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Research Article

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Design, synthesis and anticancer activity of novel hybrid compounds of imidazopyridine and quinoline/carbazole

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ABSTRACT

*A series of novel hybrid compounds of imidazopyridine and quinoline/carbazole derivatives has been prepared and evaluated in vitro against a panel of four human tumor cell lines(viz., cervical HeLa, breast MDA-MB-231, renal ACHN and colon HCT-15). Among them imidazopyridine-quinoline hybrid compounds, 3-(3-benzylimidazo[1,2-a]pyridine-2-yl)-2-chloro-6-methoxyquinoline (**8**) and 2-chloro-6-methoxy-3-(3-(4-methylbenzylimidazo[1,2-a]pyridine-2-yl)-quinoline (**12**) showed potent anticancer activity with the IC_{50} values of(0.34; 0.32; 0.39; 0.31) and (0.35; 0.29; 0.34; 0.30) respectively, **12** being the best among all the compounds synthesized In case of imidazopyridine-carbazole hybrid compounds, 3-(3-benzylimidazo[1,2-a]pyridine-2-yl)-9-ethyl-9H-carbazole(**13**) showed best activity with the IC_{50} value of (0.37; 0.41; 0.39; 0.30) followed by compound 9-ethyl-3-(3-4-methylbenzyl)imidazo[1,2-a]pyridine-2-yl)9H-carbazole (**17**)with the IC_{50} value of (0.55; 0.49; 0.60; 0.56). This preliminary study discovered that the imidazopyrine scaffold hybridized with quinoline or carbazole could be a good pharmacophore for finding novel and potent anticancer agents.*

Keywords: Hybrid, imidazopyridine, quinoline, carbazole, anticancer activity.

INTRODUCTION

In the design of new drugs, the concept of molecular hybridization is an attractive strategy. It is based on the combination of two pharmacophoric moieties of different bioactive substances to produce a new hybrid compound that is more medically effective than its individual components.[1] A single molecule containing more than one pharmacophore, each with different mode of action could be beneficial for the treatment of various diseases, in particular, cancer. [2]

The hybrid design of various heterocycles is currently an attractive strategy to find novel and potent drugs for different targets. [3] Among nitrogen-fused azoles, imidazo[1,2-*a*]pyridines have a lead role in the literature because of their wide variety of applications in various disciplines of medicinal chemistry, and display activities like anti-microbial [4], anti-viral [5], anti-inflammatory [6] and anticancer [7]. Recently imidazopyridine (**1**) showed good anticancer activity against CDC25A, CDC25B Enzymes and HT-29 HepG2 cell lines. [8]

Other nitrogen heterocycles like quinoline and carbazole, besides showing wide range of activities like anti-inflammatory, antibacterial, antioxidant, antimalarial [9-13], exhibit potent anticancer activity. For example tipifarnib (**2**), a potent anticancer drug with quinolone pharmacophore target farnesyl transferase protein. [14]

Likewise ellipticine (**3**), a carbazole alkaloid show anticancer activity by inhibiting Topoisomerase II [15] (Figure 1).

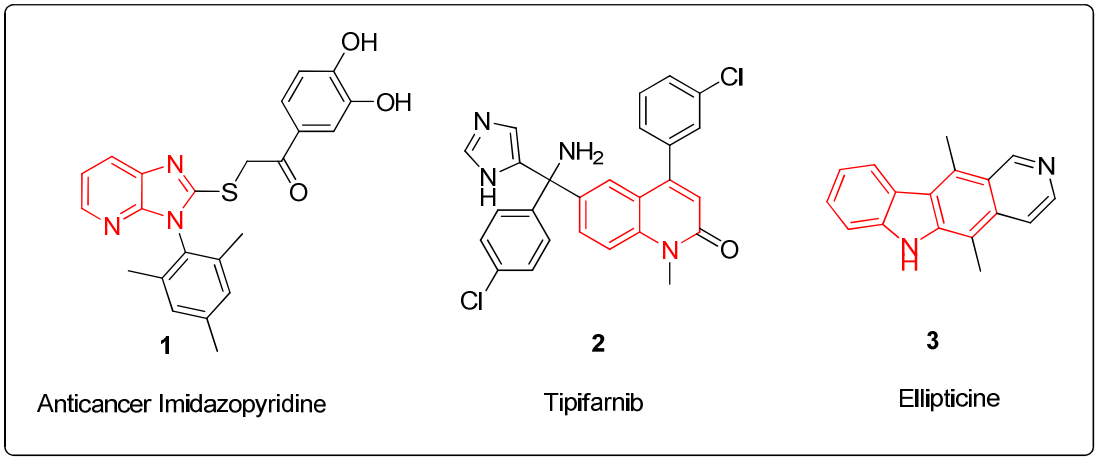


Fig. 1.Representative anticancer compounds of imidazopyridine, quinoline and carbazole

In the present study, we aim at designing and developing of new series of hybrid molecules through the combination of imidazopyridine scaffold on one partand carbazole/quinoline on another part (Figure. 2). Indeed this concept allows the fine tuning of electronic effects in the hybrid structure and provides synergistic effect to deduce structure–activity relationship.

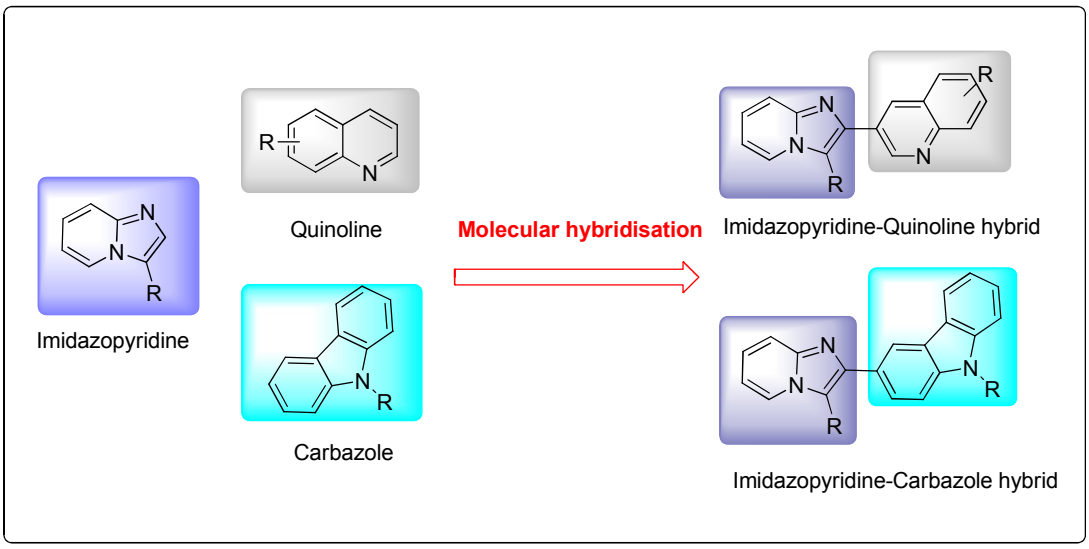


Fig. 2. Design of novel hybrid compounds of Imidazopyridine with Quinoline/Carbazole

EXPERIMENTAL SECTION

2.1. Chemistry

Melting points (m.p.) were determined on Mettler FP 51apparatus (Mettler Instruments, Switzerland) and are uncorrected. They are expressed in degree centigrade (C). The IR spectra (in KBr pellets) were recorded on a Shimadzu FT-IR 157 spectrophotometer.^{1}H NMR spectra were recorded using $CDCl_3$ as solvent and TMS as an internal standard on a Bruker400 MHz NMR spectrometer. Chemical shift values are given in δ(ppm scale). Micro analyses were performed on a Vario EL III model CHNS analyzer (Vario, Germany) at the Department of Chemistry, Bharathiar University. The purity of the products was tested by TLC with plates coated with silica gel-G

with petroleum ether, ethyl acetate and methanol as developing solvents. The purity of the compounds was checked by thin-layer chromatography(TLC) on silica gel plate using petroleum ether and ethyl acetate.

Preparation 2-chloro-6-methoxyquinoline-3-carbaldehyde (**6**)
A solution of *para*-anisidine (**18**, 5 mmol) in acetic anhydride (10 mmol) was refluxed for 2 h. The resulting solution was washed with excess water and extracted using ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to give 4-methoxyphenyl acetamide (**19**) as a yellow solid. In the next step, $POCl_3$ (60 mmol) was added drop wise to dry DMF (15 mmol) at 0-5 °C with stirring. To this mixture, compound **19** was added and stirred at 90 °C for 16 h. The mixture was poured into crushed ice, stirred for 5 min and the resulting solid was filtered, washed well with water and dried. The obtained **6** was purified by recrystallization from ethyl acetate.

2-chloro-6-methoxyquinoline-3-carbaldehyde (**6**)
white solid; m.p. 146-148 °C; Yield : 72 %; IR (KBr) ν_{max} (cm^{-1}):3026, 1684, 1626;^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.96 (s, 3H), 7.21 (d, J=7.80 Hz, 1H), 7.54 (dd, J = 8.60 Hz, 2.80 Hz, 1H), 7.96 (d, J = 8.20 Hz, 1H), 8.65 (s, 1H), 10.56(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.75, 106.47, 126.48, 126.65, 129.98, 132.55, 138.74, 145.92, 147.76, 158.90, 189.59; *Anal*. Calcd. for $C_{11}H_8ClNO_2$(221): C, 59.61; H, 3.64; N, 6.32; Found: C, 59.62; H, 3.63 ; N, 6.35 %.

General procedure for the preparation of hybrid of imidazo[1,2-a]pyridine and quinoline 8-12
Amixture of 2-aminopyridine (**4**, 1.00 mmol) and the 2-chloro-6-methoxyquinoline-3-carbaldehyde (**6**, 1.00 mmol) in absolute ethanol (5 mL) was stirred for 15 min. To this reaction mixture, was added phenylacetylene (**5**, 1.50 mmol) followed by the addition of $CuSO_4 \cdot 5H_2O$ (15 mol%) and D-glucose (30 mol%). Again ethanol (5 mL) was added to the reaction mixture and refluxed at 100 °C for 10 h. After the completion of reaction as indicated by TLC, the resultant mixture was directly adsorbed on neutral alumina(without work up) and the product was purified by column chromatography.

3-(3-Benzylimidazo[1,2-*a*]pyridine-2-yl)-2-chloro-6-methoxyquinoline (**8**)
Pale yellow solid; m.p. 191-193 °C; Yield : 74 %; IR (KBr) ν_{max} (cm^{-1}):3022, 2969, 1610, 1498, 1385, 1040, 818; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.93 (s, 3H), 4.35 (s, 2H), 6.77 (t, J = 7.80 Hz, 1H), 7.06-7.10 (m, 3H), 7.18-7.25 (m, 4H), 7.41 (dd, J = 8.60 Hz, 2.80 Hz, 1H), 7.70-7.75 (m, 2H), 7.97 (d, J = 8.40 Hz, 1H), 8.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 30.01, 55.61, 105.14, 112.59, 117.89, 123.53, 123.58, 123.92, 124.66, 126.93, 127.94, 127.99, 128.82, 128.93, 129.82, 136.20, 139.69, 140.57, 143.50, 144.92, 147.65, 158.40; *Anal*. Calcd. for $C_{24}H_{18}ClN_3O$(399): C,72.09; H, 4.54; N,8.87; Found: C, 72.05; H, 4.57 ; N, 8.78 %.

3-(3-Benzyl-6-methylimidazo[1,2-*a*]pyridine-2-yl)-2-chloro-6-methoxyquinoline (**9**)
Pale yellow solid; m.p. 200-202 °C; Yield : 76 %; IR (KBr) ν_{max} (cm^{-1}):3028, 2965, 1613, 1499, 1365, 1208, 1048, 812; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.27 (s, 3H), 3.94 (s, 3H), 4.35 (s, 2H), 7.06-7.10 (m, 3H), 7.15-7.23 (m, 4H), 7.41 (dd, J = 8.60 Hz, 2.80 Hz, 1H), 7.68-7.73 (m, 2H), 7.96 (d, J = 8.40 Hz, 1H), 8.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 18.35, 30.02, 55.62, 105.15, 112.58, 120.54, 123.60, 123.93, 124.69, 126.93, 127.94, 128.02, 128.15, 128.94, 129.80, 134.62, 136.21, 139.70, 140.55, 143.55, 144.91, 147.68, 158.42; *Anal*. Calcd. for $C_{25}H_{20}ClN_3O$(413): C,72.55; H, 4.87; N,8.57; Found: C, 72.52; H, 4.85 ; N, 8.58 %.

3-(3-Benzyl-7-methylimidazo[1,2-*a*]pyridine-2-yl)-2-chloro-6-methoxyquinoline (**10**)
Pale yellow solid; m.p. 196-198 °C; Yield : 73 %; IR (KBr) ν_{max} (cm^{-1}):3021, 2967, 1609, 1496, 1384, 1205, 1041, 815; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.40 (s, 3H), 3.95 (s, 3H), 4.36 (s, 2H),6.74 (d, J = 8.00 Hz, 1H), 7.08-7.11 (m, 3H), 7.19-7.26 (m, 4H), 7.43 (dd, J = 8.60 Hz, 2.60 Hz, 1H), 7.65-7.79 (m, 2H), 7.98 (d, J = 8.40 Hz, 1H), 8.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 21.32, 30.04, 55.62, 105.11, 112.58, 117.88, 120.51, 123.58, 123.93, 124.68, 126.94, 127.97, 128.11, 128.93, 129.81, 136.21, 137.59, 139.68, 140.59, 143.54, 144.98, 147.89, 158.40; *Anal*. Calcd. for $C_{25}H_{20}ClN_3O$(413): C,72.55; H, 4.87; N,8.57; Found: C, 72.53; H, 4.86 ; N, 8.56 %.

3-(3-Benzyl-6-chloroimidazo[1,2-*a*]pyridine-2-yl)-2-chloro-6-methoxyquinoline (**11**)
Yellow solid; m.p. 220-222 °C; Yield : 70 %; IR (KBr) ν_{max} (cm^{-1}):3025, 2968, 1612, 1501, 1366, 1206, 1046, 815; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.93 (s, 3H), 4.36 (s, 2H), 7.04-7.13 (m, 3H), 7.14-7.24 (m, 4H), 7.42 (dd, J = 8.60 Hz, 2.80 Hz, 1H), 7.71-7.86 (m, 2H), 7.96 (d, J = 8.40 Hz, 1H), 8.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 30.03, 55.63, 105.13, 112.59, 120.54, 122.44, 123.92, 124.05, 126.94, 127.95, 128.01, 128.17, 128.95,

129.82, 131.20, 136.22, 139.72, 140.58, 143.55, 144.91, 147.69, 158.43; *Anal*. Calcd. for $C_{24}H_{17}Cl_2N_3O$(433): C,66.37; H, 3.95; N,9.67; Found: C, 66.33; H, 3.96 ; N, 9.65 %.

2-Chloro-6-methoxy-3-(3-(4-methylbenzylimidazo[1,2-*a*]pyridine-2-yl)-quinoline (**12**)
Pale yellow solid; m.p. 205-207 °C; Yield : 78 %; IR (KBr) ν_{max} (cm^{-1}):3030, 2970, 1616, 1493, 1390, 1045, 812; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.34 (s, 3H), 3.95 (s, 3H), 4.36 (s, 2H), 6.77 (t, J = 7.80 Hz, 1H), 7.05-7.12 (m, 3H), 7.15-7.23 (m, 3H), 7.42 (dd, J = 8.60 Hz, 2.80 Hz, 1H), 7.70-7.76 (m, 2H), 7.97 (d, J = 8.40 Hz, 1H), 8.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 18.35, 30.02, 55.62, 105.15, 112.58, 120.54, 123.60, 123.93, 124.69, 126.93, 127.94, 128.02, 128.15, 128.94, 129.80, 134.62, 136.21, 139.70, 140.55, 143.55, 144.91, 147.68, 158.42; *Anal*. Calcd. for $C_{25}H_{20}ClN_3O$(413): C, 72.55; H, 4.87; N, 10.15; Found: C, 72.53; H, 4.86 ; N, 10.15 %.

General procedure for the preparation of hybrid of imidazo[1,2-a]pyridine and carbazole 13-17
Amixture of 2-aminopyridine (**4**, 1.00 mmol) and the 9-ethyl-9*H*-carbazole-3-carbaldehyde (**7**, 1.00 mmol) in absolute ethanol (5 mL) was stirred for 15 min. To this reaction mixture, was added phenylacetylene (**5**, 1.50 mmol) followed by the addition of $CuSO_4 \cdot 5H_2O$ (15 mol%) and D-glucose (30 mol%). Again ethanol (5 mL) was added to the reaction mixture and refluxed at 100 °C for 10 h. After the completion of reaction as indicated by TLC, the resultant mixture was directly adsorbed on neutral alumina(without work up) and the product was purified by column chromatography.

3-(3-Benzylimidazo[1,2-*a*]pyridine-2-yl)-9-ethyl-9*H*-carbazole(**13**)
White solid; m.p. 244-246 °C; Yield : 72 %; IR (KBr) ν_{max} (cm^{-1}):3011, 2986, 1620, 1494, 1391, 1044, 945; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.45 (t, J = 8.60 Hz, 3H), 4.38 (q, J = 7.20 Hz, 2H), 4.59 (s, 2H), 6.76 (t, J = 8.60 Hz, 1H), 7.19-7.24 (m, 4H), 7.43-7.51 (m, 5H), 7.76-7.79 (m, 2H), 7.88 (d, J = 7.80 Hz, 1H), 7.99-8.01 (m, 2H), 8.05 (d, J = 8.20 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 13.79, 29.76, 37.74, 105.76, 108.67, 109.17, 111.95, 117.56, 119.36, 120.05, 120.69, 120.85, 123.55, 123.75, 126.11, 126.13, 127.43, 127.55, 127.65, 129.37, 129.38, 131.31, 133.04, 134.00, 140.45, 141.03; *Anal*. Calcd. for $C_{28}H_{23}N_3$(401): C, 83.76; H, 5.77; N, 10.47; Found: C, 83.74; H, 5.77 ; N, 10.49 %.

3-(3-Benzyl-6-methylimidazo[1,2-*a*]pyridine-2-yl)-9-ethyl-9*H*-carbazole (**14**)
White solid; m.p. 255-257 °C; Yield : 75 %; IR (KBr) ν_{max} (cm^{-1}):3013, 2983, 1618, 1498, 1390, 1042, 946; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.45 (t, J = 8.60 Hz, 3H), 2.29 (s, 3H), 4.38 (q, J = 7.20 Hz, 2H), 4.59 (s, 2H), 7.19-7.24 (m, 4H), 7.43-7.51 (m, 5H), 7.76-7.84 (m, 3H), 7.99-8.01 (m, 2H), 8.05 (d, J = 8.20 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 13.80, 18.81, 29.77, 37.75, 105.77, 108.66, 109.17, 111.92, 119.36, 120.02, 120.69, 120.84, 123.56, 123.73, 126.11, 127.46, 127.55, 127.65, 128.77, 129.38, 129.38, 131.32, 132.88, 133.05, 134.01, 140.46, 141.04;*Anal*. Calcd. for $C_{29}H_{25}N_3$(415): C, 83.82; H, 6.06; N, 10.11; Found: C, 83.83; H, 6.05 ; N, 10.12 %.
3-(3-Benzyl-7-methylimidazo[1,2-*a*]pyridine-2-yl)-9-ethyl-9*H*-carbazole (**15**)

White solid; m.p. 259-261 °C; Yield : 73 %; IR (KBr) ν_{max} (cm^{-1}):3010, 2980, 1619, 1499, 1387, 1044, 948; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.44 (t, J = 8.60 Hz, 3H), 2.43 (s, 3H), 4.38 (q, J = 7.20 Hz, 2H), 4.60 (s, 2H), 6.73 (d, J = 8.40 Hz, 1H), 7.17-7.25 (m, 4H), 7.41-7.51 (m, 4H), 7.76-7.79 (m, 2H), 7.82 (d, J = 7.80 Hz, 1H), 7.98-8.01 (m, 2H), 8.07 (d, J = 8.20 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 21.60, 13.82, 29.77, 37.76, 105.76, 108.67, 109.18, 111.94, 118.09, 119.32, 120.11, 120.76, 120.85, 123.54, 123.74, 126.12, 127.44, 127.54, 127.67, 129.37, 129.39, 131.32, 133.06, 134.02, 136.71, 140.44, 141.03;*Anal*. Calcd. for $C_{29}H_{25}N_3$(415): C, 83.82; H, 6.06; N, 10.11; Found: C, 83.81; H, 6.05 ; N, 10.14 %.

3-(3-Benzyl-6-chloroimidazo[1,2-*a*]pyridine-2-yl)-9-ethyl-9*H*-carbazole (**16**)
White solid; m.p. 270-272 °C; Yield : 70 %; IR (KBr) ν_{max} (cm^{-1}):3012, 2981, 1620, 1497, 1389, 1044, 948; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.45 (t, J = 8.60 Hz, 3H), 4.38 (q, J = 7.20 Hz, 2H), 4.59 (s, 2H), 7.21-7.26 (m, 4H), 7.42-7.52 (m, 5H), 7.76-7.79 (m, 2H), 7.95-8.01 (m, 3H), 8.05 (d, J = 8.20 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 13.80, 29.77, 37.75, 105.78, 108.65, 109.17, 111.93, 120.16, 120.01, 120.68, 120.84, 123.55, 123.74, 126.12, 127.46, 127.55, 127.65, 128.78, 129.37, 129.38, 131.33, 132.89, 133.04, 134.02, 140.46, 141.04;*Anal*. Calcd. for $C_{28}H_{22}ClN_3$(435): C, 77.14; H, 5.09; N, 9.64; Found: C, 77.12; H, 5.06 ; N, 9.69 %.

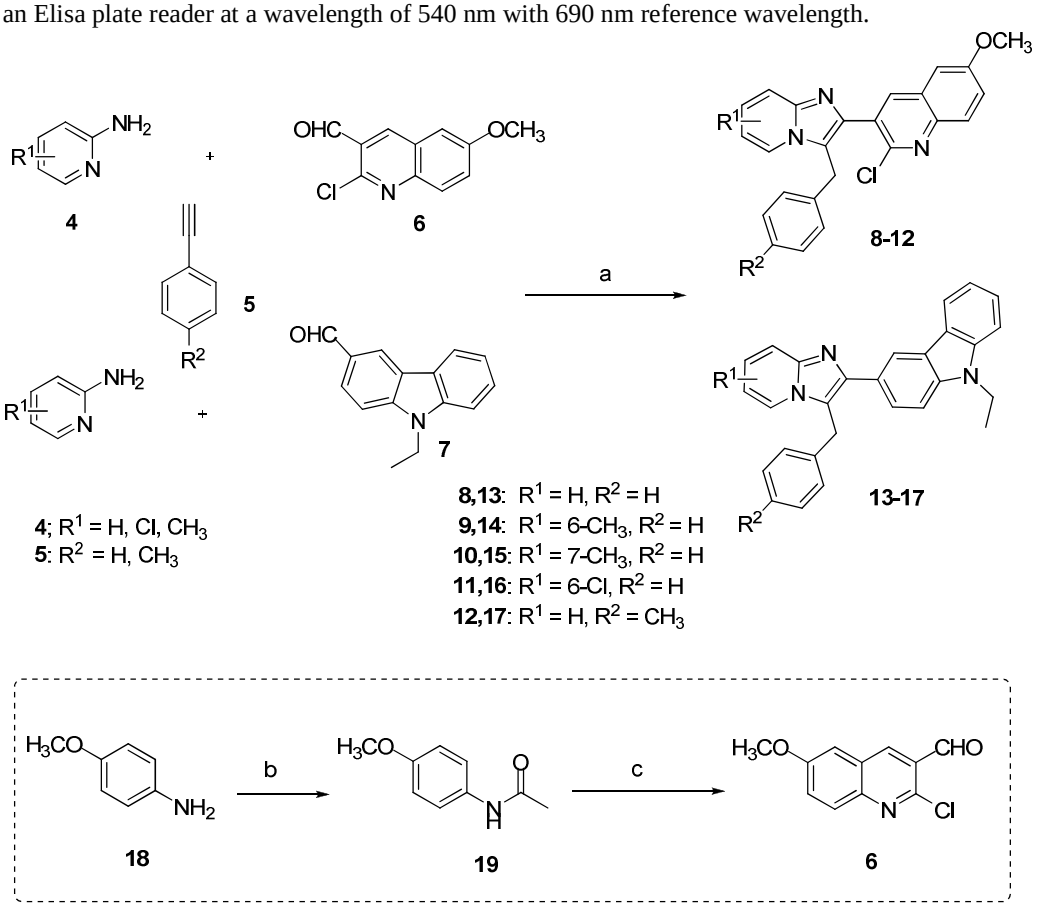
9-Ethyl-3-(3-4-methylbenzyl)imidazo[1,2-*a*]pyridine-2-yl)9*H*-carbazole (**17**)
White solid; m.p. 257-259 °C; Yield : 75 %; IR (KBr) ν_{max} (cm^{-1}):3011, 2982, 1617, 1495, 1389, 1044, 949; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.45 (t, J = 8.60 Hz, 3H), 2.33 (s, 3H), 4.38 (q, J = 7.20 Hz, 2H), 4.59 (s, 2H),

6.75 (t, J = 8.60 Hz, 1H), 7.11-7.24 (m, 4H), 7.44-7.52 (m, 4H), 7.76-7.79 (m, 2H), 7.88 (d, J = 7.80 Hz, 1H), 7.98-8.01 (m, 2H), 8.04 (d, J = 8.20 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 13.79, 20.03, 29.77, 37.75, 105.77, 108.67, 109.18, 111.97, 117.56, 119.37, 120.07, 120.68, 120.85, 123.56, 126.13, 126.13, 127.42, 127.58, 127.69, 129.38, 129.38, 131.30, 132.53, 133.05, 134.03, 140.48, 141.04; *Anal*. Calcd. for $C_{29}H_{25}N_3$(415): C, 83.83; H, 6.06; N, 10.11; Found: C, 83.82; H, 6.08 ; N, 10.10 %.

2.2. Anti-cancer activity

The anticancer screening was performed by SRB assay [18, 19]. The cell lines were grown in RPMI 1640 medium containing 10% fetal bovine serum and 2 µM L-glutamine. For present screening experiment, cells were inoculated into 96 well microtiter plates in 90 µL at 5000 cells per well. After cell inoculation, the micro titer plates were incubated at 37°C, 5%CO_2, 95% air and 100 % relative humidity for 24 h prior to addition of experimental drugs. Experimental drugs were solubilized in appropriate solvent to prepare stock of 10^{-2} concentration. At the time of experiment four 10-fold serial dilutions were made using complete medium. Aliquots of 10 µl of these different drug dilutions were added to the appropriate micro-titer wells already containing 90 µl of medium, resulting in the required final drug concentrations.

After compound addition, plates were incubated at standard conditions for 48 hours and assay was terminated by the addition of cold TCA. Cells were fixed *in situ* by the gentle addition of 50 µl of cold 30 % (w/v) TCA (final concentration, 10 % TCA) and incubated for 60 minutes at 4°C. The supernatant was discarded; the plates were washed five times with tap water and air dried. Sulforhodamine B (SRB) solution (50 µl) at 0.4 % (w/v) in 1 % acetic acid was added to each of the wells, and plates were incubated for 20 minutes at room temperature. After staining, unbound dye was recovered and the residual dye was removed by washing five times with 1 % acetic acid. The plates were air dried. Bound stain was subsequently eluted with 10 mM trizma base, and the absorbance was read on an Elisa plate reader at a wavelength of 540 nm with 690 nm reference wavelength.



Scheme 1. Preparation of hybrids of imidazo[1,2-*a*]pyridine and quinoline8-12and carbazole13-17

Reagents and conditions: a) (i) Ethanol, stirring 10 mins, (ii) $CuSO_4.5H_2O$, D-glucose, reflux, 10 h, b) acetic anhydride, reflux, 2 h, c) DMF, $POCl_3$, 90 °C, 16 h.

RESULTS AND DISCUSSION

3.1 Chemistry

In order to prepare the hybrid molecules of imidazopyridine with quinoline**8-12** and carbazole**13-17,** a multicomponent reaction (A^3-coupling and 5-exo-dig cycloisomerization) was utilized[16] in which 2-chloro-6-methoxyquinoline-3-carbaldehyde (**6**) was reacted with 2-aminopyridine (**4**) and phenylacetylene (**5**) in presence of $CuSO_4$ and D-Glucose in ethanol to afford the desired product **8-12**. 2-Chloro-6-methoxyquinoline-3-carbaldehyde (**6**) was prepared according to literature [17] in which *para*-anisidine (**18**) was acylated with acetic anhydride to **19** which was subjected to Vilsmeier-Haack reaction in presence of DMF and $POCl_3$ to afford **6**. Following that, a similar strategy was made to derive the hybrids of imidazopyridine and carbazole**13-17** by the reaction of **4, 5** and commercially available 9-ethyl-9*H*-carbazole-3-carbaldehyde (**7**) (Scheme 1).

3.2 Anti-cancer activity

All the synthesized compounds **8-17** were evaluated for their *in vitro* inhibitory activities against four human cancer cell lines (cervical HeLa, breast MDA-MB-231, renal ACHN and colon HCT-15) using SRB assay. The results as IC_{50} are mentioned in the Table 2.

Table 2.*In Vitro* anticancer activity of the synthesized compounds against three cell lines

Compound No	HeLa IC_{50} (µM)	MDA- MB-231 IC_{50} (µM)	ACHN IC_{50} (µM)	HCT-15 IC_{50} (µM)
8	0.34	0.32	0.39	0.31
9	0.59	0.56	0.61	0.63
10	0.96	0.92	1.42	1.35
11	7.34	>10	9.38	>10
12	0.35	0.29	0.34	0.30
13	0.37	0.41	0.39	0.30
14	0.57	0.58	0.60	0.78
15	0.96	1.44	1.01	>10
16	>10	8.23	>10	>10
17	0.55	0.49	0.60	0.56
Adriamycin	0.52	0.51	0.58	0.55

The initially prepared hybrid of imidazopyridine and quinoline (i.e, unsubstituted compound **8**) showed excellent anticancer activity with the IC_{50} values of (HeLa, 0.34;MDA- MB-231, 0.32; ACHN, 0.39; HCT-15,0.31) which was more than that of the standard used (Adriamycin, HeLa, 0.52;MDA-MB-231, 0.51; ACHN, 0.58; HCT-15, 0.55).The 6-methyl derivative **9** also exhibited good cytotoxicity (0.59; 0.56; 0.61; 0.63) against the four cell lines.The 7-methyl derivative **10** and 6-chloro derivative **11**, however did not show good activity. Finally the 4-methylbenzyl analog of the imidazopyridine ring **12** showed potent activity (0.35; 0.29; 0.34; 0.30).

In the next set of experiment the hybrid series of imidazopyridine and carbazole were analysed for their cytotoxicity. In this series, the unsubstituted imidazopyridine derivative **13** showed excellent activity (0.37; 0.41; 0.39; 0.30). Similarly the 6-methyl analog **14** exhibited good anticancer activity (0.57; 0.58; 0.60; 0.78). The 7-methyl derivative **15** and the 6-chloro derivative **16** did not show good activity. The 4-methylbenzyl analog **17** exhibited a moderate activity (0.55; 0.49; 0.60; 0.56).The unsubstituted imidazopyridine ring with quinoline**8**, **12** or carbazole**13,17** showed good to excellent activity.

CONCLUSION

A novel series of hybrid molecules of imidazopyridine with quinoline and carbazole were designed and synthesized in search for potent anticancer agents. Among the compounds synthesized, the imidazopyridine-quinoline hybrid molecules showed good to excellent activity againstfour human cancer cell lines (cervical HeLa, breast MDA-MB-231, renal ACHN and colon HCT-15). Particularly compound **8** and **12** showed potent anticancer activity with the IC_{50} values of(0.34; 0.32; 0.39; 0.31) and (0.35; 0.29; 0.34; 0.30) respectively, **12** being the best among all the compounds synthesized. In case of imidazopyridine-carbazole hybrid molecules, compound **13** showed best activity with the IC_{50} value of (0.37; 0.41; 0.39; 0.30) followed by compound **17**with the IC_{50} value of (0.55; 0.49; 0.60; 0.56). Thus imidazopyridine scaffold hybridized with quinoline or carbazole is a good pharmacophore for discovering novel anticancer drugs.

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