Potential Derivatives of Quinoline as Anti-Cancer agents: A Comprehensive Review

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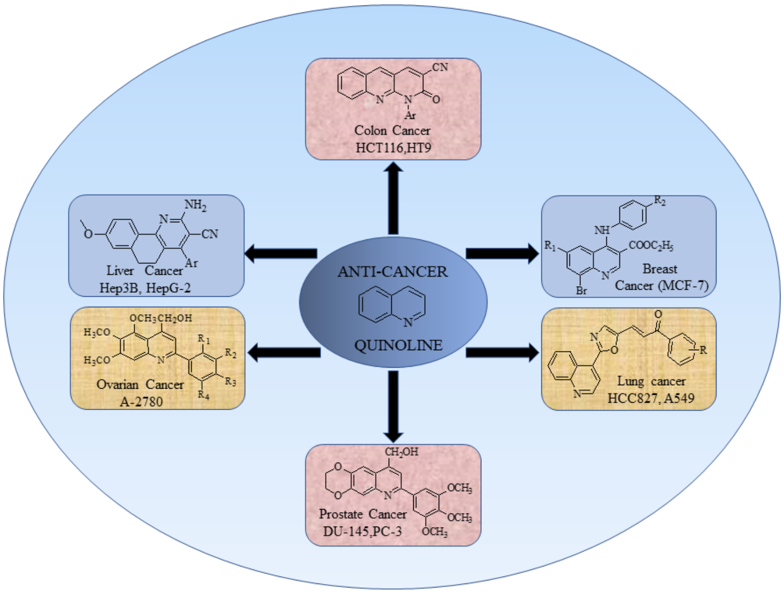
Abstract

Quinoline has gained much importance as a heterocyclic compound because it has numerous uses in both synthetic and industrial organic chemistry, it has also piqued the curiosity of academics and scientists, thus over a large period of time much research has been done and is still going on quinoline derivative as a drug to cure various types of cancer. Therefore, this review is compromised of the physiologically active quinoline derivatives showing an effective anticancer activity that will provide a brief idea to the researchers in the future for the development of a potent and effective drug molecule.

Graphical Abstract



Anticancer activity shown by Quinoline derivative on different Cancer cell lines.

Keywords: Cancer, Quinoline, Synthetic Approach, Anti-cancer Activity, Cancer Cell lines.

DOI Number: 10.14704/nq.2022.20.10.NQ55208 **NeuroQuantology 2022; 20(10): 2408-2427**

1. Introduction

Currently, cancer ranks second only to cardiovascular disease as the leading killer worldwide**[1]**.Currently, one in five men and one in six women will develop cancer, and It claims the lives of one in every eight males and one in every 10 women **[2]**.It is estimated that over 19.3 million men and women would be diagnosed with cancer across all sites, and almost 10 million dies as a result in 2020**[3]**.As the incidence of cancer rises and drug resistance to existing anti-cancer medications becomes a serious problem, researchers are focusing their efforts on finding effective cancer treatments**[4]**. Cancer is the fast development and formation of unwanted cells that grow past normal bounds, infect nearby bodily parts, and/or migrate to other distant organs via metastasis **[5-6]**. It is characterized by molecular processes such as unregulated cell proliferation **[7-8]**, cellular transformation**[9]**,inappropriate cell cycle regulation**[10-11]**, angiogenesis, and enhanced invasion with subsequent metastases **[12]**. Currently, various methods have been preferred or usedto manage cancer, such as radio and chemotherapy, which give successful results.However, a lack of cell selectivity in rare situations can cause serious immune system compromise **[13-14]**.Cancer treatment is done via different therapies and is indeed associated with a wide range of adverse effects such as alopecia, tumorigenicity, dermatitis, hepatotoxicity, developmental toxicity, mutagenicity, drug-induced cancer, alopecia, etc **[15-16]**.Natural products are widely acknowledged as an essential resource for researching chemotherapeutic and chemopreventive drugs**[17]**.The success in the treatment of cancer is still having a lot of challenges due to the increasing threats of drug resistance as well as adverse effects that make the anticancer agents less used and less effective **[18-19]**. Clinical trials are underway for a variety of anticancer drugs with novel structures, but they are currently insufficient **[20-21]**. As a result, it is critical to design and develops a novel anticancer candidate with a larger range of cytotoxicity and higher efficacy to prevent or treat this fatal disease.

Quinolinealso known as benzopyridine, 1-benzazine, and 1-azanaphthalene**[22]**,is the most common heterocyclic compound, with a variety of commercial and medical uses. Over the last 200 years, Quinoline has gotten a lot of attention from scientists**[23]**. Unique features include molecular formula, C9H7N, including its double-ring structure containing a benzo-fused pyridine molecule **[24]**. Plants have been utilized for many therapeutic purposes, including the treatment of injuries, diseases, and general health well-being since ancient timesand development**[25]**.Generally,quinoline moiety can be found in a variety of natural compounds.Natural substances with the quinoline moiety are typically pharmacologically active and have a variety of biological effects, which makes them promising therapeutic options**[26-28].** The tertiary base quinoline can combine with acids to generate a salt and is involved in several reactions with pyridine and benzene **[29]**.Several studies revealed that scholars have been interested in quinoline scaffolds because they have a wide spectrum of pharmacological and biological effects **[30]** such as antibiotic**[31-33]**, antioxidant**[34-35]**, anti-proliferative**[36-37]**,anti-inflammation**[38-39]**, antimalarial**[40-41]**, antifungal**[42-43]**, antileishmanial **[44-45]**,anticonvulsant **[46]**, etcvia severalmode of action such as growth inhibitors, apoptosis inducers, angiogenesis inhibitors, cell migration disruption, and nuclear receptor modulators **[47-49]**.Some quinazoline and quinolinealkaloids coupled with various heterocycleshave substantial anticancer action, Camptothecin is one of the most important and well-known**[50]**. Recently, several quinoline-based drugs are successfully marketed that highlights their enormous medicinal significance such as Lenvatinib (urea derivativeused in thyroid cancer treatment) **[51-52]**, topotecan (a synthetic analog of camptothecin used in the ovarian treatment, cervical, and lung cancer **[53]**, Chloroquine (antimalarial) **[54]**, bedaquiline (anti-tubercular) **[55-56],** Irinotecan (Pancreatic cancer)**[57]**, and montelukast (a styryl derivative used as anti-asthmatic). Furthermore, some quinoline-based compounds are presently under clinical investigation such as PF-254592 under phase II for Schizophrenia treatment is a selective inhibitor of PDE10A phosphodiesterase **[58]**.Based on recent studies on natural, semisynthetic, and synthetic quinoline derivatives we conclude that this moiety has a high ability to elicit anticancer activity through the various mechanisms of action**[59]**.

2. Quinoline Derivative on Different Cancer Cell lines:

Ghorab& co-workers (1) published a variety of substituted quinoline analogues and assessed their cytotoxicity in vitro against MCF-7 cancer cells. the compound with the molecular formula 4-(2-amino-4-(4-chlorophenyl)-3-cyano-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinolin-(4H)-yl) benzene-sulfonamide **(1)** was nearly the same as doxorubicin **[60]**.

Mulakayala *et al.* Anticancer effects with 6H-1-benzopyrano[4,3-b] quinolin-6-ones (2), that were demonstrated to be catalyst-free and straightforward, was tested using cancer cell lines IMR32, K564, MDA-MB 231, and Colo-205. 10,11-difluoro4,3-b-quinoline-6-one is the chemical with following formula **(2)**was found to be the most active **[61]**.

Arafa *et al.* reported the series of 5,7-dibromoquinoline**(3)** and evaluated it against the MCF-7 cell & MDA-MB231 cell lines. Compound (5,7-dibromo-quinoline-8-acyloxy) The presence of acetic acid 4-hydroxy-3-methoxy-benzylidene-hydrazide **(3)**was most potent for both cells lines **[62]**.

Marganakop *etal.,* reported Overall cytotoxicity with N-(4-acetyl-4,5-dihydro-5-(7,8,9-tetrazolo[1,5-a]-quinolin-4-yl) acetamides was tested in HeLa and MCF-7 cell lines (4). N-(4-acetyl-4,5-dihydro-5-(7-bromo-tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-thiadiazol-2-yl) and N-(4-acetyl-4,5-dihydro-5-(7-chloro-tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-thiadiazol-2-y **(4)** were had excellent activity against HeLa cell line **[63]**.

Sangani *etal.,*reported compounds (5) of the pyrazole, quinoline, and pyridine family, and tested for cytotoxicity in vitro. Specifically, amino-2,4-dicarboxylic acid (5-chloro-3-methyl-1-p-tolyl-1H-pyrazol-4-yl) -5-oxo-1-(pyridin-3-yl) two-amino-four-hydroxy-,4,5,6,7,8hexahydroquinoline-3-carbonitrile (5) (5-chloro-3-methyl-1-p-tolyl-1H-pyrazol4-yl) -7,7-dimethyl-5-oxo-1-(pyridin-3-yl) the 3-carboxyl derivative of 1,4,5,6,7,8-hexahydroquinoline **(5)** shown excellent inhibitory activity against FabH and EGFR **[64]**.

Mostafa& associatesreported antiproliferative efficacy against by the MCF-7 cell line was investigated in vitro using a range of quinoline hybrids(6,7). Three - part Mixture (quinolin-3-ylamino) (1)-(thiophen-2-yl)prop2-en-16-one(6) and (3)-(thiophen-2-yl)prop (quinolin-3-ylamino) -1-(thiophen-2-yl) prop-2-en (2-methylquinolin-4-ylamino) -1-(thiophen-2-

eISSN 1303-5150

yl)prop-2-en-1-one **(7)** showed slightly lower antiproliferative activity on cell line compared to standard doxorubicin **[65]**.

Marcelle& colleagues reported a new class of 4-quinolinylhydrazone analogs**(8)** and used the MTT assay to check it out on HL-60, SF-295, OVCAR-8, or HCT-116 primary cells. Compounds 4-(Benzylidenehydrazinyl) quinoline hydrochloride **(8)** and 4-(3-Chlorobenzylidenehydrazinyl) quinoline hydrochloride **(8)** exhibited cytotoxic activity against HCT-116 cell lines **[66]**.

Shobeiri& associatesreported A-2780, MCF-7, A-2780/RCIS, and SW480 are all human cancer cell lines and MCF-7/MX were used to assess the cytotoxicity of a series of 2-aryl-trimethoxyquinoline analogs(9). 5.6.7-trimethoxy-2-(3,4,5-trimethoxyphenyl)quinoline-4-yl) methanol **(9) showed**the most potent inhibition activity of tubulin polymerization **[67]**.

Bingul& co-workersreported a class of quinoline-based hydrazide-hydrazones**(10)** and tested cytotoxicity against Kelly neuroblastoma, SH-SY5Y, MDA-MB-23, and MCF-7 cell lines. Compound N-(3-chloro-6-methoxy-naphthalene-2-ylmethylene)-N'-(1-methylene-6-phenylsulfanyl-hexyl)-hydrazine **(10)**was found to be the most potent **[68]**.

Ahsan& co-workersreported the series of quinoline analogs**(11)** and tested for cytotoxicity was carried out against MDA-MB-435 and HeLa.Compound 1-(7-hydroxy-4-methyl-2-isoquinoline-1(2H)-yl)-3-(4-methoxyphenyl) urea **(11)** have high cytotoxicity against MDA-MB-435 and HeLa, respectively **[69]**.

Malayeri& associates reported new series of quinoline hybrids**(12)** and cell lines DU145, A549, or MCF-7 were used to determine its cytotoxicity. It's [7-(3,4,5-trimethoxy-phenyl)-2,3-dihydro-[1,4] dioxino[2,3-g] that has been linked to cancer. quinolin-9-yl] -methanol **(12)**has the highest anti-proliferative activity compared to standard (doxorubicin) **[70]**.

Alleni *et al.*,reported the class ofnovel quinoline analogs (6-phenyl-6H-chromeno [4,3-b] quinoline)**(13)** and evaluated them for anti-cancer activity. The compound 10-nitro-6-phenyl-6H-chromene [4,3-b] quinoline**(13)** showed decent anti-cancer activity on A549, MCF-7 and B16F10 cell lines **[71]**.

Okten& colleagues reported the series of substituted 5-bromo-6,8-dimethoxy-quinoline**(14,15)** and tested for cytotoxicity. Compound 5-Bromo-6,8-dimethoxy-quinoline **(14)** and N-nitrated 6,8-dimethoxy-quinoline **(15)** show excellent cytotoxicity against the HT29, A549, Hep3B, HeLa, and MCF-7 cell lines and low cytotoxicity as compared to 5-fluorouracil and cisplatin **[72]**.

Khaled& associates The family of 4-hydroxycoumarins was used to assess the antiproliferative activity against A549 and MCF-7 human cell lines (4-substituted-anilino) quinoline (16). Specifically, 8-Bromo-4- (4-chlorophenylamino) acid from the quinoline ring, carbons 3,6 3-ethyl **(16)** ester exhibited excellent activity, with standard to doxorubicin **[73]**.

Abbas& co-workers reported the series of series of quinoline-chalcone hybrid (17) and examined them on their cytotoxicity in cancer cell lines. A quinoline derivative with the molecular formula N'-((Z) (1-(4-aminophenyl)-3-(4-chlorophenyl) alkylidene) The combination of N'-((Z) -1-(4-aminophenyl)-3-(4-chlorophenyl) alkylidene) with 2-(4-

methoxyphenyl)quinoline -4-carbohydrazide (17) produces a benzamide. The 4-carboxyhydrazide of 2-(4-methyl phenyl)quinoline **(17)** found to have potent activity against A549 and K-562 cells **[74]**.

Ramya & colleagues reported the series of 2-chloro/phenoxy quinoline analogs**(18,19)** inspired by curcuminas and tested*in vitro* for their cytotoxicity towards various tumor cell lines like 4T1, HeLa, NCI-H460, HGC-27, DU-145, and PC-3. Compound1-(2-phenoxy-quinolin-3-yl)-5-(2,4,5-trimethoxy-phenyl)-penta-1,4-dien-3-one**(18)** and 1-(2-chloro-quinolin-3-yl)-5-(2,4,5-trimethoxy-phenyl)-penta-1,4-dien-3-one**(19)** give excellent activity and most potent derivative1-(2-phenoxy-quinolin-3-yl)-5-(2,4,5-trimethoxy-phenyl)-penta-1,4-dien-3-one **(18)** displayed promising cytotoxicity against all cell lines **[75]**.

Kasabian& associates Twenty different substituted pyrazole-quinoline compounds were investigated for cytotoxicity against four different types of cancer cells. To write it out chemically, it's 3-(4-Bromo-phenyl)-4-(3-nitro-phenyl)-1-phenyl. -1H-pyrazolo[4,3-c] Both the twenty-membered ring compound quinoline and the three-membered ring compound quinone exist (4-Bromo-phenyl) -4-(2,4-dimethoxy-phenyl)-1-phenyl -1H-pyrazolo[4,3-c] In comparison to the gold standard Doxorubicin, quinoline (20) had striking activity **[76]**.

Abdelbaset& co-workersreported the series of quinoline pyrroline derivatives**(21)** and evaluated antiproliferative activity. Compound 3-((6-methyl-2-(methyl-thio) quinoline-3-yl) methylene)-5-phenyl-1H-pyrrol-2(3H)-one **(21)** found to be good anti-proliferative activity **[77]**.

Jafari& associates reported new benzo- or tetrahydro benzo-[h]quinoline(22) series and tested it on A549, MCF-7, C26, or A2780 cancer cell lines. The 2-p-tolyl-benzo [h] 2'-Dimethylaminoethyl)-amide of quinoline-4-carboxylic acid **(22)** demonstrated high cytotoxicity towards all the human cancer cells **[78]**.

Hamdy *et al.,*reported a group of oxadiazole analogues (23) based on the quinolin-4-yl scaffold were investigated for their potential to inhibit tumour growth. Compound{5-[2-(4-bromophenyl)-6-methoxyquinolin-4-yl} -N-(4-nitrophenyl) - [1,3,4] cancer cell lines that express Bcl-2 and treated with oxadiazol-2-amine (23) showed sub-micromolar cytotoxicity **[79]**.

Vyas& co-workers reported a group with substituted quinoline analogues(24,25) HT-29 and MDA-MB-231 human cancer cells are treated. The chemical 2-(4-fluorophenyl)-7-methylquinoline Both 4-benzyloxymethyl-4-carboxylic acid (24) and 4-carboxylic acids benzyl ester (24) -2-(4-chloro-phenyl)-7-methyl-quinoline **(25)** showed potent activity **[80]**.

Esraa& colleaguesreported the series of benzo[h]quinoline hybrids**(26,27)** and MCF-7, HepG2, Caco-2, and In the experiment, researchers used HCT-116 cancer cell lines. Synthesis of 4-(2,4-dimethoxyphenyl)-8-methoxy-2-oxo-1,2,5,6-tetrahydrobenzo[h]quinoline-3-carbonitrile (26) and 2-amino an 8-methoxy-4-(aryl)-5,6-dihydrobenzo[h] most effective against EGFR-expressing MCF-7 cells were quinoline-3-carbonitriles (27) **[81]**.

Venkatarao& associates reported the seriesof chalcone-fused quinoline derivatives**(28)** and assessed them against the cancer cells A549, MCF-7, and A375. The compound 1-(3,4,5-trimethoxyphenyl)-3-(2-(quinoline-4-yl)oxazole-5-yl)prop-2-en-1-one**(28)** and 1-(4-chlorophenyl)-3-(2-(quinoline-4-yl)oxazole-5-yl)prop-2-en-1-one**(28)**werefound to be more active than positive control doxorubicin **[82]**.

Ribeiro& co-workers reported on the sequence compounds 2-(quinolin-4-ylmethylene) hydrazine carbothioamide analogues **(29)** and tested, against RAW-264.7, T-47D, and MCF-7 for anti-proliferative activity. Compound N-(4-ethyl phenyl)-2-(quinoline-4-ylmethylene) hydrazine carbothioamide **(29)** exhibited significant activity **[83]**.

Mirzaei& colleagues reported Huvec, A2780, MCF-7/MX, MCF-7, or A2780/RCIS normal cell lines were used to test a variety of novel quinoline chalcone derivatives (30). Compounds are one example. "3-(6-benzoyl-2-chloroquinolin-3-yl)-1-(4-methoxy phenyl)propane" 3-(6-benzoyl-2-chloroquinolin-3-yl)-2-en-1-one (30), 2-en-1-one (8-benzoyl-2-chloroquinolin-3-yl) 1- (3,4,5-trimethoxy phenyl) 3-(4-Methoxy Phenyl)prop-2-en-1-one (30) and prop-2-en-1-one (30) (8-benzoyl-2-chloroquinolin-3-yl) For both primary and secondary bacterial infections, 1-(3,4,5-trimethoxy phenyl) prop-2-en-1-one has proven to be a successful treatment and drug-resistant cancer cells (30) showed potent cytotoxicity. Research indicated that compound (30) was the most effective derivative tested **[84]**.

Kuldeep& associatesreported the series of 3-Phenyltrifluoromethyl quinoline analogs**(31)** and tetsed for *Vitro cytotoxicity* SRB assay (sulforhodamine B) against MCF-7 cell line.Compound3-(3'-amino-2'-nitro-biphenyl-3-yl)-1-[4-(2-trifluoromethyl-quinoline-4-arylamino)-phenyl]-propenone **(31)** found to be most potent **[85]**.

Katariya& colleagues reported the series of imine-linked quinoline-fused oxazole hybrids**(32)** and test for cytotoxicity in a range of NCI60 cancer cells. Compound N-(6-chloro-2-methyl-quinoline-4-yl)-N'-(2-p-tolyl-oxazole-4-ylmethylene)-hydrazine **(32)**showed significant inhibitors of Topoisomerase-I activity **[86]**.

Jin *et al.* reported sevens are a sequence (ethoxycarbonyl) -8-(arylamino)-[1,3]dioxolo[4,5-g] hybrids of quinolin-5-ium iodide (33) were examined for their cytotoxicity in vitro using SGC-7901, A-549, or Hela cell lines. Eight-amino-4-((benzyloxy) phenyl) -7- (ethoxy carbonyl) "-5-propyl-" "[1,3] "doxology" "[4,5-g]" iodide of quinolinium-5 **(33)** exhibited significant activity compare to positive control MTX and 5-FU **[87]**.

Karnik& co-workersreported and designed a class of substituted quinoline analogs **(34)** and tested for cytotoxicity on different cell lines, HCC827, HT-29, and A549 by standard MTT assay. The compound 4-(4-methyl quinoline-2-yl) phenyl 4-(chloromethyl) benzoate **(34)**has shown inhibitory activity against triple mutants of the EGFR kinase and significantly inhibited HCC827 cellproliferation compared to A431, A549, and H1975 cell lines **[88]**.

Tham& associatesreportedthe series of plinabulin-quinoline derivatives**(35,36)** and evaluated for cytotoxicity against KB, HepG2, and Lu cell lines. Compound 3,6-bis-(4-chloro-8-methyl-quinoline-2-ylmethylene)-1,4-dimethyl-piperazine-2,5-dione **(35)** and 3-(4-chloro-benzylidene)-6-

(4-chloro-8-methyl-5-nitro-quinoline-2-yl-methyl)-1-ethynyl-piperazine-2,5-dione **(36)**were found to be most potent**[89]**.

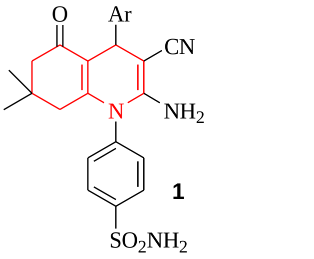
Ruoyu *et al.,* reported the series of b-methyl-4-acrylamido-quinolines **(37)** and checked for cancer-fighting properties; tested equally effective against U87MG & PC3 cell lines. Compound2,4-difluoro-N-(2-methoxy-5-(4-(4-(4-methylpiperazin1-yl) -4-oxo-but-2-en-2-yl)quinoline-6-yl)pyridine-3-yl)benzene-sulphonamide **(37)**showed comparable anti-cancer activity against U87MG and PC3 cell lines **[90]**.

Ammar& colleagues reported with HCT-116, MCF-7, HepG-2, and CACO, the sequence of quinoline-carboxamidehybrids(38). 1-(2-oxo-1,2-dihydroquinolin-3-yl) or cyano-N-2-(4-hydroxyphenyl) acrylamide (38) are two types of inorganic acrylamides (11). (4-hydroxyphenyl) -2-oxo-1,2-dihydrobenzo[b][1,8] naphthyridine-3-carbonitrile **(38)** showed good anti-proliferative activity as compared to standardDoxorubicin **[91]**.

Ren& colleaguesreported the series of acridine and quinoline analogues**(39)** and tested for cytotoxicity against HepG-2 cells. Compound N-(4-methoxyphenyl)-N-methylquinolin-5-amine **(39)** showed excellent cytotoxicity activity **[92]**.

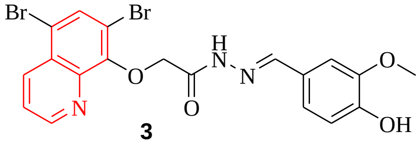
Guan& associatesreported the series of chalcone-quinoline hybrids **(40)** and tested their cytotoxicity against MCF-7, HCT-116, and MGC-803cells. Substance 1-(4-((2-methyl quinoline-4-yl) carboxy) phenyl)-3- (3,4,5-trimethoxyphenyl) prop-2-en-1-one **(40)**was found to be most potent as comparewith 5-fluorouracil **[93]**.

Kardile& co-workers the 7H-chromeno[3,2-c] series that has been reported Anti-cancer efficacy of quinoline derivatives (41) was evaluated in vitro using MCF-7 & A549 tumor cells. Compounds a-(2,2,2-trifluoroacetyl)-12-(1H-imidazol-1-yl)-2-bromo-6-(1H-imidazol-1-yl)-2-(2,2,2-trifluoroacetyl) dibenz 2-Bromo-6-(1H-imidazol-1-yl)-7-vinyl b,[1,6]naphthyridine-7(12H)-one (41) and b,[1,6]naphthyridine-7(12H)-one dibenzo[b, h]-7,12-dihydro [1,6] Excellent activity is shown for naphthyridin-7-ol (41) **[94]**.



1

Ar= C_6H_4Br-2, $C_6H_4(OCH_3)_2$-3,4



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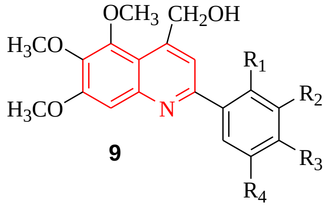
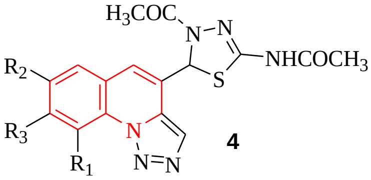


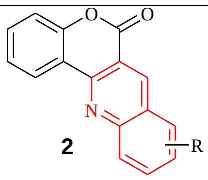
9

$\mathbf{R_1}$= H; $\mathbf{R_2}$= H,OH,OCH_3
$\mathbf{R_3}$=OCH_3,OH ; $\mathbf{R_4}$= H,OCH_3



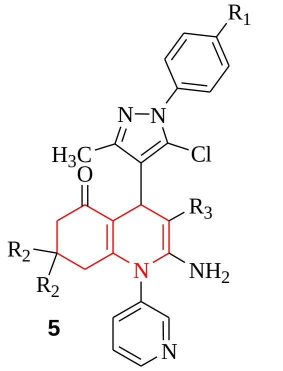
4

$\mathbf{R_1}$= H,OCH_3
$\mathbf{R_2}$= CH_3,OCH_3,Br,Cl
$\mathbf{R_3}$= H,OCH_3, CH_3



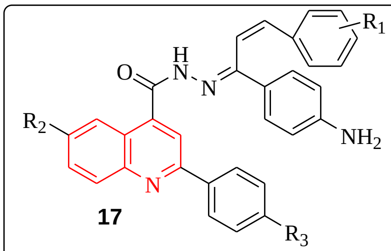
2

R= 2-OCH_3, 3,4-F, 4-Cl,
4-CH_3, 3-Br



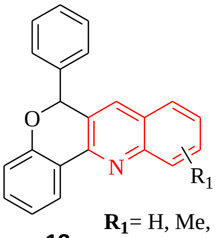
5

$\mathbf{R_1}$= H, CH_3, Cl
$\mathbf{R_2}$= H, CH_3
$\mathbf{R_3}$= CN, COOEt



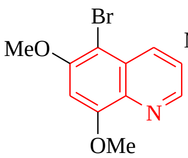
17

$\mathbf{R_1}$= H; 4-Cl; 4-OCH_3; 3,4-diOCH_3
$\mathbf{R_2}$= H; OCH_3
$\mathbf{R_3}$= H; Cl; OCH_3; Cl



$\mathbf{R_1}$= H, Me, Cl, NO_2

13



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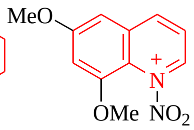

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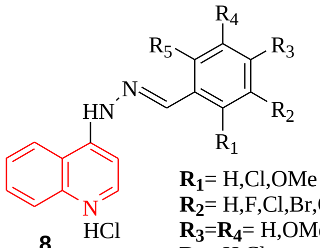
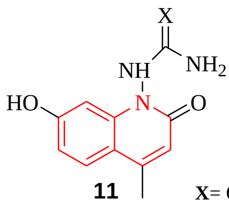
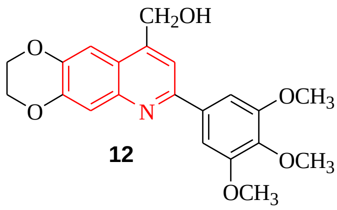


8

$\mathbf{R_1}$= H,Cl,OMe
$\mathbf{R_2}$= H,F,Cl,Br,OMe
$\mathbf{R_3}$=$\mathbf{R_4}$= H,OMe
$\mathbf{R_5}$= H,Cl



11 **X**= O, S



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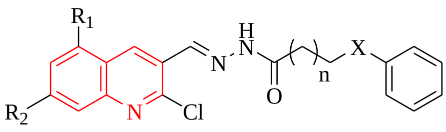
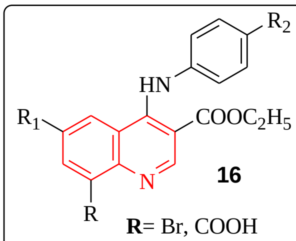


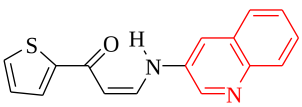
10

$\mathbf{R_1}$= $\mathbf{R_2}$= H, OMe **n**= 1, 4
X= S,O

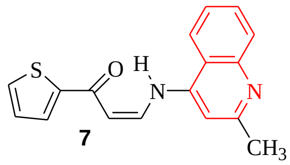


16

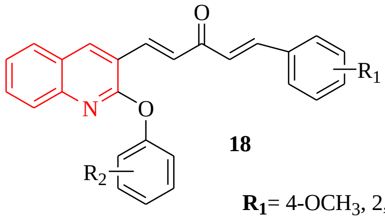
R= Br, COOH
$\mathbf{R_1}$= COOH,Br
$\mathbf{R_2}$= CH_3,OCH_3,Cl



6



7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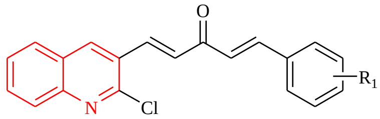
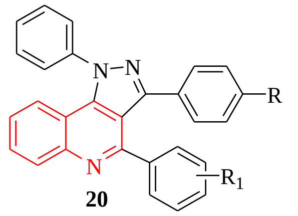
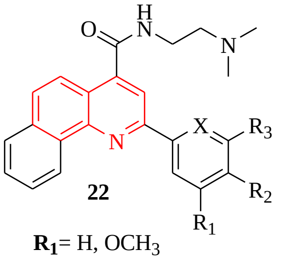

19

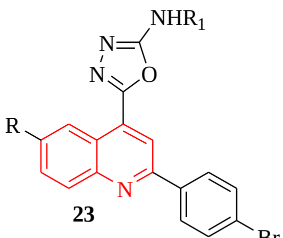
R$_1$= 4-OCH$_3$, 2,4-diOCH$_3$, 2,4,5-triOCH$_3$
R$_2$= H, 4-Br, 3-Cl, 2-CH(CH$_3$)$_2$


20

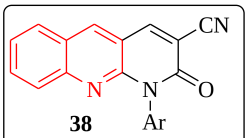
R= H, Br
R$_1$= H, CH$_3$, Cl, Br, NO$_2$, OCH$_3$


22

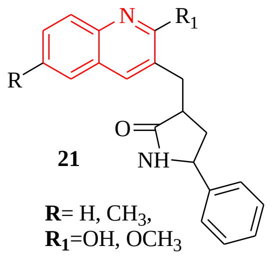
R$_1$= H, OCH$_3$
R$_2$= H, F, CH$_3$, NHCOCH$_3$,
R$_3$= H, OCH$_3$,
X = C, N


23

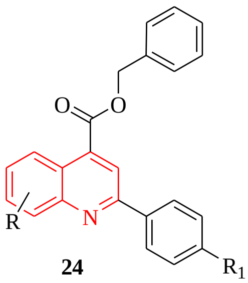
R = H, OMe
R$_1$= 4-Cl-Ph, 3,4-diCl-Ph, 4-Me-Ph, 4-NO$_2$-Ph, 3,4-diCl-Ph


38

Ar= 4-CH$_3$-C$_6$H$_4$, 4-OH-C$_6$H$_4$, 4-OH-C$_6$H$_4$


21

R= H, CH$_3$,
R$_1$=OH, OCH$_3$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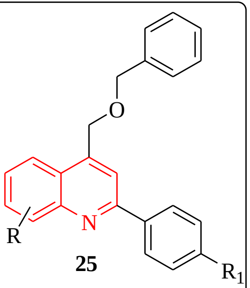
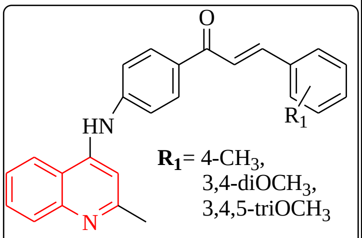
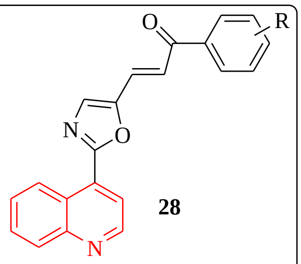

25

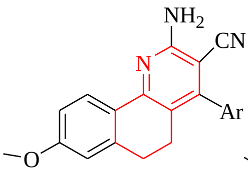
R= 6-CH$_3$, 6,7-diCl
R$_1$= Cl, F, OCH$_3$

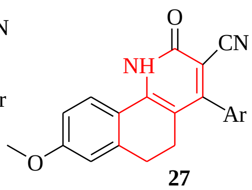

40

R$_1$= 4-CH$_3$, 3,4-diOCH$_3$, 3,4,5-triOCH$_3$

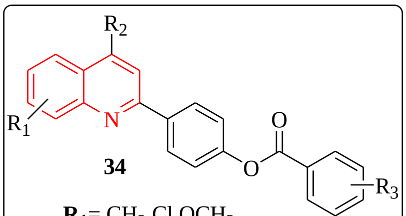

28

R= H, 3,4,5-trimethoxy; 4-chloro, 4-fluoro, 2-fluoro-4-methoxy

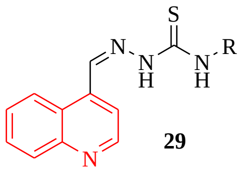

26


27

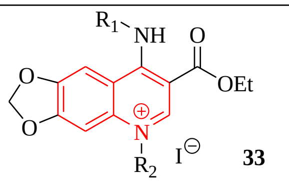
Ar= 4-MeOC$_6$H$_4$, 2,4-(MeO)$_2$-C$_6$H$_3$, 3,4-(MeO)$_2$-C$_6$H$_3$


34

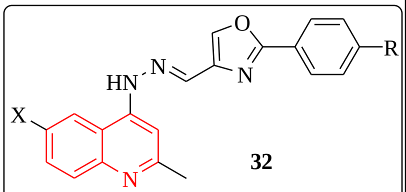
R$_1$= CH$_3$,Cl,OCH$_3$
R$_2$= CH$_3$, Ph, Cl
R$_3$= Cl, CF$_3$, CH$_2$Cl, (CH$_2$)$_2$N


29

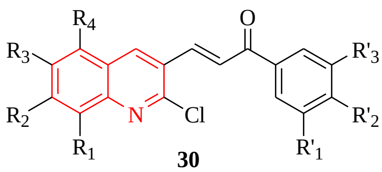
R= *p*-chloro-phenyl, *p*-ethyl-phenyl, *p*-methoxy-phenyl


33

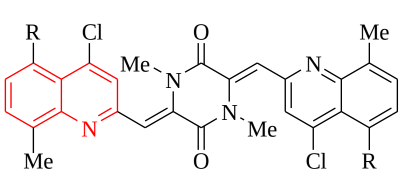
R$_1$= CH$_2$Ph, CH$_2$CH$_2$Ph, PhOCH$_2$Ph
R$_2$= CH$_2$CH$_3$, CH(CH$_3$)$_2$, CH(CH$_3$)$_2$


32

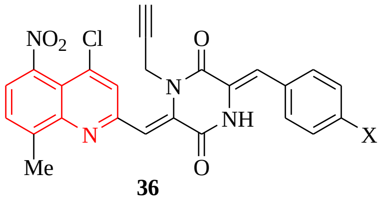
X= Br , Cl
R= H, CH$_3$, OCH$_3$, Cl, Br, F


30

R$_1$=COPh,H,COPh, **R'$_1$**=**R'$_3$**=H,OCH$_3$
R$_2$= **R$_4$**=H, **R$_3$**=H,COPh **R'$_2$**= OCH$_3$

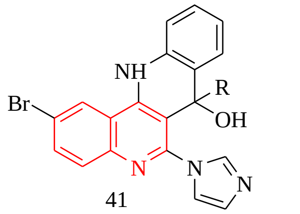


35



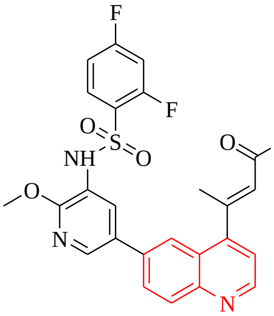
36

R= H,NO_2
X= OMe, Cl

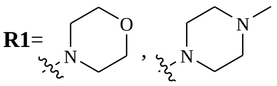


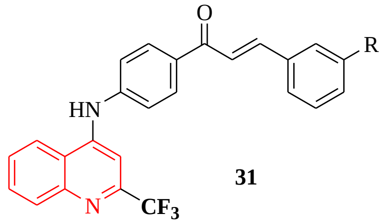
41

R= CH_3, -CH_2CH_3, -CH=CH_2, 4-Cl-C_6H_5

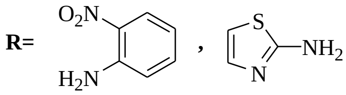


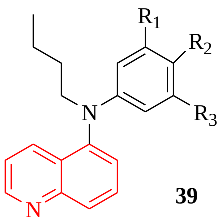
37





31





39

R_1= OCH_3, H
R_2= OCH_3,H, CN, F
R_3= H, OCH_3, Cl

Some most Potent Quinoline Derivative on Different Cancer cell lines:

Cancer Cell lines	Compounds
Cell cultures from breast cancer (MCF-7, MDA-MB-231)	1, 3,6, 7, 10,26, 27
Lung Cancer (A549, EGFR, HCC827, A431, H460, LU)	5, 13, 17
Cervical Cancer (HeLa)	4, 11, 14
Colon Cancer (HCT-116, Colo-205, HT-29, C26)	8, 22, 40
Liver Cancer (HepG-2)	28, 35, 38
Prostate Cancer (PC3, DU-145)	18, 19, 37
Erythroleukemia (K562)	2
Ovarian Cancer (A2780)	22, 30
Neuroblastoma (SH-SY5Y)	10
Gastric Cancer (SGC-7901)	33

Conclusion

This study summarizes the different Quinoline derivative showing potent anticancer activity, and further based on this study and on the published study we conclude that quinoline is a versatile molecule and have a potent anticancer activity on different cell lines. Nevertheless, this data can significantly help future researchers in the development of a better and more potent drug molecule representing a successful matrix for medicinal agents.

Conflict of Interest

All authors confirm that the information presented here is objective.

Acknowledgments

The faculty at Noida Institute of Technology have our deepest appreciation (Pharmacy Institute), Greater Noida (U.P.) for their support and guidance at every step.

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