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Design, Synthesis and Anticancer Activity of Novel Substituted (*E*)-2-Morpholinoquinoline-3-carbaldehyde-*O*-((-1-aryl-1*H*-1,2,3-triazol-4-yl)methyl)oxime Derivatives

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A new series of substituted (*E*)-2-morpholinoquinoline-3-carbaldehyde-*O*-((-1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)oxime scaffolds were synthesized from involving alkynyl quinoline oximes with various aryl azides by click reaction obtained corresponding compounds with high yields. The synthesized compounds were characterized by using IR, ^{1}H NMR, ^{13}C NMR and HRMS data. All the synthesized compounds screened anticancer activity against MCF-7, HeLa, PC-3 cell lines. All the compounds exhibited good results among them **8b**, **8g** and **8i** compounds have shown prominent anticancer activity are compared to standard drug doxorubicin.

Keywords: Quinolines, 1,2,3-Triazoles, Click reaction, Anticancer activity.

INTRODUCTION

In 2030, cancer is projected to be the leading cause of death globally, with an estimated death toll of about 17 million people. When discovered early and treated in accordance with best standards, some of the most prevalent cancer types, including breast cancer, cervical cancer, oral cancer and colorectal cancer, have high cure prospects. When the unfavourable side effects of chemotherapeutics limit their use, chemotherapy remains the most efficacious approach for cancer treatment, therefore, it is crucial for cancer research to look for safe and effective anticancer chemicals [1,2].

In medicinal chemistry, quinoline is a fascinating heterocyclic scaffold. Quinoline and its related compounds have a wide range of pharmacological effects, including antibacterial, antifungal, antitubercular, antimalarial, anticancer and choline esterase inhibitor properties [3-11]. Triazoles are desirable scaffolds among N-containing heterocycles because of their pharmacological importance. In the line of lactum antibiotics, synthetic triazoles tazobactum (**1**) and cefatrizine (**2**) exist and CAI is available on the market, as shown in Fig. 1. 1,2,3-Triazoles have been found to exhibit antibacterial [12,13], antifungal [14], anticancer [15-17] and antitubercular [18] effects. Herein, the design and synthesis of new quinoline containing 1,4-disubstituted 1,2,3-triazole hybrids *via* click reaction based on their synthetic and biological activity.

EXPERIMENTAL

Unless otherwise specified, all solvents and reagents were purchased from well-known commercial sources. The Buchi melting point instrument was used to determine the melting points in open capillaries and are uncorrected. A F_{254} silica-gel precoated aluminum sheets were subjected to thin layer chromatography with hexane/ethyl acetate (7/3) as eluent to evaluate the reactions' progress and the compounds' purity. An automated elemental analyzer, Carlo-Erba EA 1108, was used for the element analysis. The absorption spectral studies were measured by UV-visible spectrometer. IR spectra were recorded on Perkin-Elmer 100S spectrometer using KBr pellet. NMR spectra were recorded on Bruker 400 MHz spectrometer using DMSO-d_6 as solvent and TMS as an internal standard. Mass spectra (ESI) were recorded on a JEOL JMSD-300 spectrometer.

Synthesis of 2-chloroquinoline-3-carbaldehyde (2): To a cool solution of DMF (3.0 equiv.), phosphoryl chloride (4.5

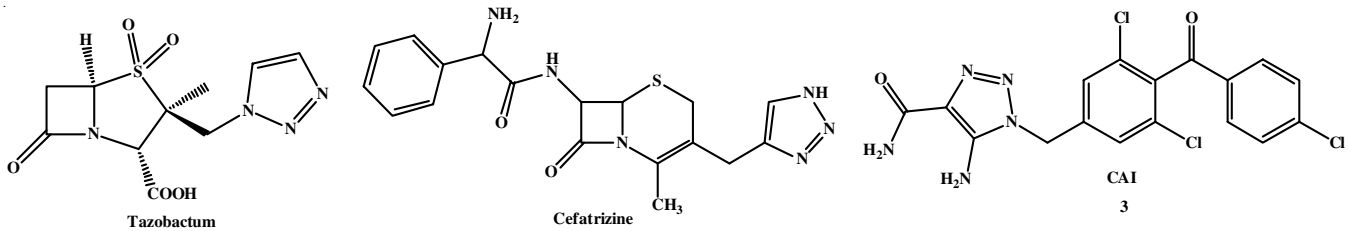


Fig. 1. Some biologically potent substituted triazole containing drug molecules in the market

equiv.) was added dropwise with stirring. In order to obtain 2-chloroquinoline-3-carbaldehyde (**2**), added acetanilide (1.0 equiv) to the above mixture and stirred at 80-90 ºC for 12 h. Following the completion of the reaction as shown by TLC, the mixture was poured into crushed ice, agitated for 5 min and the resultant solid was filtered, thoroughly washed with water, dried over anhydrous Na_2SO_4 and finally recrystallized with ethanol.

Synthesis of 2-morpholinoquinoline-3-carbaldehyde derivatives (3): A mixture of 2-chloroquinoline-3-carbaldehyde (1.0 equiv.), morpholine (1.1 equiv.) and anhydrous K_2CO_3 (2.0 equiv.) in DMF (10 mL) were charged in a 100 mL round bottom flask equipped with a mechanical stirrer and a condenser. The mixture underwent heating at 90 ºC for 2 h. Once the reaction completed, as confirmed by TLC, the mixture was transferred into 100 mL of ice-water. It was then filtered, washed thoroughly with water, dried and finally recrystallized from ethanol to yield a yellow solid.

Synthesis of (*E*)-2-chloroquinoline-3-carbaldehyde oxime (4): An ethanolic solution containing 2-chloroquinoline-3-carbaldehyde (1 mmol), hydroxyl amine hydrochloride (1.5 mmol) and sodium acetate (1.5 mmol) was introduced into a round bottom flask and then the mixture was agitated at ambient temperature for 2 h. Following the reaction's completion, as confirmed by TLC, 20 mL of ice-cold water was introduced to the reaction mixture. The product was then extracted using 25 mL of chloroform, repeated twice. The chloroform was separated through distillation using a rota-evaporator under reduced pressure, resulting in the formation of pure products.

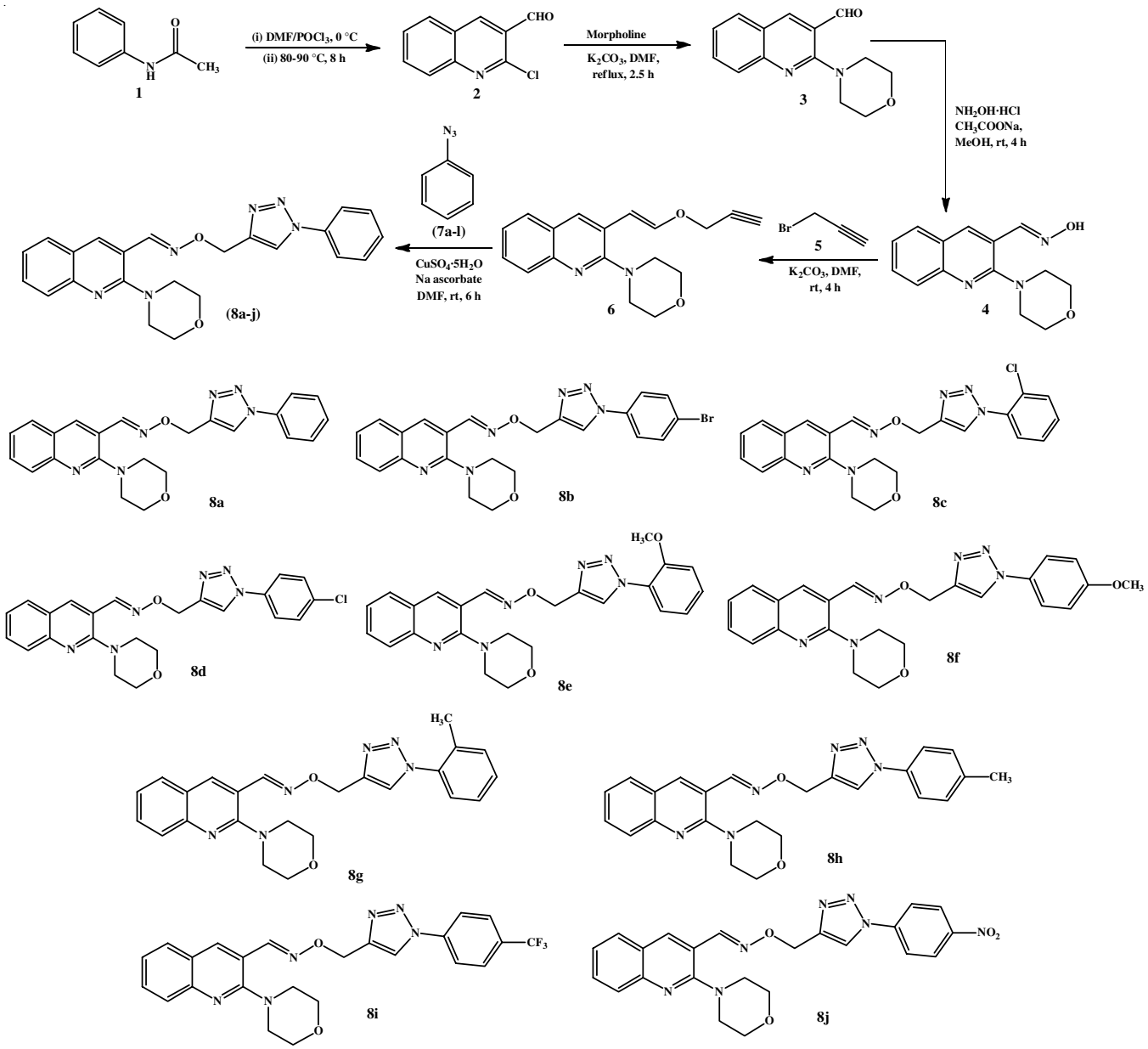
Synthesis of (*E*)-4-(3-(2-(prop-2-yn-1-yloxy)vinyl)quinolin-2-yl)morpholine (6): (*E*)-4-(3-(2-(prop-2-yn-1-yloxy)vinyl)-quinolin-2-yl)morpholine was prepared by the propargylation of (*E*)-2-chloroquinoline-3-carbaldehyde oxime (**4**) (1.0 equiv.) using propargyl bromide (1.5 equiv.) in dry DMF solvent (15 mL) was added K_2CO_3 (2.0 equiv.) at room temperature, under nitrogen atmosphere stirred for 3 h. After the complete consumption of staring material (monitored by TLC) was observed, then the reaction mixture was quenched with ice cold water and extracted with ethyl acetate. The combined organic layers was washed with water, brine and dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by silica gel column using 25% EtOAc in hexane as eluent to afford pure compound **6** in excellent yield.

Synthesis of substituted azido benzene molecules (7a-j): Substituted azido benzene derivatives **7a-j** were synthesized by adding a 5 N HCl to respective amine in CH_2Cl_2 at 0 ºC. This was followed by the gradual addition of a NaNO2 solution to the aforesaid mixture, which was then agitated at 0 ºC for 30 min. Azide (NaN_3) was introduced to the mixture at 0 ºC followed by stirring for 2 h at room temperature. Subsequently, the mixture was left undisturbed to allow for the separation of the organic and aqueous layers. The organic layer was washed with $NaHCO_3$, then with brine and solvent was then evaporated under vacuum to get the desired aryl azides **7a-j**. The azides **7a-j** were utilized in the subsequent step without undergoing any further purification.

Synthesis of (*E*)-2-morpholinoquinoline-3-carbaldehyde *O*-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8a-j): To a mixture of (*E*)-4-(3-(2-(prop-2-yn-1-yloxy)vinyl)quinolin-2-yl)morpholine (1.0 equiv.), substituted azidobenzenes **7a-j** (1.2 equiv.) in dry DMF (30 mL) was added a solution of $CuSO_4 \cdot 5H_2O$ (0.01 equiv.) and sodium ascorbate (0.01 equiv.) and the mixture was stirred for overnight at room temperature. After completion of the reaction as indicated by TLC, the reaction contents were extracted from ice-cold water and ethyl acetate (3 × 50 mL). The organic layer was washed and dried using brine and dry Na_2SO_4, respectively. The solvent was removed *in vacuo* and the obtained crude product was purified by passing through silica gel column (eluent: 30% EtOAc in hexane) to get the desired pure substituted (*E*)-2-morpholinoquinoline-3-carbaldehyde *O*-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)-oxime (**8a-j**) in 85-90% yields (**Scheme-I**).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8a): White solid, yield: 86%, m.p.: 198-200 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm: 8.42 (s, 1H), 8.31 (s, 1H), 8.08 (s, 1H), 7.78-7.73 (m, 4H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.44 –7.37 (m, 1H), 5.47 (s, 2H), 3.90-3.86 (m, 4H), 3.39 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 159.1, 147.7, 147.5, 144.9, 136.7, 130.5, 129.0, 128.1, 127.8, 125.0, 121.5, 120.7, 118.9, 77.4, 77.2, 76.8, 67.8, 67.0, 51.2. HRMS: *m/z*: 415 $(M+H)^+$. Anal. calcd. (found) % of $C_{23}H_{22}N_6O_2$: C, 66.65 (66.54); H, 5.35 (5.31); N, 20.28 (20.31); O, 7.68 (7.64).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(4-bromophenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8b): Pale yellow solid, yield: 84%, m.p.: 185-187 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.42 (s, 1H), 8.31 (s, 1H), 8.07 (s, 1H), 7.77-7.66 (m, 7H), 7.41 (s, 1H), 5.46 (s, 2H), 3.88 (s, 4H), 3.38 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 172.8, 168.5, 165.2, 156.7, 154.3, 145.3, 136.8, 133.5, 132.8, 131.5, 128.1, 126.2, 125.8, 123.4, 114.8, 71.8, 71.4, 58.8; ESI-MS: *m/z*: 493 $(M+H)^+$. Anal. calcd. (found) % of $C_{23}H_{21}N_6O_2Br$: C, 55.99 (55.94); H, 4.29 (4.34); Br, 16.20 (16.17); N, 17.03 (17.07); O, 6.49 (6.52).



Scheme-I: Synthesis of a substituted (*E*)-2-morpholinoquinoline-3-carbaldehyde *O*-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl) oxime derivatives

(*E*)-2-morpholinoquinoline-3-carbaldehyde *O*-((1-(2-chloro phenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8c): White solid, yield: 84%, m.p.: 198-200 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.40 (s, 1H), 8.32 (s, 1H), 7.89 (s, 1H), 7.73 (s, 1H), 7.67 (d, *J* = 8 Hz, 1H), 7.65-7.58 (m, 3H), 7.48-7.37 (m, 3H), 5.49 (s, 2H), 3.90 (s, 4H), 3.38 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 168.2, 164.2, 163.1, 155.3, 153.6, 144.5, 134.8, 132.5, 131.8, 130.5, 126.1, 125.1, 124.2, 122.6, 118.6, 70.2, 68.3, 55.1 ESI-MS: *m/z*: 449 $(M+H)^+$. Anal. calcd. (found) % of $C_{23}H_{21}N_6O_2Cl$: C, 61.54 (61.52); H, 4.72 (4.76); Cl, 7.90 (7.85); N, 18.72 (18.74); O, 7.13 (7.19).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(4-chloro phenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8d): Pale brown solid, yield: 88%, m.p.: 190-192 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.40 (s, 1H), 8.32 (s, 1H), 8.05 (s, 1H), 7.85 (d, 1H, *J* = 8.1 Hz), 7.76-7.73 (m, 3H), 7.67-7.64 (m, 1H), 7.62-7.52 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.42 Hz, 1H), 5.45 (s, 2H), 3.88 (s, 4H), 3.35 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 156.4, 146.2, 142.3, 140.9, 135.7, 132.4, 128.2, 126.4, 125.2, 123.2, 122.4, 122.7, 121.5, 118.6, 116.9, 76.1, 72.3, 52.2 ESI-MS: *m/z*: 449 $(M+H)^+$. Anal. calcd. (found) % of $C_{23}H_{21}N_6O_2Cl$: 61.54 (61.52); H, 4.72 (4.76); Cl, 7.90 (7.85); N, 18.72 (18.74); O, 7.13 (7.19).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(2-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8e): Brown solid, yield: 86%, m.p.: 180-182 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.41 (s, 1H), 8.32 (s, 1H), 8.21 (s, 1H), 7.84-7.79 (m, 3H), 7.76 (t, *J* = 8.5 Hz, 1H), 7.64-7.43 (m, 2H), 7.41-7.10 (m, 2H), 5.49 (s, 2H), 3.88 (m, 7H), 3.34 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 158.2, 147.1, 143.2, 141.3, 136.2, 135.3, 131.2, 128.1, 126.3, 124.2, 123.1, 121.1, 120.6, 119.6, 117.9, 76.5, 74.2, 53.2, 45.7 ESI-MS: *m/z*: 445 $(M+H)^+$. Anal. calcd. (found) % of $C_{24}H_{24}N_6O_3$: C, 64.85 (64.89); H, 5.44 (5.47); N, 18.91 (18.92); O, 10.80 (10.85).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8f): Yield 83%, m.p.: 175-177 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.40 (s, 1H), 8.33 (s, 1H), 7.90-7.84 (m, 2H), 7.73 (d, *J* = 7.1 Hz, 1H), 7.64 (t, *J* = 8.4 Hz, 1H), 7.42-7.36 (m, 5H), 5.48 (s, 2H), 3.88 (s, 4H), 3.36 (s, 4H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 156.3, 146.3, 142.8, 140.4, 135.4, 134.2, 132.1, 127.2, 125.8, 122.2, 121.6, 120.5, 119.2, 118.2, 116.2, 78.2, 76.2, 56.2, 42.7 ESI-MS: *m/z*: 445 $(M+H)^+$. Anal. calcd. (found) % of $C_{24}H_{24}N_6O_3$: C, 64.85 (64.89); H, 5.44 (5.47); N, 18.91 (18.92); O, 10.80 (10.85).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(2-methylphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8g): White solid, yield: 81%, m.p.: 170-172 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.40 (s, 1H), 8.33 (s, 1H), 7.90-7.84 (m, 2H), 7.73 (d, *J* = 8.40 Hz, 1H), 7.64 (t, *J* = 8.42 Hz, 1H), 7.42-7.36 (m, 5H), 5.48 (s, 2H), 3.88 (m, 4H), 3.36 (s, 4H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 152.4, 142.5, 141.8, 140.6, 136.9, 133.2, 131.9, 126.6, 124.3, 121.5, 121.1, 120.2, 119.1, 118.1, 117.2, 76.2, 71.2, 52.2, 32.6 ESI-MS: *m/z*: 429 $(M+H)^+$. Anal. calcd. (found) % of $C_{21}H_{21}N_6O_2$: C, 64.77 (64.82); H, 5.44 (5.47); N, 21.5821.63); O, 8.22 (8.20).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8h): light yellow solid, yield: 78%, m.p.: 203-205 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.40 (s, 1H), 8.33 (s, 1H), 7.90-7.84 (m, 2H), 7.73 (d, *J* = 8.40 Hz, 1H), 7.64 (t, *J* = 8.42 Hz, 1H), 7.42-7.36 (m, 5H), 5.48 (s, 2H), 3.88 (m, 4H), 3.36 (s, 4H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 151.2, 141.2, 141.1, 139.2, 137.2, 132.1, 131.6, 125.8, 124.6, 120.8, 120.1, 119.2, 119.1, 117.1, 116.2, 76.8, 68.2, 51.1, 31.8, ESI-MS: *m/z*: 429 $(M+H)^+$. Anal. calcd. (found) % of $C_{21}H_{21}N_6O_2$: C, 64.77 (64.82); H, 5.44 (5.47); N, 21.58 (21.63); O, 8.22 (8.20).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(4-triflouromethyl phenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8i): Brown solid: yield 78%, m.p.: 168-170 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.41 (s, 1H), 8.33 (s, 1H), 8.15 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.83-7.74 (m, 3H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 8.42 Hz, 1H), 7.39 (t, *J* = 8.42 Hz, 1H), 5.47 (s, 2H), 3.87 (s, 4H), 3.34 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 169.8, 157.5, 152.4, 149.6, 146.6, 141.8, 139.8, 136.2, 132.5, 128.9, 126.6, 122.2, 120.5, 118.1, 117.4, 79.6, 72.4, 68.1, 58.3, ESI-MS: *m/z*: 483 $(M+H)^+$. Anal. calcd. (found) % of $C_{24}H_{21}N_6O_2F_3$: C, 59.75 (59.69); H, 4.39 (4.43); F, 11.81 (11.84); N, 17.42 (17.45); O, 6.63 (6.68).

(*E*)-2-Morpholinoquinoline-3-carbaldehyde *O*-((1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl)oxime (8j): Brown solid, yield: 78%, m.p.: 183-185 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.44 (s, 1H), 8.41 (d, *J* = 8.0Hz, 2H), 8.33 (s, 1H), 8.19 (s, 1H), 8.02 (d, *J* = 8.2 Hz, 2H), 7.76 (s, 1H), 7.67 (d, *J* = 8.0Hz, 1H), 7.62 (t, *J* = 8.42 Hz, 1H), 7.40 (t, *J* = 8.42, 1H), 5.47 (s, 2H), 3.88 (s, 4H), 3.35 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 162.2, 160.1, 155.2, 148.2, 141.2, 140.2, 137.5, 136.2, 132.2, 126.2, 124.2, 123.3, 118.2, 116.2, 114.2, 72.1, 71.5, 64.1, 52.3, ESI-MS: *m/z*: 460 $(M+H)^+$. Anal. calcd. (found) % of $C_{23}H_{21}N_7O_4$: C, 60.12 (60.16); H, 4.61 (4.63); N, 21.34 (21.38); O, 13.93 (13.90).

Cytotoxic activity: The synthesized compounds containing a quinoline linked triazole nucleus were assessed for their anticancer efficacy against three cancer cell lines (MCF-7, PC3 and Hela) using the MTT assay. The assessment of the synthesized compounds' anticancer activity was conducted by a two-step *in vitro* screening process. Initially, all the compounds were evaluated at two concentrations (5 and 10 μM) against the aforementioned three cell lines. The goal was to determine the most efficient chemicals by evaluating their level of cancer cell growth inhibition after 48 h of incubation.

Cell culture: The MCF-7 cells were cultivated in RPMI-1640 medium containing 10% FBS, whereas the PC-3 and HeLa cells were kept in MEM medium which also contained 10% FBS. All the cell lines were grown in a humidified environment with 5% CO_2 at 37 ºC. The stock solutions of the compounds were prepared in DMSO solvent and then applied to the cell culture at the required concentrations. The DMSO concentration did not exceed 1:1,000 in the final culture.

MTT assay: The MTT test was used to assess the cytotoxic activity of the synthesized compounds [19]. The synthesized stock solutions of the compound were diluted with culture medium. A density of 5×10^3 cells per well was used to seed the cells in 96-well plates. After incubation until confluency was achieved, each well was treated with 100 mL of media containing synthesized compounds as needed and left to incubate for 48 h. Then, after incubating for an additional 4 h, the MTT working solution (5 mg/mL) was applied to every well. Careful removal of the medium and addition of 200 mL DMSO occurred at the end of incubation. This was followed by the measurement of the optical density at 490 nm and 630 nm using a microplate reader (MODEL). In order to determine the percentage of cell growth inhibition, the following equation was applied:

$$\text{Inhibition } (\%) = \left(1 - \frac{(\text{Sample group } OD_{490} - \text{Sample group } OD_{630})}{(\text{Control group } OD_{490} - \text{Control group } OD_{630})}\right) \times 100$$

The IC_{50} values were calculated with Graph pad prism software and standard deviations of the IC_{50} values were obtained from at least three independent experiments.

RESULTS AND DISCUSSION

The initial screening study revealed that 6 out of the total 10 compounds exhibited significant anticancer activity with a range of 70-85% of cancer cell growth inhibition than the rest of the compounds (Table-1). Later, the selected compounds based on their anticancer activity were tested further with more number of concentrations so as to determine the IC_{50} value of the compounds which is a parameter used for the evaluation and comparison of the potency of the compounds with the standard drug used in this study. The IC_{50} values of the selected compounds were presented in Table-2 and found to be in the range of 2.85 μM, 4.07 μM and 3.35 μM against MCF-7, PC-3 and HeLa cancer cell lines respectively. Whereas the IC_{50} value of the standard drug, doxorubicin was found to be 2.71 μM (MCF-7), 4.01 μM (PC-3) and 3.21 μM (HeLa). These results showed that the selected compounds are more sensitive towards MCF-7 cancer cell lines than PC-3 and HeLa cancer cell lines.

TABLE-1
THE % GROWTH INHIBITORY ACTIVITIES OF THE SYNTHESIZED COMPOUNDS (**8a-j**) AGAINST MCF-7, HeLa AND PC-3 CELL LINES

Compd. No.	MCF-7		PC-3		HeLa	
	5 µM	10 µM	5 µM	10 µM	5 µM	10 µM
8a	62	70	59	63	60	66
8b	90	95	79	86	80	88
8c	89	94	76	84	78	85
8d	87	92	74	80	76	82
8e	67	72	63	69	66	71
8f	68	74	64	70	67	72
8g	83	89	72	79	73	80
8h	74	81	67	73	69	75
8i	92	96	80	88	82	90
8j	63	71	60	65	61	67
Doxorubicin	93	98	76	86	82	90
Control	10	10	10	10	10	10

(a) Values are average of three determinations and deviation of data results is 10-20%; (b) All compounds were dissolved in DMSO for testing; (c) MCF-7 breast cancer cell lines; (d) PC-3 prostate cancer cell lines; (e) HeLa cervical cancer cell lines.

TABLE-2
IC_{50} VALUES OF SELECTED COMPOUNDS WITH THE STANDARD DRUG DOXORUBICIN

Compd. No.	IC_{50} (µM ± SEM)		
	MCF-7	PC-3	HeLa
8b	2.98 ± 0.01	4.16 ± 0.08	3.41 ± 0.02
8c	3.14 ± 0.06	4.21 ± 0.03	3.53 ± 0.06
8d	3.28 ± 0.02	4.47 ± 0.09	3.68 ± 0.04
8g	3.47 ± 0.07	4.51 ± 0.05	3.82 ± 0.01
8h	3.85 ± 0.04	5.11 ± 0.09	4.17 ± 0.02
8i	2.85 ± 0.01	4.07 ± 0.07	3.35 ± 0.07
Doxorubicin	2.71 ± 0.03	4.01 ± 0.05	3.21 ± 0.01

Conclusion

Based on click reaction, novel quinoline containing 1,4-disubstituted 1,2,3-triazole hybrids *e.g.* ((*E*)-2-morpholino-quinoline-3-carbaldehyde *O*-((1-phenyl-1*H*-1,2,3-triazol-4-yl)-methyl)oxime derivatives) were successfully synthesized and characterized. The adopted method is believed to be effective and can contribute to the design of the new molecule for potential drug applications. The synthesized compounds were evaluated for their *in vitro* anticancer activity against pathogenic strains. All the compounds shown good activity, however, compounds **8a**, **8g** and **8i** had shown the excellent results.

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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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