 1598 (C=C), 1583 (C=N), 738 (C-Cl);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 7.29 (d,  $J = 8.4$  Hz, 2H, Ar-H), 7.34 (m, 2H, Ar-H), 7.43 (d,  $J = 6.8$  Hz, 2H, Ar-H), 7.48 (d,  $J = 8.4$  Hz, 1H, Ar-H), 7.62 (d,  $J = 8.4$  Hz, 2H, Ar-H), 7.67 (m, 3H, Ar-H), 7.84 (d,  $J = 8.8$  Hz, 1H, Ar-H), 7.87 (d,  $J = 8.4$  Hz, 1H, Ar-H), 9.14 (s, 1H, Ar-H), 9.16 (d,  $J = 4.0$  Hz, 1H, Ar-H), 10.46 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 122.66, 124.69, 124.74, 125.60, 127.07, 127.53, 127.83, 127.93, 128.51, 128.54, 128.61, 129.01, 129.10, 129.18, 129.32, 130.08, 130.29, 132.83, 133.04, 134.10, 137.51, 138.53, 138.62, 141.44, 141.59, 143.87, 145.69; MS (*m/z*): calcd. 465.07, found 465.95 [M+1].

**3-[4,5-Bis(4-methoxyphenyl)-1*H*-imidazol-2-yl]-2-chlorobenzo[*h*]quinoline (4d):** Pale yellow solid; yield: 90%; m.p.: 162-163 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3426 (N-H), 3052 (Ar-H), 2837 (-OCH<sub>3</sub>), 1611 (C=C), 1585 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 3.82 (s, 3H, -OCH<sub>3</sub>), 3.84 (s, 3H, -OCH<sub>3</sub>), 6.83 (m, 4H, Ar-H), 7.44 (m, 4H, Ar-H), 7.69 (m, 3H, Ar-H), 7.83 (d,  $J = 8.8$  Hz, 1H, Ar-H), 7.89 (d,  $J = 6.8$  Hz, 1H, Ar-H), 9.16 (d,  $J = 7.2$  Hz, 1H, Ar-H), 9.24 (s, 1H, Ar-H), 10.36 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 49.95, 108.30, 108.58, 117.69, 119.37, 119.42, 120.36, 122.13, 122.56, 123.20, 123.62, 124.82, 125.70, 125.97, 128.70, 133.04, 135.28, 138.53, 140.14; MS (*m/z*): calcd. 491.13, found 492.01 [M+1].

**2-Chloro-3-(4,5-diphenyl-1*H*-imidazol-2-yl)benzo[*h*]quinoline (4e):** Yellow solid; yield: 94%; m.p.: 196-197 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3450 (N-H), 3053 (Ar-H), 1602 (C=C), 1580 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 7.28 (m, 6H, ArH), 7.50 (d,  $J = 7.2$  Hz, 2H, Ar-H), 7.69-7.76 (m, 5H, Ar-H), 7.81 (d,  $J = 8.8$  Hz, 1H, Ar-H), 7.88 (d,  $J = 7.2$  Hz, 1H, Ar-H), 9.15 (d,  $J = 7.6$  Hz, 1H, Ar-H), 9.22 (s, 1H, Ar-H), 10.46 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 117.47, 119.38, 120.30, 121.96, 122.17, 122.41, 122.49, 122.59, 122.91, 122.99, 123.10, 123.63, 123.72, 124.75, 125.18, 128.72, 128.97, 133.21, 133.39, 135.92, 138.54, 140.25; MS (*m/z*): calcd. 431.11, found 432.01.

**3-[4,5-Bis(4-methylphenyl)-1*H*-imidazol-2-yl]-2-chlorobenzo[*h*]quinoline (4f):** Off white solid; yield 73%; m.p.: 185-187 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3413 (N-H), 3054 (Ar-H), 2852 (-OCH<sub>3</sub>), 1611 (C=C), 1583 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 2.35 (s, 3H, -CH<sub>3</sub>), 2.39 (s, 3H, -CH<sub>3</sub>),

7.13 (d,  $J = 8.0$  Hz, 2H, ArH), 7.19 (d,  $J = 8.0$  Hz, 2H, ArH), 7.38 (d,  $J = 8.0$  Hz, 2H, ArH), 7.58 (d,  $J = 7.6$  Hz, 2H, ArH), 7.69 (m, 3H, ArH), 7.80 (d,  $J = 8.8$  Hz, 1H, ArH), 7.87 (d,  $J = 6.8$  Hz, 1H, ArH), 9.14 (d,  $J = 7.2$  Hz, 1H, ArH), 9.19 (s, 1H, ArH), 10.42 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 21.27, 30.97, 113.92, 123.01, 124.73, 125.64, 127.44, 127.65, 127.88, 128.13, 128.85, 128.94, 129.07, 129.68, 130.16, 131.61, 134.05, 136.83, 138.09, 138.45, 138.55, 140.90, 143.94, 145.50; MS (*m/z*): calcd. 459.14, found 460.12 [M+1].

**2-Chloro-3-[5-(2-chlorophenyl)-4-(3,4-dimethoxyphenyl)-1*H*-imidazol-2-yl]benzo[*h*]quinoline (4g):** Pale yellow solid; yield: 86%; m.p.: 176-177 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3417 (N-H), 2055 (Ar-H), 2832 (-OCH<sub>3</sub>), 1610 (C=C), 1586 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 3.75 (s, 3H, -OCH<sub>3</sub>), 3.86 (s, 3H, -OCH<sub>3</sub>), 6.78 (d,  $J = 8.4$  Hz, 2H, Ar-H), 7.14 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.46 (m, 2H, Ar-H), 7.44 (d,  $J = 6.4$  Hz, 1H, Ar-H), 7.55 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.70 (m, 4H, Ar-H), 7.87 (d,  $J = 6.4$  Hz, 1H, Ar-H), 9.14 (d,  $J = 7.6$  Hz, 1H, Ar-H), 9.22 (s, 1H, Ar-H), 10.70 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 55.50, 55.82, 109.46, 110.47, 111.04, 111.32, 118.05, 119.81, 122.89, 124.27, 125.59, 126.81, 126.97, 127.51, 127.93, 128.94, 129.73, 130.08, 132.62, 133.51, 134.07, 138.45, 140.24, 141.29, 144.09, 145.61, 148.70; MS (*m/z*): calcd. 525.10, found 525.97 [M+1].

**2-Chloro-3-[4,5-di(furan-2-yl)-1*H*-imidazol-2-yl]benzo[*h*]quinoline (4h):** Brown solid; yield: 80%; m.p.: 153-155 °C; FT-IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3436 (N-H), 3055 (Ar-H), 1601 (C=C), 1586 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 6.54 (s, 2H, Ar-H), 6.91 (d,  $J = 2.4$  Hz, 1H, Ar-H), 7.10 (d,  $J = 2.4$  Hz, 1H, Ar-H), 7.51 (d,  $J = 13.2$  Hz, 2H, Ar-H), 7.72 (m, 3H, Ar-H), 7.80 (d,  $J = 8.8$  Hz, 1H, Ar-H), 7.86 (d,  $J = 8.0$  Hz, 1H, Ar-H), 9.12 (d,  $J = 12.0$  Hz, 1H, Ar-H), 9.15 (s, 1H, Ar-H), 10.73 (s, 1H, NH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm: 107.50, 108.39, 111.48, 112.16, 124.67, 124.76, 127.51, 127.91, 129.01, 129.11, 138.80, 141.67, 141.93; MS (*m/z*): calcd. 411.07, found 411.97 [M+1].

## Biological activity

**Antioxidant activity:** The antioxidant activity study of compounds **4a-h** was carried out by using the DPPH method. Synthesized compounds were first dissolved in DMSO and then diluted with methanol to obtain the concentrations 10, 50 and 100  $\mu\text{g/mL}$ . A 5 mL of 0.1 mM methanolic solution of DPPH was added to the above stock solutions and shaken vigorously. The solutions were allowed to remain in the absence of light at the ambient temperature for 20 min. Subsequently, the samples were assessed for absorbance at a wavelength of 517 nm, with butylated hydroxy anisole (BHA) serving as the reference standard. Free radical scavenging activities were calculated using the following formula:

$$\text{Antioxidant activity (\%)} = \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \times 100$$

**Cytotoxicity study:** Using the MTT cell viability assay method, the *in vitro* cytotoxicity activity of each synthesized compounds **4a-h** was assessed against the colo-205, HeLa, and A549 cell lines. Using the appropriate media that contained

10% FBS, the cell count was adjusted to  $1.0 \times 10^5$  cells/mL after the monolayer cell culture was trypsinized. The diluted cell solution (100  $\mu$ L) containing 50,000 cells/well was added to every well of the 96-well microtiter plate. Following 24 h, once a partial monolayer had developed, the supernatant was discarded. The monolayer was then rinsed with medium once again and 100  $\mu$ L of various compound concentrations were added to the partially formed monolayer in microtiter plates. A 5% CO<sub>2</sub> environment was used to incubate the plates at 37 °C for 24 h. The test solutions in the wells were removed after incubation and 100  $\mu$ L of MTT (5 mg/10 mL of MTT in PBS) was added to every well. A 5% CO<sub>2</sub> atmosphere was used to incubate the plates for 4 h at 37 °C. To dissolve the formazan that had formed, 100  $\mu$ L of DMSO was added after the supernatant had been removed and the plates were gently shaken. A microplate reader operating at 590 nm was used to determine the optical density (OD). The percentage growth inhibition was calculated using the following formula:

$$\text{Inhibition (\%)} = 100 - \left( \frac{\text{OD of sample}}{\text{OD of control}} \right) \times 100$$

## RESULTS AND DISCUSSION

A series of 2-chlorobenzo[*h*]quinoline containing imidazoles (**4a-h**) with different substituent's at 4- and 5-positions have been synthesized and characterized. Initially, 2-chlorobenzo[*h*]quinoline-3-carbaldehyde was synthesized from naphthalen-1-amine by acetylation reaction followed by the reaction with Vilsmeier reagent. The final hybrid derivatives were successfully achieved by the one-pot multi-component cyclocondensation of 2-chlorobenzo[*h*]quinoline-3-carbaldehyde (**3**), substituted benzil and ammonium acetate in ethanol solvent using catalytic amount of acetic acid. The chemical structures of the synthesized compounds were established by <sup>1</sup>H/<sup>13</sup>C-NMR, FT-IR and mass spectral studies. Compound **4a** showed the stretching frequencies of 3383 cm<sup>-1</sup> for N-H bond, 1601 cm<sup>-1</sup> for C=C bond and 1581 cm<sup>-1</sup> for C=N bond of imidazole ring. <sup>1</sup>H NMR spectrum of the same compound showed singlet at  $\delta$  3.76 ppm, which corresponds to -OCH<sub>3</sub> and singlet at  $\delta$  10.50 ppm for N-H proton. The aromatic protons of the compound **4a** were appeared in the range of  $\delta$  6.84 to 9.18 ppm. In the <sup>13</sup>C NMR spectrum, the number of carbon peaks are correlated with compound **4a**. Mass

spectrum of the compound **4a** showed a peak at 492.01 (*m/z*), which corresponds to [M+1] ion.

**Antioxidant activity:** All the synthesized compounds **4a-h** were screened for their antioxidant activity by DPPH method. Among the synthesized 2-chlorobenzo[*h*]quinoline containing 2,4,5-trisubstituted imidazole derivatives, compounds **4a** and **4d** containing electron releasing methoxy groups and compound **4e** exhibited the good antioxidant activity as compared to the others. The results of the antioxidant activity of synthesized compounds **4a-h** are presented in Table-1.

Compd. No.	Concentration ( $\mu$ g/mL)		
	10	50	100
<b>4a</b>	44.00	49.07	53.53
<b>4b</b>	41.78	47.96	50.80
<b>4c</b>	42.52	44.62	50.68
<b>4d</b>	42.27	45.98	52.04
<b>4e</b>	43.39	46.72	54.88
<b>4f</b>	39.68	48.95	50.80
<b>4g</b>	43.76	45.74	48.70
<b>4h</b>	41.04	48.70	51.92
<sup>a</sup> BHA	54.27	70.10	91.82

<sup>a</sup>BHA = butylated hydroxy anisole as a reference standard

**Cytotoxicity study:** The cytotoxicity study revealed that compound **4a** with electron donating -OCH<sub>3</sub> group exhibited significant inhibition of 57.86%, 58.18% and 53.77% against Colo-205, HeLa and A549 human cancer cell lines, respectively at 320  $\mu$ g/mL. Compound **4f** comprising electron donating -CH<sub>3</sub> group showed 53.77% inhibition on Colo-205 and 60.64% inhibition on HeLa cell lines at 320  $\mu$ g/mL. Compound **4c** with chloro group showed 52.97% inhibition against HeLa cell line. The Doxorubicin used as a reference standard. The results of cytotoxicity study on compounds **4a-h** against Colo-205, HeLa and A549 cell lines are presented in Fig. 1.

## Conclusion

In this study, a series of 2-chlorobenzo[*h*]quinoline containing imidazole derivatives from one-pot multi-component synthesis using 2-chlorobenzo[*h*]quinoline-3-carbaldehyde, ammonium acetate and 1,2-diketones in the presence of acetic

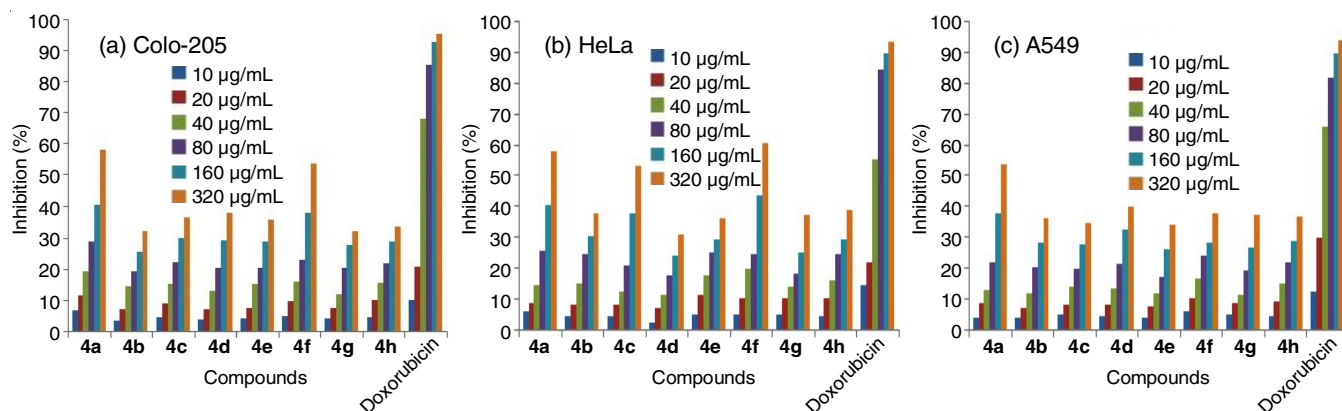


Fig. 1. Cytotoxic activity of compounds **4a-h** against (a) Colo-205 cell line, (b) HeLa cell line and (c) A549 cell line



acid as a catalyst in ethanol solvent. All synthesized imidazoles are characterized by  $^1\text{H}$  &  $^{13}\text{C}$  NMR, FT-IR and mass spectra. The synthesized compounds were evaluated *in vitro* cytotoxicity studies against colo-205, HeLa, A549 human cancer cell lines. Among the tested samples, compound **4a** has showed good cytotoxicity in all the three cell lines *i.e.*, Colo-205, HeLa and A549. Compound **4f** has shown the excellent cytotoxicity in Colo-205 and HeLa cell lines, whereas compound **4c** exhibited good cytotoxicity only in HeLa cell lines at 320  $\mu\text{g}/\text{mL}$ . The antioxidant activities are also performed by DPPH free radical scavenging assay method and only three compounds **4a**, **4d** and **4e** exhibits significant antioxidant activity compared with reference standard BHA.

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#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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