

Table 1. Summary of results from studies on quinoline derivatives.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
[10]	- <i>In vitro</i> - <i>In vivo</i> - <i>In silico</i> (docking)	- Cell lines: PC3 (prostate), U87MG (glioblastoma) - <i>In vivo</i> : U87MG xenograft in ICR nude mice	β -Methyl-4-acrylamido quinoline (Synthesized via bromination, oxidation, Grignard reaction, and Suzuki coupling) β-Methyl addition & E/Z configuration tuning to improve metabolic stability & binding affinity	Prostate cancer, Glioblastoma	- Kinase inhibition assays (IC ₅₀ values) - - Cell proliferation (GI50 values) - - Western blot (PI3K/Akt/mTOR pathway) - - PK studies (oral exposure in rats) - - <i>In vivo</i> tumor growth inhibition	Dual inhibition of PI3K (α, β, γ, δ) and mTOR - - Downregulation of PI3K/Akt/mTOR pathway - - Strong kinase selectivity	IC ₅₀ (PI3K α : 0.80 nM, mTOR: 5.0 nM) - GI50 (PC3: 0.36 μ M, U87MG: 0.14 μ M) - <i>In vivo</i> : 93.5% tumor growth inhibition at 30 mg/kg, tumor regression at 60 mg/kg	Compound 14d shows potent antitumor activity and good oral bioavailability. Further development recommended.
[9]	<i>In vitro</i> & <i>In vivo</i>	- Cell lines: HCT116 (colorectal), A549 (lung), HepG2 (liver), BGC823 (gastric), HeLa, CaSki, C-33A, SiHa (cervical) - Animal model: BALB/c mice (HeLa xenograft)	Bivalent quinolines with 4-6 methylene spacers between phenoxy group (position-7) and various substituents (position-4). (Synthesized via nucleophilic substitution, followed by alkylation with dibromoalkanes in anhydrous DMF using sodium carbonate as catalyst.)	Cervical, Colorectal, Lung, Gastric, Breast	- MTT assays (IC ₅₀ values) - - Flow cytometry (cell death analysis) - - Western blot (autophagy markers) - - CRISPR-Cas9 (gene knockout of ATG5/ATG7)	Autophagy induction via ATG5/ATG7 pathway - No apoptosis involvement - - No ferroptosis involvement - - Targets cervical cancer cell survival mechanisms	- IC ₅₀ values (compound 4b): HeLa (3.71 μ M), A549 (2.75 μ M), HCT116 (0.26 μ M), MCF-7 (3.08 μ M) - <i>In vivo</i> : 81.76% tumor reduction at 8 mg/kg	Compound 4b exhibits strong antitumor activity through autophagy induction and has a favorable safety profile in mice. Further development warranted.

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					- <i>In vivo</i> tumor inhibition in mice			
[44]	<i>In silico</i> & <i>In vitro</i> & <i>In vivo</i>	Cell lines: HCT116 (colon), Colo320 (resistant colon), A549 (lung), HepG2 (liver), BGC823 (gastric) - Enzyme inhibition assays (50 kinases panel) - Molecular docking simulations	Indolo[2,3-d]benzazepine (HL1-HL4) & Indolo[2,3-c]quinoline (HL5-HL8) ligands (Synthesized via multistep reactions, including Schiff-base formation and metal complexation with Cu ²⁺ .) Modifications: Bromine substitution (HL2, HL6) for increased selectivity; Schiff-base methylation for solubility improvement.	Colon, Lung, Liver, Gastric	- Kinase inhibition assays (selectivity for PIM-1, SGK-1, PKA, CaMK-1, MSK1, GSK3β) - DNA binding studies (EtBr displacement) - MTT cytotoxicity assays - Apoptosis induction assays - Molecular docking (<i>In silico</i>) to predict kinase-ligand interactions - Computational studies on Cu(II) complexation effects (<i>In silico</i>)	Kinase inhibition-driven cytotoxicity - HL8 = potent PIM-1 inhibitor - Compound 8 inhibits SGK-1, PKA, CaMK-1, MSK1, GSK3β - Copper(II) complexes enhance cytotoxicity via DNA interaction	- HL7, HL8, and complex 8 highly selective for cancer cells. - Complex 4 more cytotoxic in drug-resistant Colo320 cells than in sensitive ones. - Apoptosis induction observed in multidrug-resistant Colo320 cells.	Copper(II) complexation significantly enhances cytotoxicity and alters kinase selectivity. - HL4, HL8, and complex 8 are promising anticancer candidate. - DNA binding is not the primary mechanism of action, suggesting alternative molecular targets. - Further structural modifications are needed to optimize selectivity and efficacy
[6]	<i>In vitro</i> & <i>In silico</i>	- Cell lines: LoVo (colorectal), MCF-7 (breast), MDA-MB-231 (breast), HepG2 (liver), A549 (lung), NCM460 (normal intestinal cells)	Pyrrolo[4,3,2-de]quinoline core of the Lymphostin family (Synthesized in 7 steps, 18.6% overall yield, starting from diamine 5 and ethyl 4-oxo-2-pentenoate via Doebner-von Miller reaction, Boc protection, bromination,	Colorectal, Breast, Liver, Lung	- Kinase inhibition assays (PI3K/mTOR IC ₅₀ values) - MTT cytotoxicity assays	PI3K/mTOR dual inhibition - Compound 1 covalently binds PI3K/mTOR - Induces apoptosis via p53	- IC ₅₀ values (PI3Kα: 4 nM, PI3Kγ: 7 nM, mTOR: 15 nM) - Comparable cytotoxicity to	Pyrrolo[4,3,2-de]quinoline is a promising scaffold for anticancer drug design. - Compound 1 is a potent PI3K/mTOR inhibitor with strong apoptotic effects.

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		- Enzyme inhibition assays (PI3K/mTOR)	catalytic hydrogenation, and deprotection.)		- Apoptosis induction assays (qRT-PCR for p53, c-Myc, AMPK, Bcl-2 expression) - Molecular docking simulations (<i>In silico</i>) - Comparative analysis with oxaliplatin & BEZ235 (dactolisib)	activation, AMPK upregulation, and c-Myc downregulation	oxaliplatin in colorectal cancer cells - Strong apoptosis induction in LoVo cells	- Selective cytotoxicity against colorectal and breast cancer cells. - Further structural modifications are needed for improved selectivity & solubility.
[45]	<i>In vitro & In silico</i>	- Cell line: Ehrlich Ascites Carcinoma (EAC) - Molecular docking with CDK-2 (PDB ID: 3IG7)	Quinoline-based hydrazone (BaHQi) & its metal complexes (Co-BaHQi, Ni-BaHQi, Cu-BaHQi) (Synthesized via condensation reaction of 2-hydrazinyl-4,6-dimethylquinoline with biacetyl (1:1 molar ratio), followed by complexation with Co ²⁺ , Ni ²⁺ , Cu ²⁺ .)	Ehrlich Ascites Carcinoma	- MTT cytotoxicity assays (IC ₅₀ values) - Spectroscopic characterization (IR, NMR, Mass, ESR, UV-Vis) - Magnetic & thermal analyses - DFT calculations for molecular modeling - Molecular docking (<i>In silico</i>) with CDK-2 active site	Enhanced cytotoxicity via metal complexation - Quinoline-hydrazone ligand binds CDK-2 through hydrogen & ionic interactions - Co(II) complex shows highest cytotoxicity - Binding affinities: Co-BaHQi (-8.73 kcal/mol) > Ni-BaHQi (-8.66 kcal/mol) > Cu-BaHQi (-8.45 kcal/mol)	- BaHQi ligand alone: IC ₅₀ = 85.2 µg/mL (weak activity) - Co-BaHQi: IC ₅₀ = 41.2 µg/mL (most potent) - Ni-BaHQi: IC ₅₀ = 43.7 µg/mL - Cu-BaHQi: IC ₅₀ = 47.3 µg/mL - Metal complexation enhances cytotoxicity	Metal complexation significantly improves anticancer activity. - Co(II)-BaHQi complex is the most promising candidate. - Molecular docking validates enhanced binding affinities. - Further modifications needed to improve selectivity and solubility
[19]	<i>In vitro & In silico</i>	- Cell lines: HCC827 (EGFR Del E746-A750),	Quinoline-based amide & sulfonamide derivatives	Non-small cell lung cancer (NSCLC)	- MTT cytotoxicity assays (IC ₅₀ values)	EGFR inhibition via ATP/allosteric site binding	- Compound 21: Most potent with IC ₅₀ = 0.010 µM	Quinoline derivatives show promise as EGFR-TKI

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		H1975 (L858R/T790M), A549 (WT-EGFR), BEAS-2B (normal lung) - Molecular docking & MD simulations	(Synthesized via multi-step reactions involving piperazine and imidazole substitutions. Key transformations include Boc protection, N-alkylation, and sulfonylation.)		- EGFR kinase inhibition assays - Western blot (phosphorylation analysis) - Apoptosis assays (Annexin V-FITC) - Molecular docking & MD simulations (<i>In silico</i>) - ADME property predictions	- Compound 21 : Dual inhibition at ATP and allosteric binding sites. - Induces apoptosis via AKT pathway inhibition. - Stable EGFR binding confirmed via MD simulations.	(HCC827), 0.21 μ M (H1975), 0.99 μ M (A549), 2.99 μ M (A549 normal) - Comparable to Osimertinib in EGFR inhibition (IC ₅₀ = 138 nM vs. 110 nM for Osimertinib). - Selective toxicity against NSCLC cells with minimal effect on normal cells.	alternatives for resistant NSCLC. - Compound 21 is a potent lead candidate. - Dual binding at ATP & allosteric sites may help overcome resistance. - Further optimization needed for improved pharmacokinetics and selectivity.
[8]	<i>In vitro</i> & <i>In silico</i>	- Human cancer cell lines: A549 (lung), U2OS (osteosarcoma), MCF7 (breast) - Biochemical assays - X-ray crystallography	-Quinoline-based analogs with methylamine, methylpiperazine substitutions on rings B, C, D; Compounds 6, 8, 9, 11, 12, 13 analyzed	Lung (NSCLC), osteosarcoma, breast cancer	- MTase-Glo assay - IC ₅₀ evaluation - DNA intercalation assays - Enzyme inhibition (DNMT1, CamA, glycosylases, polymerases) - Western blot (p53, p21, γ H2AX)	Inhibition of multiple DNA-modifying enzymes (DNMT1, polymerases, BER glycosylases) - DNA intercalation - Activation of p53 pathway and DNA damage response	- Compound 11 : selective cytotoxicity in A549 cells - Upregulation of p21 and γ H2AX - p53-dependent DNA damage	Quinoline derivatives, especially compound 11 , are promising antitumor agents via DNA intercalation and multi-enzyme inhibition; suitable for cancers with functional p53.
[31]	<i>In vitro</i> & <i>In silico</i>	Cell lines: MCF-7, MDA-MB-231, MCF-10A, LAN-5, HeLa, H292, 16HBE - NCI 60 tumor panel - Docking on HSP90 and ER	1,3,4-substituted pyrrolo[3,2-c] quinoline derivatives - 4g with benzodioxol group - 4h brominated - 4i with di-Cl-OH-Ph - 5 with Cl-propyl chain in position 1	Breast, CNS, Melanoma, Renal, Leukemia, Lung, Cervical	- MTS assay - Cell cycle analysis - Clonogenic assay - ROS measurement - Cell viability assay	- Cell cycle arrest in S phase - Apoptosis induction - ROS increase - HSP90 and ER binding (<i>In silico</i>)	Compound 4g active across 5 tumor panels at 10 μ M - Selective action - Apoptotic effects - Better activity than other analogs	- Compound 4g shows potent and selective antiproliferative activity - Low toxicity in healthy cells - Promising for breast and other cancers

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					- Molecular docking (HSP90/ER)			- Targets HSP90 and ER
[46]	<i>In vitro & In silico</i>	- HepG2 human liver carcinoma cells - Docking on HepG2-related protein target (PDB: 5EQG)	Quinoline derivatives with allyl, amino acid esters, carboxamides, hydrazones, and thio-ether groups - Key compound: 15d (2-(allylthio)-N-tetradecylquinoline-4-carboxamide)	Hepatocellular carcinoma (HepG2)	- Synthesis & structural characterization (NMR, IR, MS, elemental analysis) - Molecular docking (binding energies with 5EQG target) - <i>In vitro</i> cytotoxicity assays (IC ₅₀ determination)	- Binding to 5EQG protein (GLUT1) - H-bond and π -interactions with active site residues - Impacts cellular metabolism and viability	- Compound 15d showed highest activity: IC ₅₀ = 6.529 μ g/mL (close to doxorubicin: 4.059 μ g/mL) Better binding affinity than other analogs (-34.48 kcal/mol)	Compound 15d is a potent and promising anticancer agent against HepG2 - Strong docking interaction - Encouraged for further development
[7]	<i>In vitro & In vivo</i>	- Cell lines: HeLa, SiHa, C-33A (cervical), MiHa (normal) - Nude mice (xenograft model) - Molecular docking & CETSA	- Trifluoromethyl quinoline derivative (FKL117) - Designed and synthesized in-house - Targets HDAC1	Cervical cancer	- MTT assay - Flow cytometry (apoptosis, cell cycle) - Colony formation assay - Western blot - CETSA - Immunofluorescence - <i>In vivo</i> tumor volume and histology	- Inhibits HDAC1 expression and activity - Increases acetylation of histone H3 & H4 - Induces apoptosis (\uparrow Bax, \downarrow Bcl-2) - Arrests G2/M phase (\uparrow cyclin B1, \downarrow CDC2) - HMGB1 cytoplasmic translocation	- IC ₅₀ (HeLa) = 0.022 μ M - SI (selectivity index) = 14.5 - Tumor weight & volume significantly reduced in mice - No significant toxicity to major organs	- FKL117 selectively targets HDAC1 - Promotes histone acetylation - Induces apoptosis and cycle arrest in cervical cancer cells - Safe and promising HDAC1 inhibitor for cervical cancer therapy
[34]	<i>In vitro & In vivo</i>	- SK-OV-3 (ovarian cancer), T24, HepG2, MGC80-3 - Normal cells: WI-38, HL-7702 - Xenograft mouse model	- Quinoline Schiff base ligands (H-L1, H-L2, H-L3) with 2-fluorophenyl group - Cu(II) complexes: Cu1, Cu2, Cu3 (tetrahedral/square planar)	- Ovarian cancer (SK-OV-3), bladder, liver, gastric	- MTT assay - Flow cytometry (apoptosis, cell cycle) - JC-1 (mitochondrial potential)	- Cu(II) reduced to Cu(I) by GSH \rightarrow Fenton-like reaction $\rightarrow \cdot$ OH - Induction of ROS, ER stress, Ca ²⁺ overload - Mitochondrial dysfunction	- Cu1 and Cu2 show higher cytotoxicity than cisplatin - IC ₅₀ (SK-OV-3): Cu1 = 5.27 μ M, Cu2 = 9.40 μ M - Tumor inhibition in mice: Cu1 (48%), Cu2 (58%)	- Cu1 and Cu2 are promising chemodynamic therapy agents - Induce apoptosis via oxidative stress, mitochondrial and ER pathways

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					- ROS & OH detection - Western blot - <i>In vivo</i> tumor model	- Caspase 3/9 activation	- Low toxicity to normal cells	- Effective and selective <i>In vitro</i> and <i>In vivo</i>
[47]	<i>In vitro</i> & <i>In vivo</i>	- Cell lines: Huh7 (liver), MCF-7 (breast), SGC-7901 (gastric), MCF-7/ADM (resistant), HUVECs (normal) - Nude mice orthotopic Huh7 tumor mod	- 6-aryl-4-(3,4,5-trimethoxyphenyl)quinoline derivatives - Scaffold designed to mimic and rigidify CA-4 - Key compound: 14u with indole B-ring	- Hepatocellular carcinoma - Breast cancer - Gastric cancer	- MTT assay - Cell cycle & apoptosis (flow cytometry) - Tubulin polymerization assay - Colchicine competition assay - Immunofluorescence - Molecular docking - <i>In vivo</i> tumor growth & H&E staining	- Inhibits tubulin polymerization - Binds to colchicine site - Induces G2/M arrest - Triggers apoptosis (Annexin V/PI) - Disrupts microtubules	- Compound 14u : IC ₅₀ = 0.03 μM (Huh7), 0.13 μM (MCF-7), 0.18 μM (SGC-7901) - 14u active on MCF-7/ADM (IC ₅₀ = 0.52 μM) - Low toxicity to HUVECs (IC ₅₀ = 5.82 μM) - <i>In vivo</i> : strong tumor reduction without weight loss	- Compound 14u is a potent and selective colchicine-site tubulin inhibitor - Effective <i>In vitro</i> and <i>In vivo</i> - Well tolerated and adheres to drug-likeness criteria
[48]	<i>In vitro</i> & <i>In vivo</i>	- T24 (bladder cancer), SK-OV-3, MGC80-3, HepG2 - Normal cells: WI-38, HL-7702 - Xenograft model in BALB/c mice	- 12 halogenated quinoline Schiff base ligands (H-L1 to H-L12) - Corresponding Cu(II) complexes Cu(L1) ₂ to Cu(L12) ₂ - Key derivatives: Cu(L4) ₂ and Cu(L10) ₂ (fluorinated at R2 and R4)	- Bladder cancer (T24) - Also tested on ovarian, liver, gastric	- MTT assay - Apoptosis & cell cycle (flow cytometry) - ROS & •OH detection (DCFH-DA, MitoROS probes) - Western blot (Bax, Bcl-2, caspases, ER stress proteins) - Cellular uptake (ICP-MS)	- CDT via GSH depletion and Cu(II) → Cu(I) → •OH generation - Mitochondrial dysfunction, ER stress - Bax/Bcl-2 modulation, caspase 3/9 activation - Inhibition of autophagy flux (↑LC3B-II, ↑p62)	- Cu(L4) ₂ and Cu(L10) ₂ show better IC ₅₀ than cisplatin in T24 (≈9.6–9.7 μM) - Cu(L10) ₂ had best uptake and <i>In vivo</i> efficacy (tumor inhibition 58.8%) - No significant weight loss or organ toxicity	- Cu(L10) ₂ is a potent CDT agent combining ROS generation and autophagy inhibition - Superior pharmacokinetics and selectivity make it a promising anticancer candidate

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					- <i>In vivo</i> tumor growth & histology - Pharmacokinetics (C _{max} , AUC, t _{1/2})			
[49]	<i>In vitro</i> & <i>In vivo</i>	- NCI-60 human tumor cell line panel (9 cancer types) - RPMI-8226 cell line (apoptosis/necrosis study) - WI-38 normal cells	- Diarylurea and diarylamide derivatives - Quinoline core with morpholine or dimethylamino side chains - Terminal aryl substitutions (e.g., 4-F-3-CF ₃ , 4-Cl-3-CF ₃ , 3,5-bis-CF ₃) - Key compounds: 1j , 1k , 11	- Broad spectrum: leukemia, NSCLC, colon, CNS, melanoma, ovarian, renal, prostate, breast	- MTT assays - GI ₅₀ and TGI (dose-response) - C-RAF kinase inhibition (IC ₅₀) - Kinase selectivity panel - Caspase-3/7 & LDH assays - Solubility, logD, Caco-2 permeability - Molecular docking	- Selective inhibition of C-RAF kinase (IC ₅₀ : 1j = 67 nM) - Apoptosis and necrosis induction via caspase-3/7 and LDH - High selectivity over off-target kinases	- 1j-1 more potent than sorafenib in >50 cancer cell lines - 11 : strongest cytotoxicity (GI ₅₀ = 0.84 μM in RPMI-8226) - Strong inhibition in multiple tumor types - Minimal effect on WI-38 normal cells	1j-1 are potent and selective C-RAF inhibitors with broad-spectrum anticancer activity - Compound 11 is most promising: potent, selective, soluble, permeable, and effective <i>In vitro</i> and <i>In vivo</i>
[50]	<i>In vitro</i> & <i>In vivo</i>	- Cell lines: MCF-7 (breast cancer), MCF-12A (normal) - <i>In vivo</i> : DMBA-induced breast cancer in Wistar rats - Molecular docking & MD simulation with EGFR	- 5-(4-chloroquinolin-3-yl)methylene)-2-(piperazin-1-yl)-1,3-thiazol-4(5H)-ones - Substituted piperazine groups (alkyl, aryl, alkoxy) in compounds 8a-8i - Key compound: 8i (ethoxymethyl piperazine)	Breast cancer	- MTT assay (cytotoxicity) - EGFR-TK inhibition (Kinase-Glo) - Molecular docking (Schrödinger) - MD simulation (GROMACS) - <i>In vivo</i> evaluation: tumor volume, body weight, antioxidants, histology	- EGFR-TK inhibition (8i : 87.5%) - Binding to EGFR (Lys745, Asp855, Phe723) - ↑ SOD, catalase, glutathione - ↓ lipid peroxidation and tumor growth	- Compound 8i : IC ₅₀ = 36.2 μM (MCF-7), non-toxic to MCF-12A - Tumor volume reduced by 52.71% at 150 mg/kg - Antioxidant markers restored - Comparable to methotrexate	- Compound 8i is a potent EGFR-TK inhibitor - Shows selective anticancer activity with low toxicity - Effective <i>In vitro</i> and <i>In vivo</i> ; supports further development

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[51]	<i>In vitro</i> (NMR-based binding assay)	- Recombinant β -Catenin armadillo domain (residues 141–end) - TCF4 peptide (residues 13–50)	- 2-Amino-4-(2-chloroquinolin-3-yl)-7-hydroxy-4H-chromene-3-carbonitrile (compound 3a) - Chromene-quinoline scaffold	Colorectal cancer	- Water-LOGSY NMR assay - 1D ^1H NMR - Competition assay with TCF4	- Selective reversible binding of compound 3a to β -Catenin - No interaction with TCF4 - Does not disrupt β -Catenin/TCF4 complex - Potential allosteric modulation	- Signal inversion in Water-LOGSY confirms binding to β -Catenin - Interaction remains in presence of TCF4	- Compound 3a is a promising β -Catenin-targeted ligand - Potential scaffold for anticancer drug development against colorectal cancer
[52]	<i>In silico</i> & <i>In vitro</i>	- Cell lines: A549 (lung cancer), MCF-7 (breast cancer) - Computational docking: c-Abl kinase (PDB: 1IEP)	- Quinoline-amidrazone hybrids (10a–10l) - Derived from 6-aminoquinoline and cyclic amines (piperazine, morpholine, etc.) - Key active compounds: 10d and 10g	Lung cancer and breast cancer	- MTT assay (IC_{50} determination) - Molecular docking (LibDock, c-Abl kinase) - ADMET prediction (Discovery Studio) - Toxicity prediction (Daphnia EC_{50} , TOPKAT)	- Predicted inhibition of c-Abl kinase via interaction with active site residues: - Hydrogen bonds with Met318, Thr319, Asp382 - π - π stacking with Phe382 - Acceptable pharmacokinetics but high aquatic toxicity.	- 10d: IC_{50} = 43.1 μM (A549) - 10g: IC_{50} = 59.1 μM (MCF-7) - Other compounds less active (IC_{50} > 100 μM) - 10d and 10g = non-carcinogenic	Compounds 10d and 10g are most promising leads - Likely act via c-Abl kinase inhibition - Further <i>In vivo</i> validation and optimization needed due to high aquatic toxicity
[17]	<i>In vitro</i> & <i>In vivo</i>	- MiaPaCa-2 & PANC-1 (PDAC cell lines) - MRC-5 (normal) - Zebrafish xenograft model	- 4-aminoquinoline derivatives (compounds 1–3) - Derived from antimalarial scaffolds with favorable toxicological profile	Pancreatic ductal adenocarcinoma (PDAC)	- MTT assay - Flow cytometry (apoptosis, cycle) - Mitochondrial membrane potential (MMP) - ROS/mROS quantification - Immunostaining (LC3, LAMP1, p62)	- Increased apoptosis via mitochondrial pathway - Elevated ROS and mitochondrial ROS levels - Loss of mitochondrial membrane potential (depolarization) - Upregulation of LC3-II and p62 (autophagy inhibition)	- Compounds 1–3 active at nanomolar to low micromolar range - Compound 1 most potent: induced apoptosis in 35% (PANC-1), 25% (MiaPaCa-2) - Inhibited tumor growth and metastasis in zebrafish model	- 4-aminoquinolines are promising anti-PDAC agents - Dual action: induction of apoptosis and inhibition of autophagy - Compound 1 is most potent and least toxic

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					- <i>In vivo</i> zebrafish model (toxicity & metastasis)	- Altered lysosomal function - Low general toxicity (LC50 > 60 μM for compound 1)		
[53]	- <i>In vitro</i> & <i>In silico</i>	- MCF-7 (breast), HCT-116 (colon), A549 (lung), NIH3T3 (normal fibroblasts) - DFT calculations and molecular docking (DNA intercalation)	- Coumarin-quinoline hybrids complexed with Re(I) tricarbonyl core - Re(I)-CO ₃ complexes with bidentate coumarin-quinoline ligands (L1-L4)	Breast, colon, lung cancer	- MTT assay (IC ₅₀) - Selectivity index (SI) - UV-Vis spectroscopy - DNA interaction studies - Molecular docking on DNA	- Likely DNA intercalation through π-π stacking of planar ligand - Mitochondrial dysfunction and ROS elevation inferred - DFT supports stable DNA binding conformatio	Complex 5dRe most potent: IC ₅₀ = 4.5 μM (MCF-7), SI = 7.8 - Lower cytotoxicity on NIH3T3 (normal) cells - Structure-activity relation favors L1/L2 ligands	Coumarin-quinoline-Re(I) complexes are effective and selective anticancer agents - Complex 5dRe is most promising - DNA targeting and redox-active metal core enhance efficacy
[11]	- <i>In vitro</i> & <i>In vivo</i> & <i>In silico</i>	- Cell lines: OCI-Ly10, SU-DHL-2 (ABC-DLBCL) - Xenograft in nude mice - SHP-1 truncation mutants - ITC, SAXS, CETSA - Molecular docking & MD simulations	- Thieno[2,3-b]quinoline core with procaine or procainamide side chain - Best compound: 3b , with 8-methyl substitution - SAR confirms methyl at position 8 and procaine are critical for activity	Diffuse large B-cell lymphoma (ABC-DLBCL)	- SHP-1 enzymatic activity assays (EC50 = 5.48 μM for 3b) - Western blot (p-STAT3) - Flow cytometry (apoptosis) - CETSA (cellular thermal shift) - Xenograft tumor model (SU-DHL-2) - Molecular docking and MD with SHP-1	- Allosteric activation of SHP-1 via N-SH2 and C-terminal domain interaction - Inhibition of p-STAT3 signaling pathway - H-bonding with Gln87 and His51 confirmed by docking and mutagenesis - Conformational shift from closed to open SHP-1 structure	- 3b induced dose-dependent apoptosis in OCI-Ly10 and SU-DHL-2 - Reduced p-STAT3 levels in both cell lines - Inhibited tumor growth <i>In vivo</i> (SU-DHL-2 xenograft) - No significant toxicity observed <i>In vivo</i>	- Compound 3b is a direct, selective allosteric SHP-1 activator - First validation of SHP-1 activation alone as therapeutic strategy in ABC-DLBCL - Promising scaffold for further development of anticancer agents targeting STAT3 via SHP-1
[12]	<i>In vitro</i> & <i>In silico</i>	- Cell lines: SMMC7721 (liver), HCT116, HT-29, TFK-1	- Quinoline-thiosemicarbazone hybrids: Complex 1: [Cu(qcpt)(PPh ₃) ₂ Br]·2CH ₃ CN	- Liver (principal), colorectal, bile duct	- MTT assay (IC ₅₀) - Flow cytometry: apoptosis, cell cycle, ROS, Ca ²⁺ , Δψ _m	- Complex 1: - Enters cells and accumulates in nuclei and mitochondria	- IC ₅₀ (SMMC7721) = 1.58 μM for complex 1 - More active than cisplatin	- Complex 1 shows potent dual-targeting activity: DNA damage and mitochondrial dysfunction

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		- Spectroscopic and docking studies with ctDNA	Complex 2: [Cu ₂ (qcapt)(Ac) ₂ (CH ₃ OH)] - Ligands contain quinoline-2-carboxaldehyde-pyridine-thiosemicarbazone		- DNA binding: EB displacement, CD, docking - DNA cleavage assay	- Induces ROS production and Ca ²⁺ overload - Causes mitochondrial membrane depolarization and ATP depletion - Intercalates DNA (K _{app} ≈ 4 × 10 ⁶ M ⁻¹) - Cleaves DNA in the presence of H ₂ O ₂	- Induces S-phase cell cycle arrest - Triggers apoptosis: 29.5% (2.5 μM), 62.8% (5 μM)	- Acts through ROS generation, ATP loss, and DNA intercalation - Promising anticancer candidate with strong apoptotic effects
[54]	<i>In vitro</i>	- Cell lines: HCT116 (colon), TFK-1 (bile duct), SMMC7721 (liver), L-02 (normal liver) - DNA interaction (CT-DNA, pBR322)	- Complexes [Cu(btmbq)Br] ₂ (1) and [Cu(btmbq)Cl] ₂ (2) - Ligand: btmbq (benzotriazolyl-methyl-quinoline-benzimidazole hybrid)	- Colon (principal), bile duct, live	- MTT assay (IC ₅₀) - Flow cytometry (apoptosis, cell cycle, ROS, Ca ²⁺ , Δψ _m) - ICP-MS (cellular Cu uptake) - CD, EB displacement, DNA cleavage - Cyclic voltammetry	- DNA intercalation and oxidative cleavage (pBR322) - ROS and Ca ²⁺ overload - Collapse of mitochondrial membrane potential - ATP depletion - G2 phase cell cycle arrest - Induction of apoptosis	- Complex 1: IC ₅₀ = 10.1 μM (HCT116), more active than cisplatin (12.4 μM) - Lower toxicity on normal L-02 cells than cisplatin - Induces G2 arrest and apoptosis (up to 52%)	Complex 1 is a potent dual-target agent: DNA and mitochondria - Antitumor effects linked to ROS generation, mitochondrial dysfunction, and DNA damage - Promising scaffold for further anticancer development
[55]	<i>In silico</i> (DFT, docking, ADMET)	- Molecular docking with Bcl-2, Caspase-3, EGFR, mTOR, PI3K (PDB IDs: 6OOK, 5I9B, 2J6M, 4DRH, 4TV3)	- Benzimidazo methoxy quinoline-2-one ligand (BMQ) - Metal complexes: Co-Q, Ni-Q, Cu-Q, Zn-Q and Co-Im, Ni-Im, Cu-Im, Zn-Im - Coordination via imidazole-imine or quinoline-nitrogen	- Target: proteins involved in various cancers (e.g. Bcl-2 in lymphoma, EGFR in lung, PI3K in glioblastoma)	- DFT (Gaussian 16) - Molecular descriptors (FMO, MEP) - Molecular docking (AutoDock Vina) - ADMET prediction (SwissADME, pkCSM)	- Im-metal complexes show stronger binding than Q-metal - Ni-Im: best electrophilicity, softness, lowest HOMO-LUMO gap - Strong hydrogen bonding	- Ni-Im and Co-Im have best docking scores (e.g. Ni-Im with mTOR: -8.7 kcal/mol) - ADMET shows good oral bioavailability, BBB permeability, low toxicity - Im-complexes more	- BMQ-metal complexes, especially Ni-Im and Co-Im, are promising lead compounds - High stability, reactivity, and drug-likeness support anticancer potential - Strong candidate scaffolds

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
						and pi stacking interactions with protein active sites - Active residues involved: ARG146, PHE104, TYR2105, SER629, etc.	favorable pharmacologically than Q-complexes	for protein-targeted cancer drug design
[56]	<i>In vitro</i> & <i>In silico</i>	Cell lines: HepG2 (liver), SK-LU-1 (lung), MCF-7 (breast) - Docking on EGFR (PDB: 4HJO)	- Zerumbone-quinoline conjugates (compounds 16a–k) - Substitution on quinoline ring (e.g. Cl, OCH ₃ , NO ₂) - Linked at position C-15 of zerumbone via ether linker	Liver, lung, breast cancer	- MTT assay (IC ₅₀ values) - Docking studies with EGFR - SAR analysis of substituents	- EGFR binding via π - π stacking and hydrogen bonding - Better activity with electron-withdrawing groups (e.g. NO ₂) - Molecular docking shows interaction with EGFR active site	- Compound 16j: IC ₅₀ = 1.02 μ g/mL (HepG2), 1.31 μ g/mL (SK-LU-1), 1.09 μ g/mL (MCF-7) - Higher activity than parent zerumbone	- Quinoline conjugates of zerumbone show potent and selective anticancer activity - 16j highlighted as lead compound - Valid scaffold for future EGFR-targeting agents
[57]	<i>In vitro</i> & <i>In silico</i>	- Cell lines: MCF-7 (ER ⁺ breast), Ishikawa (endometre)	- Quinoline core with acrylic acid side chain - Ketone linker to improve pharmacokinetics - Series 18a–q and 24a–g	- ER positive breast cancer	- MTT assay (IC ₅₀) - Western blot (ER degradation) - RT-qPCR, ERE-luciferase assay - Fluorescence microscopy - Molecular docking	- Induces degradation of ER α via proteasome-dependent mechanism - Suppresses estrogen signaling - Triggers immunogenic cell death, evidenced by increased calreticulin exposure, elevated HMGB1 release, and enhanced extracellular ATP levels	- 18j: IC ₅₀ = 0.15 μ M (MCF-7) - 24d: stronger ER α degradation at 10 μ M - Activity comparable to fulvestrant	- Quinoline-based SERDs 18j and 24d are highly effective at degrading ER α - Demonstrate dual action through hormonal suppression and immunogenic cell death - Strong candidates for development in ER ⁺ breast cancer immunotherapy
[58]	<i>In vitro</i> - <i>In silico</i> (DFT, QSAR)	Cell line: HepG2 (liver cancer)	- Pentacyclic quinolino[3',4':5,6]pyrano[3,2-c]quinoline - Derivatives 5–7 and 11–13	Hepatocellular carcinoma (HepG2)	- MTT assay for IC ₅₀ - DFT: HOMO-LUMO, hardness, softness, electrophilicity	- Activity linked to softness, ΔE (gap), E_{HOMO} , E_{LUMO} - Higher softness and lower ΔE = greater cytotoxicity	- Compound 13: IC ₅₀ = 5.76 μ M - Compounds 5–7, 11–12: IC ₅₀ = 6–9 μ M	- Novel chromone-quinoline hybrids exhibit promising <i>In vitro</i> cytotoxicity

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			via nucleophilic ring opening of chromone moiety - Various amine substituents (methylamine, benzylamine, etc.)		- QSAR correlations with IC ₅₀	- No cellular mechanism directly tested	- All better than Cisplatin control (17.86 μM)	- Electronic descriptors accurately predict activity - Compound 13 = best lead for further optimization
[21]	- <i>In vitro</i> - <i>In vivo</i> - <i>In silico</i> (crystal docking)	- Cell lines: MV4-11 (AML), CT26 (colon), 293-WT, 293-dKO - Mouse models: CT26 (Balb/c), MV4-11-luc (NSG)	- Quinoline-6-carbonitrile scaffold - Key compound: 20a (Senexin C) - Modifications: substitutions on quinoline ring and linker optimization	- Acute myeloid leukemia (AML) - Colon cancer	- Lanthascreen binding assay - NFκB reporter assay - Luciferase reporter in MV4-11-luc - PK/PD and tissue distribution studies - Crystal structure docking (PDB: 4F7S)	- CDK8/19 inhibition via ATP-competitive binding - Nitrile group interacts with hinge region (Ala100) - Downregulates transcriptional targets: MYC, CXCL8, CCL12, KLF2	- Inhibits MV4-11 proliferation (IC ₅₀ = low μM) - Tumor regression <i>In vivo</i> (CT26, MV4-11-luc) - Selective for CDK8/19 over other CDKs - 20–40× higher tumor vs plasma drug levels	- Senexin C (20a) is a potent and selective CDK8/19 inhibitor - Demonstrates strong tumor-targeting and oral bioavailability - Promising candidate for further clinical development
[25]	- <i>In vitro</i> - <i>In vivo</i> - <i>In silico</i> (docking)	- Cell lines: A549 (lung), H1299, MDA-MB-231, MCF-7, HT-29, H1975 (EGFR mutant) - <i>In vivo</i> : A549 xenograft in nude mice - Normal: HEK-293, PBMCs, H9c2 (cardiac)	Quinoline-bridged hydroxamates (Designed via e-pharmacophore approach) – Quinoline cap + hydroxamic acid (ZBG) – Linker length variation + phenyl/methoxy modifications	Lung, breast, colon, resistant lung cancer	- Topo I/II inhibition (decatenation & relaxation assays) - HDAC1/6/8 isoform profiling (IC ₅₀) - Docking on hTopoIIα, HDAC1/6/8 - 2D/3D culture, flow cytometry (ROS, JC-1) - Western blot, qPCR - <i>In vivo</i> xenograft tumor suppression	Dual inhibition of Topo I/II and HDAC1 - No DNA intercalation - Induction of ROS, mitochondrial dysfunction - Activation of mitophagy & autophagy - Inhibition of Topo-HDAC protein-protein interaction	IC ₅₀ : - A549: < 1 μM - H1975: 250 nM <i>In vivo</i> : - 67% tumor inhibition @15 mg/kg - 84% tumor inhibition @30 mg/kg - No toxicity to HEK-293 or cardiac cells	Compound 5c is a potent multi-target anticancer agent with excellent <i>In vitro</i> and <i>In vivo</i> efficacy, low toxicity, and strong HDAC1 selectivity. Highly promising for future development.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
[59]	- <i>In vitro</i> - <i>In vivo</i> -like assays (HUVEC, migration/invasion) - Spectroscopic & structural	- Cell lines: HeLa, NCI-H460, HepG-2, BGC-823 - Normal cells: HUVEC - Crystal structure confirmed via XRD	Cu(I)-quinoline Schiff base complexes [Cu ₂ (L1) ₂ (μ-Br) ₂] and [Cu ₂ (L1) ₂ (μ-Cl) ₂] - Ligand L1: 4-methyl-N-(quinolin-2-ylmethyl)aniline - In situ reduction of Cu(II) to Cu(I) during synthesis	Cervical (Hela), Lung (NCI-H460), Liver (HepG2), Gastric (BGC-823)	- X-ray diffraction - UV-Vis, IR, HRMS - DNA binding & cleavage assays - MTT, Colony assay - ROS, ΔΨ _m , apoptosis (Hoechst, JC-1) - Cell cycle, Transwell, angiogenesis (Matrigel)	- Self-activated DNA cleavage (via hydroxyl radicals) - Binds DNA ($K_b \approx 10^5 M^{-1}$) - Generates ROS, disrupts ΔΨ _m - Induces apoptosis via mitochondrial dysfunction - Inhibits migration, invasion, and angiogenesis	- IC ₅₀ (μM): – Complex 1: 14.3–30.5 – Complex 2: 14.8–27.1 – Both ~5–7× less toxic to HUVEC than oxaliplatin - High cellular uptake (ICP-OES) - Colony formation ↓ >70% in most lines - TGI & angiogenesis inhibition confirmed	Complexes 1 and 2 show broad-spectrum <i>In vitro</i> antitumor activity with low toxicity and strong mitochondrial apoptosis induction. Promising multifunctional copper-based leads for cancer therapy.
[60]	- <i>In vitro</i> - <i>In silico</i> (docking, MD, MM-PBSA) - ADME/T prediction	- Cell lines: A549 (lung), HT-29, HCT116 (colorectal), MCF-7 (breast), A2780 (ovarian) - No <i>In vivo</i> model	Quinoline-based benzamide derivatives (10a–t): – Quinoline "Cap" with 2-methyl or aryl groups – 4-position: benzamide linker – ZBG: o-phenylenediamine – Designed as HDAC pharmacophore (Cap-Linker-ZBG)	Colorectal (HT-29, HCT116), breast, lung, ovarian	- MTT assay (cytotoxicity) - HDAC inhibition (Pan-HDAC assay) - Docking (HDAC1/HDAC3) - MD simulation - MM-PBSA binding energy - SwissADME, pkCSM analysis	- HDAC inhibition (Pan-HDAC): compounds 10a , 10b , 10c most potent - 10a binds HDAC1/3 active site better than Entinostat - Interacts with Zn ²⁺ + catalytic residues - Good stability and H-bond profile in MD	- IC ₅₀ (cytotoxicity): 10a: 8.6 μM (HCT116), 14.5 μM (HT-29) 10b: 9.9 μM (HCT116), 12.02 μM (HT-29) - HDAC inhibition IC ₅₀ : 10a: 1.1 μM (HCT116), 2.99 μM (HT-29) Better than Entinostat in some metrics	10a (simplest, 2-methyl) and 10b (methyl-substituted) are the most potent. Low steric hindrance → better HDAC binding. Good leads for pan-HDAC inhibition & colorectal cancer therapy. <i>In silico</i> ADMET supports oral bioavailability.
[61]	- <i>In vitro</i> - <i>In vivo</i> - <i>In silico</i> (SAR modeling)	- Cell lines: B16–F10 (melanoma), A549, HepG2, MCF-7 - <i>In vivo</i> : B16–F10 mouse model	Trimethoxyanilino-substituted pyrimidine & quinazoline derivatives – Substituents at 2-/4-position – Focus on compound 2k : 1-methyl-1H-indolyl at position 2	Melanoma, lung, liver, breast	- MTT assays (IC ₅₀ values) - Tubulin polymerization inhibition - Immunofluorescence (β-tubulin)	- Inhibits tubulin polymerization (IC ₅₀ = 22.23 μM) - Induces G2/M arrest (82.4% at 200 nM)	- 2k IC ₅₀ (μM): B16–F10: 0.098 A549: 0.135 HepG2: 0.109 MCF-7: 0.259 - <i>In vivo</i> tumor inhibition:	Compound 2k is a potent microtubule polymerization inhibitor with comparable efficacy to colchicine. Shows strong <i>In vitro</i> and <i>In vivo</i> activity with good safety profile.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
			– Structural simplification based on colchicine		- Flow cytometry (G2/M arrest, apoptosis) - Wound healing assay - <i>In vivo</i> tumor growth (C57BL/6 mice)	- Triggers apoptosis (Annexin V assay) - Disrupts cytoskeleton (β -tubulin staining) - Reduces cell migration	57.9% (15 mg/kg), 79.6% (30 mg/kg) - No toxicity observed in mice	Promising candidate for further development.
[62]	- <i>In vitro</i> - <i>In vivo</i> (xenograft) - (tumor spheres) - <i>In silico</i> (docking)	- Cell lines: MDA-MB-231, A549, OVCAR-3, HeLa, MCF-10A - <i>In vivo</i> : MDA-MB-231 xenografts in nude mice	QUM prodrugs of 8-HQ: - Alkylation at quinoline N \rightarrow QUM-1–QUM-4 - Dual-masked (QUM-5–QUM-9) via N & O groups - Stimuli: H ₂ O ₂ , β -Glc, UV, etc. - QUM-1 (H ₂ O ₂), QUM-4 (β -Glc), QUM-5 (UV/H ₂ O ₂)	Breast (MDA-MB-231), Lung, Cervical, Ovarian	- HPLC, NMR, UV-Vis - MTT, JC-1 ($\Delta\psi$ m), EdU - Apoptosis, ROS, ATP, Ca ²⁺ , γ -H2A.X - tumor sphere assay - <i>In vivo</i> tumor model - Hepato/renal toxicity evaluation	- Stimulus-responsive 8-HQ release - Selective cytotoxicity via ROS elevation - Disruption of mitochondrial membrane potential - Reduction in ATP levels - Increase in intracellular calcium - Enhanced apoptosis - QUM-5: dual-stimulus control improves safety	- QUM-1 IC ₅₀ (μ M): MDA-MB-231: 0.83 A549: 3.48 OVCAR-3: 6.63 HeLa: 11.20 MCF-10A: >10 - QUM-5 <i>In vivo</i> : 63.1% tumor inhibition @ 20 mg/kg - QUM-4 more selective than O-masked counterpart QU-4 - QUM-4 uptake enhanced via GLUT transporters - Minimal toxicity observed in liver and kidney vs 8-HQ	QUM-based dual-masked prodrugs offer cancer-specific release with high efficacy and safety. QUM-1 and QUM-4 show strong tumor selectivity. QUM-5 achieves synergistic activation and reduced systemic toxicity.
[63]	- <i>In vitro</i> - <i>In vivo</i> (xenograft) - <i>In silico</i> (docking)	- Cell lines: KYSE30, KYSE70, KYSE270, KYSE450 (ESCC) - Normal: HUVEC - <i>In vivo</i> : KYSE30 xenograft in nude mice	4-phenyl-5-quinolinyl isoxazole analogues – Inspired by CA-4 (colchicine site inhibitor) – Three scaffold series (A, B, C) – Lead: C11 (2-methyl-quinoline, para-methoxyphenyl)	Esophageal squamous cell carcinoma (ESCC)	- MTT, colony formation - Tubulin polymerization (cell-free + IF) - EBI competition assay - Flow cytometry (G2/M arrest, apoptosis)	- Binds colchicine site on β -tubulin - Inhibits tubulin polymerization - Arrests G2/M phase - Induces apoptosis (Caspase-3/7/9, cleaved-PARP)	- IC ₅₀ (C11): – KYSE30: 13 nM – KYSE70: 14 nM – HCT116, MGC-803: 14–26 nM - <i>In vivo</i> : – Tumor inhibition: 6 mg/kg (strong), 12 mg/kg > CA-4 – No liver/kidney toxicity	Compound C11 is a potent microtubule polymerization inhibitor targeting the colchicine site. Shows excellent <i>In vitro</i> & <i>In vivo</i> activity against ESCC with a strong safety profile.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
					- RTCA proliferation - <i>In vivo</i> tumor growth - Liver/kidney safety markers	- Inhibits cell migration	- No significant body weight loss	Promising lead for CA-4-based anticancer drug development.
[27]	- <i>In vitro</i> - <i>In vivo</i> (MCA205 allograft in mice) - <i>In silico</i> (docking on HDAC8 and tubulin)	- Cell lines: HCT116, HT-29 (resistant), A549, MCF-7, K562R (MDR), MCA205 <i>In vivo</i> : MCA205 fibrosarcoma model (intratumoral injection)	Quinoline-2-carbonitrile hydroxamic acids - Hydroxamate ZBG - Csp ² -Csp ² linkers - N-Me cap vs. C=CH ₂ analogs - Lead: 12a, 12d	Colon, breast, lung, leukemia (MDR), fibrosarcoma	- MTT (IC ₅₀), HDAC isoform profiling (HDAC6, 8, 11) - Flow cytometry (cell cycle, apoptosis) - JC-1 (mitochondrial membrane), γH2AX - Tubulin polymerization, docking, WB (SMC3) - <i>In vivo</i> tumor regression, survival	- Dual inhibition: colchicine-site tubulin + HDAC8/6/11 - Causes G2/M arrest, mitochondrial depolarization - Caspase-dependent apoptosis - HDAC8 selective (IC ₅₀ : 150–280 nM) - Inhibits DNA repair (γH2AX ↑)	- 12a IC ₅₀ (nM): HCT116: 0.5 HT-29 (resistant): 0.6 K562R (MDR): sub-nM - <i>In vivo</i> (MCA205): 70% tumor regression at 0.5 mg/kg intratumoral - No systemic toxicity observed	2a and 12d are potent second-generation dual HDAC/tubulin inhibitors with broad-spectrum cytotoxicity, MDR-resistance circumvention, and favorable metabolic stability. Excellent candidates for clinical development.
[64]	- <i>In vitro</i> - Transcriptomics (RNA-seq) - <i>In silico</i> (docking, PPI network)	- Cell line: BGC823 (gastric cancer) - No <i>In vivo</i> model used	Benzimidazole-quinoline Cu(II) complex (Complex 1): - Cu(p-2-bmq)Cl ₂ - p-2-bmq = 2-((1-(pyridin-2-yl)-1H-benzimidazol-2-yl)methyl)quinoline - Previously synthesized & structurally confirmed	Gastric cancer	- MTT, JC-1 (mitochondrial membrane potential), AO/EB & Hoechst staining - Flow cytometry (apoptosis, cell cycle) - Transwell & scratch assay - ROS detection - RNA-seq, GO & KEGG analysis - Docking to GNG7 mode	- Induces oxidative stress & ROS accumulation - Causes mitochondrial dysfunction and loss of mitochondrial membrane potential - G2/M phase cell cycle arrest - Activates apoptosis pathways - Inhibits migration & invasion	- Inhibits BGC823 proliferation dose-dependently - IC ₅₀ : not numerically stated, but compared to cisplatin (less cytotoxic) - Strong apoptosis induction (up to 75%) - G2/M arrest + invasion inhibition confirmed	Complex 1 exhibits promising antiproliferative activity via mitochondrial dysfunction and multi-pathway modulation. Transcriptomic insights support its potential as a copper-based chemotherapeutic agent. Strong candidate for future targeted therapy development.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
						- DEGs affect p53, MAPK, mTOR, AMPK, TNF signaling	- Transcriptomics: 6050 DEGs, 478 hub genes - Docking score = -9.18 kcal/mol with GNG7	
[65]	- <i>In vitro</i> - <i>Ex vivo</i> - <i>In silico</i> (DFT, docking) - Transcriptome reference	- Cell line: DL (T-cell lymphoma, murine) - Normal: thymocytes - No <i>In vivo</i> model	Quinoline-dipyrrin Ru(II) arene complexes - R1: η6-benzene - R2: η6-p-cymene - Ligand: 2-chloro-3-bis(pyrrolylmethyl)quinoline	T-cell lymphoma (murine DL)	- MTT, Trypan blue - Wright-Giemsa (apoptosis) - UV-Vis, EB displacement - DNA thermal denaturation - JC-1, viscosity, protein binding - DFT (HOMO/LUMO), docking - BSA interaction (3D, synchronous fluorescence)	- Intercalation with DNA (UV-vis, viscosity, EB) - Binding to BSA (1:1, Kb = 6.1×10^4 – 7.6×10^4 M ⁻¹) - Induces apoptosis (membrane blebbing) - G2/M arrest, mitochondrial potential loss - Static quenching and conformational shift in BSA	- IC ₅₀ (μM): R1: 30 R2: 20 - R2 > R1 in all assays - R2 more lipophilic (logP ↑) - Apoptosis in 75% of DL cells - No cytotoxicity on normal thymocytes	R1 and R2 show dual DNA-protein binding via intercalation and static protein interaction. R2 more potent due to better lipophilicity and protein affinity. Effective & selective cytotoxins for T-cell lymphoma with minimal off-target toxicity.
[66]	- <i>In vitro</i> - <i>In vivo</i> (xenograft) - Transcriptomics - <i>In silico</i> (docking, SAR, NMR)	- Cell lines: KMS-11, OPM2, RS4:11, HL-60, THP-1, MOLM13, etc. - <i>In vivo</i> : KMS-11 MM xenografts (oral)	Quinoline-5,8-dione analogs (14a-m, 15a-m) - Substituted at C-6/C-7 with diverse amines & linkers - Lead: 15a (but-2-ynoyl tail, C-6 substituted) - Based on DA3003-1 scaffold	Multiple myeloma, leukemia (ALL, AML), lymphoma	- NSD2 enzymatic assay - MTT/CCK-8 (viability) - RT-PCR, ChIP-qPCR - RNA-seq (GO/KEGG) - Apoptosis (FC, WB) - PK studies (AUC, T _{1/2} , F%) - NMR (STD, CPMG)	- Selective NSD2 inhibition (IC ₅₀ : 0.23 μM) - Suppresses H3K36me2 in gene promoters - Blocks transcription of NSD2 target genes (TGFA, MET...) - Alters mTOR, Hippo, FoxO signaling - Induces apoptosis (Bid/Bim ↑, Bcl-xl ↓)	- IC ₅₀ (KMS-11): 0.27 μM - Active in NSD2 mutant cell lines (OPM2, RS4:11) - Less active in wild-type (HL-60: 2.6 μM; Daudi: 12.8 μM) - <i>In vivo</i> (oral): TGI = 56–58.4% at 75–150 mg/kg - No weight loss or toxicity observe	15a is a potent, selective, orally bioavailable NSD2 inhibitor. Demonstrates strong <i>In vitro</i> and <i>In vivo</i> efficacy via epigenetic modulation. High-value candidate for hematologic malignancies with NSD2 dysregulation

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					- Xenograft (tumor growth, toxicity)	- Minimal off-target methyltransferase inhibition		
[67]	- <i>In vitro</i> - <i>In silico</i> (molecular docking)	- Cell lines: HT29 (colon), MCF7 (breast), HepG2 (liver) - Normal: Hs27 (fibroblasts) - No <i>In vivo</i> model	Benzo[h]quinoline-3-carbonitrile derivatives (CMMP, CNMP, CPMP, CRMP, CTMP) - 2-amino-4-substituted (e.g., NO ₂ -Ph, Me ₂ N-Ph, Naphthyl) - Most active: CNMP (2)	Colon, breast, hepatocellular carcinoma	- MTT assay (LC50) - Molecular docking with cancer proteins: 3EQM (breast), 3IG7 (colon), 4FM9 (liver) - Docking scores, H-bond, hydrophobic interaction	- CNMP showed strong docking scores with all 3 targets: - Breast: -7.55 kcal/mol - Colon: -6.90 kcal/mol - Liver: -6.90 kcal/mol - H-bonds to Trp141, Arg145, Arg435 (3EQM) - Nitro substitution key to binding and cytotoxicity	- LC50 (μM) for CNMP: - MCF7: 8.24 - HT29: 21.23 - HepG2: 26.15 - Comparable or better than doxorubicin in colon - CTMP also potent: LC50 (MCF7) = 10.12 μM - CPMP & CRMP less active	CNMP (2) and CTMP (5) exhibit potent <i>In vitro</i> anticancer activity, supported by strong docking with key cancer targets. Nitro and naphthyl substituents enhance activity. CNMP proposed as a promising scaffold for further anticancer development
[42]	- <i>In silico</i> (DFT, ADMET, docking) - No <i>In vitro</i> / <i>In vivo</i> yet	- 11 cancer-associated protein targets (CDK2, PI3K, EGFR, etc.) - Compared with doxorubicin	8-Nitroquinoline hydrazides (6a-6c) - Core: 2-cyano-N'-(8-nitroquinolin-4-ylidene)acetohydrazide - Substituents at C6: H (6a), Cl (6b), Me (6c) - Best: 6c (methyl group)	Computationally predicted across multiple cancer types: colon, breast, lung, CNS	- DFT: FMO, MEP, HOMO-LUMO, global reactivity descriptors - ADMET: SwissADME, ProTox-3.0 - Docking (PyRx, Discovery Studio) vs 11 oncogenic proteins - Binding site analysis, drug-likeness (Lipinski), radar plot	- 6c shows best drug-likeness (Lipinski compliant, bioavailability radar positive) - Binds strongly to CDK2 (-8.7 kcal/mol) and PI3K (-7.5 kcal/mol) - Stable π-π, H-bond & hydrophobic interactions - Nitro and hydrazide groups form active site interactions	- 6c: best docking vs doxorubicin for CDK2, PI3K - All compounds absorbed via GI tract, not BBB-permeable - 6c shows low predicted toxicity (only CYP1A2 inhibition) - LD50 for 6c = 1000 mg/kg (moderate)	6c shows potent dual kinase binding (CDK2 & PI3K) with strong pharmacokinetics and safety profile. Validated for further <i>In vitro</i> / <i>In vivo</i> evaluation as a cancer drug lead. In-silico studies strongly support its anticancer potential.
[38]	- <i>In vitro</i> - <i>In vivo</i> (xenograft, MDA-MB-231)	- Cell lines: MDA-MB-231, MCF-7, A549, A549/CDDP, WI-38 - <i>In vivo</i> : xenograft mouse model (MDA-MB-231)	- Cycloplatinated (II) complexes Pt-1-Pt-4 - C [^] N isoquinoline alkaloid ligand	Triple-negative breast cancer (TNBC)	- MTT, IC ₅₀ , resistance factor - ICP-MS (uptake), log P (shake flask)	- Induces autophagy and ferroptosis, both validated by LC3-II ↑, p62 ↓, GPX4 ↓ - Ferroptophagy-dependent	- Pt-3: IC ₅₀ (MDA-MB-231) = 2.24 μM - More active than cisplatin (lower IC ₅₀ , better RF)	Pt-3 induces ferroptophagy-dependent ferroptosis in TNBC through selective ROS and iron metabolism modulation.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
	- <i>In silico</i> (docking, lipophilicity)		- Ancillary N ^N ligands: phenanthroline (Pt-3), bipyridine (Pt-2), etc. - Lead compound: Pt-3		- Autophagy/ferroptosis inhibition assays - Western blot (LC3, p62, GPX4) - ROS, LPO, MDA assays - Confocal microscopy (autophagy vacuoles) - <i>In vivo</i> tumor inhibition & toxicity	ferroptosis via FTH degradation - ROS ↑, lipid peroxidation ↑, labile iron pool ↑ - Uptake via energy-dependent nonendocytic mechanism - Selective for cancer vs normal cells	- Resistance factor (Pt-3) = 1.44 vs cisplatin = 7.12 - <i>In vivo</i> : 65.3% tumor inhibition (vs 43.1% for cisplatin) - No weight loss or acute toxicity observed	Exhibits superior activity, selectivity, and safety profile compared to cisplatin. Strong candidate for ferroptosis-based metal anticancer therapy.
[23]	- <i>In vitro</i> - <i>In vivo</i> (MV4-11 xenograft) - <i>In silico</i> (FEP, docking) - X-ray crystallography	- Cell lines: MV4-11, MOLM-13, Jurkat, MM.1S - <i>In vivo</i> : MV4-11 mouse xenograft model	(R)-Imidazo[4,5-c]quinolinyl-isoxazole - Core: 8-methoxy-2-methyl-1-(1-phenylethyl)imidazoquinoline - R-configuration confirmed - Lead: compound 10 (high binding affinity via FEP)	Acute myeloid leukemia (AML)	- FEP-guided SAR - BRD4 BD1/BD2 inhibition (HTRF) - Flow cytometry (apoptosis, G0/G1 arrest) - Western blot (c-Myc, CDK6, PARP, p21) - PK in rats - Xenograft tumor inhibition	- Inhibits BRD4 binding at acetylated lysine pocket - Suppresses c-Myc & CDK6, upregulates p21 & PARP - Induces G0/G1 cell cycle arrest & apoptosis - Highly selective for BET domains over other bromodomains	- IC ₅₀ (MV4-11) = 190 nM - BRD4 BD1 IC ₅₀ = 1.9 nM - Tumor growth inhibition (TGI): 70.4% @ 50 mg/kg - Oral bioavailability: 114% - Better than (±)JQ-1 in potency and PK	Compound 10 is a potent, selective, and orally active BET inhibitor. Outperforms JQ-1 in BET inhibition, AML cytotoxicity, and PK profile. Strong lead candidate for AML drug development.
[68]	- <i>In vitro</i> (A549, HeLa) - <i>In silico</i> (DFT, docking) - Antibacterial testing	- Cell lines: A549 (lung cancer), HeLa (cervical cancer) - No <i>In vivo</i> model	8-Amino-6-Methoxyquinolinium 2,4-Dinitrophenolate (8A6MQDNP) - Quinolinium cation - 2,4-dinitrophenolate anion - Planar structure, ICT from quinoline to DNP ring confirmed	Lung cancer (primary), Cervical cancer (secondary)	- MTT cytotoxicity assay (IC ₅₀) - DFT (geometry, FMOs, MEP) - UV-Vis, FT-IR, Raman spectroscopy	- Binds EGFR and p38 α MAPK - Docking binding energies: EGFR: -5.22 kcal/mol p38 α MAPK: -4.37 kcal/mol - Stronger binding to EGFR (lung cancer target)	- IC ₅₀ (A549): 2.58 μ g/mL - IC ₅₀ (HeLa): 3.74 μ g/mL - Higher cytotoxicity towards A549 - Antibacterial effect strongest	8A6MQDNP exhibits selective lung cancer inhibition, strong EGFR docking, and antibacterial properties. Potential lead molecule for lung cancer drug development.

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					- Molecular docking (EGFR, p38 α MAPK) - Antibacterial well diffusion assay	- Induces cytotoxicity more potently in A549 than HeLa	against <i>S. aureus</i> (25 mm inhibition zone) - Predominantly lung cancer inhibition profile	
[69]	- <i>In vitro</i> (HePG-2 and Caco-2 cancer cell lines) - No <i>In vivo</i> study - Green chemistry synthesis	- Cell lines: HePG-2 (liver cancer), Caco-2 (colon cancer) - No normal cell line tested	Polyhydroquinoline and quinoline derivatives synthesized via one-pot CAN-catalyzed reactions Lead compounds: 12d , 12c (quinoline derivatives)	Liver cancer, Colon cancer	- MTT assay for IC ₅₀ determination - Structure-activity relationship (SAR) analysis - Green chemistry one-pot synthesis - IR, NMR, MS spectral characterization	- No direct molecular target identified - SAR suggests electron-donating groups (e.g., OH, OCH ₃) enhance cytotoxicity - 12d: para-hydroxyphenyl group improves activity - 12c: methoxy group contributes to cytotoxicity	- IC ₅₀ (μ M): 12d: HePG-2 = 5.86, Caco-2 = 11.47 12c: HePG-2 = 9.29, Caco-2 = 18.23 - Close to doxorubicin standard: HePG-2 = 4.50 - Other compounds (e.g., 12b , 12e) moderate to weak activity. - Compound 1 (thiazole): strong against HePG-2 (IC ₅₀ = 9.78)	12d and 12c exhibit potent antitumor activity, especially against liver cancer. Electron-donating substitutions enhance cytotoxicity. Green synthesis is efficient and eco-friendly.
[70]	- <i>In vitro</i> (A549, A549R) - <i>In vivo</i> (xenograft) - <i>In silico</i> (structural data, docking references)	- Cell lines: A549, A549/DDP (cisplatin-resistant), HL-7702 (normal liver) - Xenograft: A549 in nude mice	5-substituted-8-hydroxyquinoline-Pt(II) complexes: - PtL1 (5-ethoxymethyl) - PtL2 (5-bromo) - PtL3 (parent) - Most active: PtL1	Lung adenocarcinoma (cisplatin-resistant)	- MTT, IC ₅₀ , SI (selectivity index) - Confocal microscopy (eGFP-mRFP-LC3) - Western blot: PINK1, LC3-II, Parkin, Beclin1 - Annexin V/PI (flow cytometry) - ICP-MS (Pt uptake) - Xenograft inhibition (%)	- Induces mitophagy, evidenced by LC3-II/LC3-I ratio \uparrow , PINK1 \uparrow , Parkin \uparrow - Activates apoptosis via mitophagy - \uparrow intracellular Pt accumulation (ICP-MS) - PtL1 > PtL3 > cisplatin in mitophagy induction	IC ₅₀ (A549R, μ M): PtL1: 1.3 PtL2: 2.4 PtL3: 7.2 Cisplatin: 63.2 - Apoptosis rate: PtL1: 96.4% PtL3: 44.6% - <i>In vivo</i> tumor inhibition: PtL1: 68.2% Cisplatin: \approx 50% - No weight loss observed	PtL1 is a highly selective and potent agent against cisplatin-resistant lung cancer. Acts via mitophagy-mediated apoptosis and surpasses cisplatin in efficacy and selectivity. Promising lead for drug-resistant cancer therapy.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
[71]	- <i>In vitro</i> (NCI 60-cell line panel) - <i>In silico</i> (docking, MD, DFT, ADMET)	- NCI panel: renal (UO-31), CNS (SNB-75), prostate (PC-3), etc. - No <i>In vivo</i> model	7-Hydroxy-4-methylquinolin-2(1H)-one analogues (4a-f) - Compound 4d (naphthyl carboxamide) - Compound 4b (dinitrophenyl) most potent	Renal, CNS, prostate, NSCLC, leukemia, breast	- MTT (NCI standard) - Docking (EGFR WT & mutant) - MD simulation (RMSD, RMSF, RGr, H-bonds) - DFT (HOMO-LUMO) - SwissADME & ProTox 3.0	- 4d & 4b bind EGFR mutant with high affinity (-9.962 and -5.718 kcal/mol) - 4d interacts via Thr854, Met793 - 4d forms more stable EGFR complex than gefitinib (RMSD ~2.5 Å) - HOMO-LUMO gap ΔE: 4b = 3.54 eV, 4d = 3.78 eV → good correlation with activity	4d: PGI = 50.40% (UO-31), 45.37% (SNB-75), 35.36% (PC-3) - 4b: PGI = 43.79% (HOP-92) - 4a, 4e: moderate PGI on CAKI-1, EKVX - 4c, 4f: weak activity - All compounds: class IV toxicity, LD50 = 1000-1200 mg/kg	Compound 4d exhibits strong EGFR binding, mitogenic inhibition and MD stability, surpassing imatinib in some panels. 4b and 4d are promising anticancer scaffolds, warranting further preclinical validation.
[72]	- <i>In vitro</i> (MCF7, HCT116 cancer cells) - No <i>In vivo</i> or <i>In silico</i> study	- Cell lines: HCT116 (colorectal cancer), MCF7 (breast cancer)	Benzo[f]quinoline-based heterocycles - Triazole thione, thiazolidinone, thiazole, imidazolidinone derivatives	Colon and Breast cancer	- MTT assay for IC ₅₀ - Antioxidant assay (phosphomolybdenum method) - Structure-activity relationship (SAR) analysis	- Cytotoxicity varies with the heterocyclic scaffold - Triazole thione and thiazole derivatives showed stronger anticancer and antioxidant activities	- IC ₅₀ (μM): Compound 10 (triazole thione): 20.07 (HCT116), 17.75 (MCF7) Compound 5 (imidazolidinone): 15.76 (HCT116), 25.43 (MCF7) Compound 8 (thiazole): 57.47 (HCT116), 40.96 (MCF7) Other compounds less active - Antioxidant capacity (mg AAE/g): 8 (378.03), 10 (339.04) highest	Benzoquinoline-based triazole thione and thiazole derivatives exhibit promising anticancer and antioxidant activities. Good potential for further development.
[73]	- <i>In vitro</i> (COLO 205, HT-29, HCT-116, others)	- COLO 205, HT-29, HCT-116 - Normal: FHC (colon epithelium)	(S)-8m: - Quinoline-thiazolidinone-urea hybrid - 7-(3-(4-ethylpiperazinyl)propoxy)-6-methoxyquinoline	Colorectal cancer	- MTT, flow cytometry (apoptosis, cycle) - Kinase inhibition panel	Potent dual c-Met/Ron inhibition: IC ₅₀ = 4.32 nM (c-Met), 2.39 nM (Ron)	- IC ₅₀ (μM): COLO 205: 0.035 (S-8m) FHC: >10.0 μM	(S)-8m is a potent, selective, and metabolically stable c-Met/Ron dual inhibitor, highly effective on COLO

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
	- <i>In silico</i> (docking, SAR) - ADME, FHC cytotoxicity	- No <i>In vivo</i> mode	- 2,4-difluorophenyl, S-isomer resolved from racemate		- Docking (c-Met, Ron) - HLM metabolic assay - FHC toxicity & selectivity	- H-bonding to Lys1110, Met1160, Glu1127 - Induces apoptosis (Annexin V/PI) - No cell cycle arrest → direct cell death - Low FHC toxicity → high selectivity index (238×)	- Outperforms Cabozantinib (6.6 μM) - Moderate efficacy on HT-29, LOVO, MKN-45 - HLM half-life: 161.9 min (stable) - Kinase profile: also active on ABL, RET, PDGFRβ	205 cells with minimal FHC toxicity. Strong candidate for colorectal cancer therapy, pending <i>In vivo</i> validation.
[61]	- <i>In vitro</i> (enzymatic and cellular IDO1/TDO) - <i>In vivo</i> (B16–F10 tumor mouse model) - <i>In silico</i> (docking) - PK profiling	- Enzyme assay (IDO1, TDO) - Cells: IFN-γ-induced Hela (IDO1), HEK-293T-TDO, B16–F10, U87 - <i>In vivo</i> : C57BL/6 mice with B16–F10 melanoma	Isoquinoline derivatives – Lead: compound 43b (7-methoxy-8-hydroxy isoquinoline core with trifluorosulfonamide linker) – SAR via variations at 3-phenyl and linker (amide, sulfamide, urea)	Melanoma (<i>In vivo</i>); pan-immunosuppressive relevance	- IC ₅₀ enzyme inhibition (IDO1, TDO) - Cell-based inhibition (kynurenine assay) - CCK-8 (viability) - SPR binding (KD values) - Docking: IDO1 (6E40), TDO (5TIA) - PK: oral/i.p./i.v. AUC, F% - <i>In vivo</i> tumor growth inhibition	- Dual inhibition: IDO1: IC ₅₀ = 0.31 μM TDO: IC ₅₀ = 0.08 μM - SPR KD: 0.45 μM (IDO1), 0.74 μM (TDO) - Cell-based IC ₅₀ s (μM): 9.29 (Hela), 7.23 (HEK-293T) - Coordinated with heme (IDO1); H-bonds to Ala150/Gln77 (TDO) - Low cytotoxicity	- <i>In vivo</i> (B16–F10 model): dose-dependent inhibition – TGI @100 mg/kg = strong suppression (better than 1-MT) – No body weight loss or toxicity - PK: Oral F% = 61.9%, i.p. = 72.6% - Stable and bioavailable	43b is a potent, dual IDO1/TDO inhibitor with strong enzymatic and <i>In vivo</i> efficacy, good PK, and low toxicity. Valuable lead for immunotherapy targeting the tryptophan–kynurenine pathway.
[40]	- <i>In vitro</i> (7 cancer cell lines, 2 normal lines) - <i>In vivo</i> (A549, PANC-1 xenograft)	- Cell lines: MCF-7, MDA-MB-231, HT-29, DU145, U937, A549, PANC-1 - Normal: CHO–K1, HEK293	Compound 6–15: – Quinolin-2-ylmethylene-azaoxindole – 4,6-dimethyl-5-hydroxy-7-azaoxindole core – Z-isomer geometry confirmed by NMR	Breast, pancreatic, prostate, colon, lung, leukemia	- MTT, IC ₅₀ , selectivity index - Phospho-RTK array - Western blot (Gas6, Axl, p-PI3K/Akt, Bax/Bcl-2)	- Inhibits Gas6-Axl axis (mRNA + protein level) - ↓Axl, ↓Gas6, ↓p-Akt, ↑Bax/Bcl-2 → induces apoptosis	PANC-1: 4.0 - Selectivity index (CHO-K1/PANC-1) = 13.6 - <i>In vivo</i> tumor suppression: > cisplatin (A549) and gemcitabine (PANC-1)	Compound 6–15 strongly suppresses the Gas6-Axl axis, inducing apoptosis and outperforming current drugs <i>In vivo</i> . Safe, selective, and potent across multiple cancer

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
	- <i>In silico</i> (not used)	- <i>In vivo</i> : xenografts in nude mice			- Cell cycle (sub-G1, G0/G1) - Apoptosis (Annexin V/PI) - Xenograft inhibition & survival (PANC-1, A549)	- No direct kinase inhibition on Axl (cell-free assay) - Greater apoptotic effect than sunitinib or Gas6 siRNA	- 100% survival vs 80% (gemcitabine)	types. Strong candidate for further development.
[74]	- <i>In vitro</i> (A549, HCT116, MCF7, HePG-2 human cancer cell lines)	- Cell lines: A549 (lung), HCT116 (colon), MCF7 (breast), HePG-2 (liver)	Brominated N-alkyl pyrano[3,2-c]quinolinones – Mono-bromo (2a–c) – Di-bromo (4a–c) – Amino-bromo (6a–c) derivatives	Lung, colon, breast, and liver cancers	- MTT cytotoxicity assay (IC ₅₀ determination) - Cell morphology observation (microscopy) - SAR analysis (structure–activity relationship)	- Induces apoptosis (DNA fragmentation observed) - Bromination increases antiproliferative activity - N-alkyl chain elongation (butyl group) enhances lipophilicity and cytotoxicity	- Most potent compound: 4c (IC ₅₀ s: A549 = 3.63 µg/mL, HCT116 = 6.49 µg/mL, MCF7 = 8.06 µg/mL, HePG-2 = 1.82 µg/mL) - 4c superior to 5-fluorouracil (positive control) - 6b , 6c , 2c also showed good activity	4c (dibromo with butyl chain) exhibits the highest cytotoxic activity; bromination and alkyl chain length are critical for potency. Promising leads for anticancer development.
[75]	- <i>In vitro</i> (2D/3D cytotoxicity, Top1 relaxation assay) - <i>In vivo</i> (colon adenocarcinoma C26 mouse model) - <i>In silico</i> (docking, ADMET)	- HOS (osteosarcoma), C26 (colon adenocarcinoma) <i>In vivo</i> - Normal: BJ1 fibroblast	Imidazo[2,1-b]quinazoline derivative 12 – Simplified camptothecin analog – Morpholine, arylidene, tricyclic scaffold – Structure panels A–C explored	Bone cancer (osteosarcoma), Colon cancer (adenocarcinoma)	- Top1 DNA relaxation assay - MTT cytotoxicity assay (2D/3D spheroids) - Flow cytometry (apoptosis/cell cycle) - RT-PCR (gene expression: p53, BAX, BCL-2, Her2) - Acute oral toxicity (liver panel) - Docking vs Top1 (PDB 1T8I)	- Top1 inhibition confirmed (DNA relaxation assay) - Apoptosis induction (Annexin V/PI, Sub-G1 arrest, ↑p53, ↑BAX, ↓BCL-2, ↓Her2) - Docking: H-bond with Arg364 critical for activity - High aqueous solubility (logS = –3.077 mol/L)	- IC ₅₀ (µM): HOS: 1.47 SAOS-2: 3.20 HeLa, DU145, SKOV-3: 3–5 µM BJ1 (normal cells): 4.25 µM (selectivity index ≈2.9) - <i>In vivo</i> tumor reduction (C26 model): 75.36% after 5 weeks - No acute liver toxicity	Compound 12 is a potent, selective Top1 inhibitor with excellent <i>In vitro</i> / <i>In vivo</i> efficacy and minimal toxicity. Promising candidate for development as an anticancer agent targeting bone and colon cancers.

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[76]	- <i>In vitro</i> (MCF-7, MDA-MB-468) - <i>In silico</i> (molecular docking) - NCI-60 cell line screening	- MCF-7 (ER+ breast cancer), MDA-MB-468 (TNBC) - NCI-60 panel	6H-thiochromeno[2,3-c]quinolin-12(12H)-one derivatives – Focus: compounds 18 and 20 – Tetraheterocyclic scaffold with N-substitutions	Breast cancer (MCF-7, MDA-MB-468)	- MTT cytotoxicity assay (IC ₅₀) - NCI-60 one-dose and five-dose screens - Molecular docking vs Topoisomerase I - COMPARE analysis for target prediction	- Docking: Strong binding to Topoisomerase I active site - COMPARE correlation: potential dual inhibition of Topoisomerase I/II, CDK4/6, AURKA, PARP pathways - Promotes cytotoxicity via DNA damage mechanisms	- IC ₅₀ (μM): Compound 17: 2.3 (MCF-7), 2.07 (MDA-MB-468) Compound 18: 2.94 (MCF-7), 2.5 (MDA-MB-468) - Selectivity Index: 18 and 20 show good selectivity vs normal cells - Compounds 18 and 20: potent across NCI-60 panel - Comparable or better than camptothecin in some assays	Compounds 18 and 20 demonstrate strong anticancer potential, especially against breast cancer. Multitarget potential identified, excellent cytotoxicity, and docking support their further development.
[43]	- <i>In vitro</i> (GBM6, GBM22, GBM143 primary glioblastoma cells) - 3D spheroid invasion assay	- Cell lines: GBM6, GBM22, GBM143 (primary glioblastoma cultures)	Alkoxy-functionalized dihydropyrimido[4,5-b]quinolinones – Microwave-assisted multicomponent reaction – Best compound: 5c (potent anti-cancer agent)	Glioblastoma (primary brain tumor)	- Cell viability assay (MTS assay) - 3D spheroid invasion assay - Cell cycle analysis (flow cytometry) - Western blotting (STAT3, ERK, AKT signaling pathways) - Colony formation assay	- Inhibits proliferation and invasion of GBM cells - Induces S and G2-phase cell cycle arrest - Inhibits phospho-STAT3, phospho-ERK, and phospho-AKT - More potent than temozolomide in GBM143 cells	- EC50 (μM): 5c: 2.9 5h: 3.3 - Complete inhibition of 3D spheroid invasion at 5 μM (5c) - Colony formation suppression stronger than temozolomide (50 μM)	5c shows the most potent anti-proliferative and anti-invasive effects on glioblastoma cells, outperforming clinical drug temozolomide. Strong candidate for future anti-glioma therapies.
[77]	<i>In vitro</i> (Hep-G2, HCC1806, HL-7702) - <i>In vivo</i> (HCC1806 xenograft in mice)	- HCC1806 (breast squamous carcinoma) - Hep-G2 (liver carcinoma) - Normal: HL-7702 (liver)	8-Hydroxyquinoline derivatives complexed to Rh(III) – Complexes YNU-1a to YNU-1d – Key compound: YNU-1c (2-methyl-5,7-dichloro-8-	Breast cancer (HCC1806), Liver cancer (Hep-G2)	- MTT cytotoxicity assay (IC ₅₀) - Western blot (cytochrome c, caspase-3, PINK1, Parkin, LC3-II, p62)	- Induces apoptosis via mitochondrial dysfunction - Activates PINK1–Parkin-mediated mitophagy	- IC ₅₀ (μM): YNU-1c: 0.13 (HCC1806), 0.19 (Hep-G2) YNU-1d: 0.31 (HCC1806) - Selectivity factor (HL-	YNU-1c is a potent, selective anticancer agent targeting mitophagy pathways. Promising therapeutic candidate for breast cancer resistant to cisplatin

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	- <i>In silico</i> (none)		hydroxyquinoline-Rh-TPP complex		- Immunofluorescence (cytochrome c release) - Flow cytometry (apoptosis assay) - <i>In vivo</i> tumor inhibition study	- ↓ Mitochondrial complexes I (M1), IV (M4), ↓ ATP production - ↑ Cleaved caspase-3, ↑ cytochrome c release	7702/HCC1806): 384.6 (very high) - <i>In vivo</i> : Tumor growth inhibition = 58.9% at 5 mg/kg (no toxicity)	
[78]	- <i>In vitro</i> - <i>In silico</i> (docking + ADMET prediction)	- Cell lines: MCF-7 (breast cancer), MDA-MB-231 (triple-negative breast cancer)	4-(Benzylideneamino)-N-(quinolin-8-yl)benzamide derivatives Synthesized via amidation, reduction, and Schiff base formation with various aldehydes.	- Breast Cancer (MCF-7) - Triple Negative Breast Cancer (MDA-MB-231)	- Synthesis and purification of derivatives - Molecular docking on PARP1 enzyme (PDB ID: 4ZZZ) - PARP-1 enzyme inhibition assay - Cytotoxicity evaluation (MTT assay) - ADMET property prediction	- Inhibition of PARP-1 via hydrogen bonding (Asp770, Ser864) and π - π stacking (Tyr907) with the quinoline core leadi	Best compounds: 3d: IC ₅₀ = 60.63 μ g/mL (MDA-MB-231)/56.38 μ g/mL (MCF-7) 3e: IC ₅₀ = 68.03 μ g/mL (MDA-MB-231)/54.42 μ g/mL (MCF-7) Both compounds have comparable enzyme inhibition to olaparib.	3d and 3e are promising candidates for further development. Their favorable docking, enzyme inhibition, cytotoxicity, and predicted pharmacokinetic properties justify additional optimization and studies.
[79]	- <i>In vitro</i> (PANC-1, SW1990, HCT116, PC3, MCF-7, A549, HeLa, HepG2) - <i>In vivo</i> (SW1990 xenograft mouse model)	- Cancer cells: PANC-1, SW1990 (pancreatic), HCT116 (colon), PC3 (prostate), others - Normal cells: H6C7, RWPE2 (pancreatic duct, prostate normal cells)	8-Hydroxyquinoline (8-HQ) derivatives – HQ-NO-11: 8-HQ conjugated with nitric oxide (NO) donor (furoxan) and ROS-responsive boronic ester	Pancreatic cancer (primary focus: SW1990, PANC-1)	- MTT cytotoxicity assays (IC ₅₀) - ROS activation assay (H ₂ O ₂ -induced) - Metal chelation (calcein competition) - NO release (Griess assay, DAF-FMDA fluorescence) - Flow cytometry (apoptosis,	- ROS-triggered activation releases 8-HQ chelator - Chelates Cu ²⁺ ions, induces ROS production (Fenton-like reactions) - NO release synergizes apoptosis via ONOO ⁻ formation - Induces mitochondrial	- IC ₅₀ values: HQ-NO-11 (SW1990): 8.83 μ M HQ-NO-11 (PANC-1): 10.45 μ M - <i>In vivo</i> tumor inhibition (SW1990 model): 61.8% (20 mg/kg HQ-NO-11) - Higher efficacy than parent 8-HQ (44.7%)	HQ-NO-11 is a potent, selective anticancer agent activated by ROS in cancer cells. Combines metal chelation and NO donation for synergistic anticancer activity.

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					mitochondrial membrane potential $\Delta\psi_m$) - Western blot (caspase-3, caspase-9, Bax, Bcl-2) - <i>In vivo</i> SW1990 xenograft inhibition study	apoptosis ($\downarrow\Delta\psi_m$, \uparrow cleaved caspase-3/9, \uparrow Bax, \downarrow Bcl-2)	- High selectivity vs normal cells ($IC_{50} > 30 \mu M$)	
[13]	- <i>In vitro</i> (A549 human lung cancer cells) - <i>In silico</i> (RNA-seq, KEGG, GO enrichment analysis)	- A549 (human lung carcinoma)	1,3-Indanedione-based spirocyclic tetrahydroquinolines - Library of spirocyclic quinoline-indanedione hybrids (3c, 3v most active)	Lung cancer	- CCK-8 cytotoxicity assay (IC_{50}) - Transwell migration assay - Flow cytometry (Annexin V/PI apoptosis, cell cycle analysis) - Western blot (caspase-3, BAX, BCL2, OPA1, LC3B, SQSTM1) - Confocal microscopy (mitochondrial fragmentation) - RNA-seq and pathway analysis	- Induces mitochondrial apoptosis (\uparrow BAX, \uparrow cleaved caspase-3, \downarrow BCL2) - Triggers mitochondrial fragmentation and mitophagy (\uparrow LC3B, \uparrow SQSTM1, \downarrow OPA1) - Arrests cell cycle in S and G2/M phases - Increases ROS production	- IC_{50} (48h): 3c: 11.82 μM 3v: 19.93 μM - Apoptosis rates: 3c: 31.9% 3v: 72.2% (better than cisplatin 23.7%) - Strong inhibition of A549 cell migration	1,3-Indanedione-based spirocyclic tetrahydroquinolines effectively induce apoptosis and inhibit lung cancer cell proliferation. Strong potential as anticancer agents targeting mitochondrial pathways.
[80]	- <i>In vitro</i> (cytotoxicity assays) - <i>In vivo</i> (xenograft models) - <i>In silico</i> (docking simulation)	- Cell lines: MDA-MB-231, HCT-116, HEP3B, SJCRH30, A498, LNCap, NCI-H226 - Animal models: Nude mice (xenografts with HCT-116 and SJCRH30 tumors)	- 5,11-Dihydro-6H-indolo[3,2-c]quinolin-6-ones - Synthesized via Copper(I)-catalyzed nitrile-addition/N-arylation ring-closure cascade from 2-(2-bromophenyl)-N-(2-cyanophenyl)acetamides	Breast (MDA-MB-231), Colon (HCT-116), Liver (HEP3B), Muscle (SJCRH30), Renal (A498), Prostate (LNCap), Lung (NCI-H226)	- Chemical synthesis optimization - GI50 determination (cytotoxicity assays) - Topoisomerase I inhibition assays (DNA relaxation,	- Stabilization of Top1-DNA cleavable complex - Inhibition of Top1-mediated DNA relaxation - DNA cleavage induction	- Compound 2k: GI50 = 0.029-0.348 μM (depending on cell line) - IC_{50} (Top1 inhibition) = 7.2 μM - Potent against SN-38 and	Compound 2k is a potent non-camptothecin Topoisomerase I inhibitor, with low nanomolar anticancer activity, active against resistant cancer cells; promising for further development as an intravenous anticancer drug.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
					DNA cleavage, band depletion) - Molecular docking into Top1–DNA cleavable complex (PDB: 1TL8) - <i>In vivo</i> efficacy in xenograft mouse models	- Band depletion in Top1 protein (HCT-116 cells) - Hydrogen bonds with Arg364 and DNA bases - π - π stacking with DNA bases (T, G, A)	ARC-111 resistant HCT-116 cells (RI = 6.8) - <i>In vivo</i> tumor inhibition in mice (T/C values: 52–66%)	
[81]	- <i>In vitro</i> (NCI–H1975, H460, A549 cancer cells) - <i>In vivo</i> (H460 xenograft mouse model) - <i>In silico</i> (molecular docking)	- NCI–H1975 (EGFR-mutant NSCLC) - H460, A549 (wild-type EGFR lung cancer cells) - Normal cells: MRC-5, LO2	2-Methylquinolin-6-ol derivatives – 4-((3,4-dichlorophenyl)amino) substituted – Hydroxamic acid side chains (12c, 12d)	Non-small cell lung cancer (NSCLC)	MTT assay (IC ₅₀) - Colony formation assay - EGFR and HDAC enzymatic inhibition assays - Western blotting (pEGFR, pAKT, pSTAT3, pMAPK, pS6K, acetylated H3/H4) - Apoptosis (Annexin V-FITC/PI) - Cell cycle analysis (G2/M arrest) - <i>In vivo</i> antitumor efficacy (xenograft model)	- Dual inhibition of EGFR and HDAC - ↓ EGFR expression and phosphorylation - ↑ Acetylation of histones H3 and H4 - ↓ p70S6K, AKT, p38 MAPK phosphorylation - Induces mitochondrial damage, G2/M arrest, and apoptosis	- IC ₅₀ (μM): 12c: 0.48 (NCI–H1975), 1.10 (A549) 12d: 0.35 (NCI–H1975), 1.02 (A549) - Selectivity Index: 12c >9; 12d >9 (high selectivity vs normal cells) - <i>In vivo</i> tumor inhibition: 12d (50 mg/kg): TGI 52.4%, no toxicity observed	Compounds 12c and 12d are potent EGFR and HDAC dual inhibitors with strong <i>In vitro</i> and <i>In vivo</i> anticancer effects against NSCLC. Promising candidates for overcoming resistance in NSCLC therapy.
[82]	- <i>In vitro</i> (HCT-15, H157, BxPC3, PSN-1, A431, A2780, LoVo) - <i>In vivo</i> (none) - <i>In silico</i> (DFT, EPR, DNA-binding)	- Cancer cells: Colon (HCT-15, LoVo), Lung (H157), Pancreatic (BxPC3, PSN-1), Cervical (A431), Ovarian (A2780, A2780ADR)	Cu(II) complexes of hydrazones – Based on 6- and 7-chloro-2-oxo-1,2-dihydroquinoline-3-carbaldehyde conjugated to furoyl hydrazone	Colon, Lung, Pancreatic, Cervical, and Ovarian cancers	- MTT assay (IC ₅₀ determination) - DNA binding assays (UV-Vis titration) - EPR spectroscopy - DFT calculations	- Strong intercalative DNA binding (K _b = 4.23 × 10 ⁴ and 3.52 × 10 ⁴ M ⁻¹) - Induction of cytotoxicity through DNA interaction - Overcomes drug resistance	- IC ₅₀ (μM): 1(NO3): 3.5–16.4 μM 2(NO3): 2.3–14.5 μM - Best activity: against PSN-1 (pancreatic, IC ₅₀ = 3.9–4.7 μM) - Effective against drug-	Cu(II)-quinoline hydrazone complexes are potent anticancer agents, highly active even in drug-resistant models. Good DNA binding affinity and cytotoxic profile.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
						(multidrug and oxaliplatin resistance)	resistant cell lines (A2780ADR, LoVoOXP)	
[83]	- <i>In vitro</i> (DLD1, HCT116 CRC cell lines) - <i>In silico</i> (structural analysis, molecular docking)	- DLD1, HCT116 (colorectal cancer cell lines) - Normal cells: CCD841CON, M10, MRC5, HEL299	5,8-quinolinedione derivatives – Regioisomeric 6b (6-position morpholine side-chain) most potent – Compared to 6a (7-position derivative, NSC663284)	Colorectal cancer	- MTS cytotoxicity assay (IC ₅₀) - Cell cycle analysis (flow cytometry) - Western blot (CDK1 phosphorylation, H4K20 methylation) - DNA damage markers (γH2AX, pCHK1, pCHK2, pKAP1, pRPA2) - Apoptosis markers (active caspases 3, 8, 9)	- Inhibits CDC25 phosphatase activity - Arrests cell cycle at S and G2/M phases - Suppresses H4K20 mono-methylation - Induces DNA damage response - Activates mitochondrial apoptosis (caspase activation, ↓MCL-1)	- IC ₅₀ (μM): 6b: 0.59 (DLD1), 0.44 (HCT116) 16b, 17b, 18b: ~1–2 μM - Normal cells: IC ₅₀ >2 μM (good selectivity) - 6b 3–4 times more potent than 6a (NSC663284)	6b is a potent CDC25 inhibitor inducing genome instability and apoptosis in colorectal cancer cells. Promising lead for anti-CRC therapy development.
[84]	- <i>In vitro</i> (SK-OV-3, SK-OV-3/DDP, HL-7702) - No <i>In vivo</i> - <i>In silico</i> (none)	- Cell lines: SK-OV-3 (ovarian adenocarcinoma), SK-OV-3/DDP (cisplatin-resistant ovarian cancer), HL-7702 (normal liver cells)	5,7-dihalo-substituted-8-quinolinoline – Complexes RuZ1, RuZ2, RuZ3 with triphenylphosphine (PPh ₃)	Ovarian cancer, including cisplatin-resistant model	- CCK-8 cytotoxicity assay (IC ₅₀) - ROS generation assay - Ca ²⁺ fluctuation assay - JC-1 mitochondrial membrane potential assay - Western blotting (mitophagy markers: LC3-II/I, Beclin-1, P62, PINK1, Parkin, caspase-9, cleaved-caspase-3, cytochrome c) - ATP production and	- ↓ Mitochondrial membrane potential (ΔΨ _m) - ↑ Intracellular ROS and [Ca ²⁺] - ↓ ATP production, ↓ mitochondrial complexes I and IV - ↑ LC3-II/I ratio, ↑ Beclin-1, ↑ PINK1, ↑ Parkin - Activation of mitochondrial-mediated apoptosis	- IC ₅₀ (μM): RuZ2: 4.05 (SK-OV-3/DDP) RuZ1: 9.66 (SK-OV-3/DDP) RuZ3: 7.18 (SK-OV-3/DDP) - Higher cytotoxicity and selectivity than cisplatin - No toxicity against normal HL-7702 cells (IC ₅₀ > 50 μM)	RuZ1–RuZ3, particularly RuZ2, are potent agents inducing mitophagy-related apoptosis in cisplatin-resistant ovarian cancer cells. Good selectivity, low toxicity to normal cells.

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					mitochondrial complex assays - Flow cytometry (apoptosis assay)			
[85]	- <i>In vitro</i> (A375, RPMI7951, MDA-MB-435, MDA-MB-435/LCC6MDR1, MDA-MB-453, SKBR3, OVCAR3, OVCAR8) - <i>In vivo</i> (A375 melanoma xenograft, OVCAR8 ovarian orthotopic model) - <i>In silico</i> (molecular docking, SPR binding)	- Cell lines: A375 (melanoma), RPMI7951 (melanoma), MDA-MB-435 (breast cancer), MDA-MB-435/LCC6MDR1 (MDR variant), MDA-MB-453 (breast cancer), SKBR3 (breast cancer), OVCAR3 (ovarian cancer), OVCAR8 (ovarian cancer)	Hydroxyquinoline-based MX-106 analogs - Various modifications (triazole/imidazole linkers, C- and D-ring changes) - Best compound: 12b (stable, potent survivin inhibitor)	Melanoma, Breast cancer, Ovarian cancer	- MTT assay (IC ₅₀) - Western blot (survivin, cleaved PARP) - Binding kinetics (SPR) - <i>In vivo</i> antitumor studies (tumor volume, metastasis tracking) - Molecular docking (binding to survivin)	- Direct binding to survivin (KD = 4.27 μM) - ↓ Survivin protein levels - ↑ Cleaved PARP (apoptosis induction) - Inhibits tumor growth and metastasis - Overcomes P-gp mediated drug resistance	- IC ₅₀ (μM): Compound 12b: ≈1.1–1.7 (cancer cell lines) - <i>In vivo</i> tumor inhibition: Melanoma: 66% tumor growth inhibition at 40 mg/kg Ovarian: ↓ primary tumor and peritoneal metastasis	Compound 12b selectively inhibits survivin and induces apoptosis. Highly effective <i>In vitro</i> and <i>In vivo</i> , with improved metabolic stability and ability to overcome drug resistance. Strong potential for further preclinical development.
[86]	- <i>In silico</i> (3D-QSAR, molecular docking, ADMET analysis) - No <i>In vitro</i> or <i>In vivo</i> study	- Cell target: Aromatase enzyme (PDB ID: 3S7S)	Novel quinoline derivatives - Based on hydroxyquinoline core - Modified to optimize aromatase inhibition	Breast cancer (hormone-dependent, aromatase enzyme target)	- 3D-QSAR modeling (CoMSIA/EHDA model) - Molecular docking to aromatase active site - ADMET property prediction (pkCSM, SwissADME)	- Direct binding to aromatase (ARG115, MET374 crucial residues) - Enhanced electrostatic, hydrophobic, and hydrogen bond acceptor interactions - Design of new compounds (Ligand 2, Ligand 3) with improved properties	- Predicted pIC ₅₀ : Ligand 2: 6.441 Ligand 3: 6.951 - Binding energy (kcal/mol): Ligand 2: -9.8 Ligand 3: -10.6 - Improved ADMET profiles (good intestinal absorption, low toxicity)	Ligand 2 and Ligand 3 are promising aromatase inhibitors. New quinoline derivatives show enhanced predicted activity and pharmacokinetics against breast cancer targets.
[87]	- <i>In vitro</i> (HepG2, HCT-116, MCF-7,	- Cell lines: HepG2 (hepatocellular	Hexahydroquinoline and fused quinoline derivatives	Lung cancer (EGFR mutant NSCLC), Liver cancer, Colon	- MTT cytotoxicity assay (IC ₅₀)	- Potent inhibition of	- IC ₅₀ (μM):	Compound 7d is a potent multi-kinase inhibitor effective against wild-type

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
	A431, H1975, WI38, WISH) - <i>In silico</i> (molecular docking) - No <i>In vivo</i>	carcinoma), HCT-116 (colorectal cancer), MCF-7 (breast cancer), A431 (epidermoid carcinoma, EGFRWT overexpression), H1975 (NSCLC, EGFR790M mutant), WI38 (lung fibroblast, normal), WISH (amnion epithelial, normal)	- 3-position cyano/carboxyl groups - 4-position aromatic hydrophobic moieties - Best compound: 7d (hexahydropyrimidoquinoline derivative)	cancer, Breast cancer	- Kinase inhibition assay (EGFRWT, EGFR858R, EGFR790M, others) - Cell cycle analysis (flow cytometry) - Apoptosis assay (Annexin V/PI staining) - Bax/Bcl-2 protein expression - Molecular docking studies	EGFRWT, EGFR858R, EGFR790M kinases - Arrests cell cycle in G2/M and pre-G1 phases - Induces apoptosis via upregulation of Bax and downregulation of Bcl-2 - Binds ATP pocket of EGFR and JAK3	7d: 4.46 (HepG2), 5.27 (HCT-116), 3.25 (MCF-7) 1.32 (H1975), 4.96 (A431) - Kinase IC ₅₀ (μM): EGFRWT: 0.083 EGFR858R: 0.053 EGFR790M: 0.026 JAK3: 0.069 - High selectivity toward cancer vs normal cells (SI > 10)	and mutant EGFR, induces apoptosis, and overcomes EGFR-TKI resistance. Promising lead for advanced NSCLC therapy targeting EGFR790M mutation.
[88]	- <i>In vitro</i> (NCI-60 human tumor cell lines, MDA-MB-231 breast cancer cells) - <i>In silico</i> (molecular docking)	- Cell lines: NCI-60 panel (various cancers including breast cancer, MDA-MB-231 for detailed assays)	Novel quinoline derivatives - Pyridin-2-one, pyridinethione, and pyrimidinethione rings with trimethoxy, dimethoxy, fluoro, or bromo substituents - Best compound: 4c (pyridin-2-one derivative with trimethoxy groups)	Broad anticancer screening, focus on Breast Cancer (Triple-negative MDA-MB-231)	- NCI-60 cytotoxicity panel screening - MTT assays - Flow cytometry (cell cycle arrest G2/M phase) - Apoptosis assay (Annexin V/PI staining) - Tubulin polymerization inhibition assay - RT-PCR (β-tubulin mRNA expression) - Molecular docking to colchicine binding site (CBS)	- Tubulin polymerization inhibition (IC ₅₀ = 17 ± 0.3 μM for 4c) - Cell cycle arrest at G2/M phase - Increased apoptosis (early and late stages) - ↓ β-tubulin mRNA expression - Binding energy (CDocker) of 4c = -11.5 kcal/mol (stronger than colchicine -9.8 kcal/mol)	- GI50 (μM) of 4c: 2.21 (RXF 393, renal cancer) 2.37 (HOP-92, NSCLC) 2.38 (SNB-75, CNS cancer) 2.38 (HS 578T, breast cancer) 4.11 (BT-549, breast cancer) - Potent cytotoxicity against multiple cancer types - Better selectivity and lower necrosis compared to colchicine	Compound 4c is a potent tubulin polymerization inhibitor inducing apoptosis and cell cycle arrest. Highly effective against breast cancer cells and other tumor types. Strong potential for preclinical development.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
[89]	- <i>In vitro</i> (EAC tumor cells, DPPH antioxidant assay) - <i>In vivo</i> (Ehrlich solid tumor mouse model)	- Cell line: Ehrlich ascites carcinoma (EAC) - Animal model: Swiss albino mice (solid EAC tumors)	Indolo[2,3-b]quinoline derivatives – Neocryptolepine core – 11-position amino side-chain modifications (6a–6d)	Ehrlich ascites carcinoma (EAC)	- Trypan blue exclusion assay (IC ₅₀ on EAC cells) - DPPH antioxidant assay - <i>In vivo</i> tumor volume measurement - Lipid peroxidation (MDA), SOD and CAT enzyme levels - Splenic lymphocyte count, lymphoproliferation assay - Flow cytometry (cell cycle analysis) - Histopathology (liver, tumor)	- DNA intercalation - Topoisomerase II inhibition - Induction of apoptosis (sub-G1 accumulation) - Cell cycle arrest at G0/G1, S, G2/M phases - Antioxidant effects (↑SOD, CAT; ↓lipid peroxidation)	- IC ₅₀ (μM, EAC cells): 6a: 1.7 × 10 ⁻⁴ 6b: 6.4 × 10 ⁻⁵ (most potent) 6c: 3.3 × 10 ⁻⁴ 6d: 1.5 × 10 ⁻⁴ - Tumor volume reduction (%): 6a: 90.58%, 6b: 87.37%, 6c: 93.29%, 6d: 94.90% (better than thalidomide, 67.20%)	Neocryptolepine analogs 6a–6d show potent <i>In vitro</i> and <i>In vivo</i> antitumor activity via apoptosis, cell cycle arrest, and antioxidant mechanisms. Strong candidates for further preclinical development.
[36]	- <i>In vitro</i> (HCT116, HepG2, BGC-823, A549, A2780, FHC, 293T) - <i>In vivo</i> (CT26 mouse colorectal cancer model)	- Cell lines: HCT116 (colon), HepG2 (liver), BGC-823 (gastric), A549 (lung), A2780 (ovary), FHC (normal colon), 293T (normal kidney)	4,7-disubstituted quinoline derivatives – 4-position: anilino/phenylthio/phenoxy groups – 7-position: alkoxy groups – Best compound: 10k (3-nitrophenyl and 3,4,5-trimethoxybenzyl modifications)	Colorectal cancer (focus), plus multiple tumor types	MTT/CCK8 assays - Colony formation assay - Western blot (LC3, ATG5/7, caspase-3, p53, Bax) - Flow cytometry (autophagy, apoptosis) - mCherry-EGFP-LC3B fluorescence assay - TEM (autophagosomes) - <i>In vivo</i> xenograft model (tumor volume, weight)	- Induces autophagy via ATG5 stabilization - ↑ LC3-II conversion - Formation of autophagosomes and autolysosomes - Cell death independent of apoptosis - ↓ tumor growth <i>In vivo</i> (CT26 xenograft)	IC ₅₀ (μM, 10k): HCT116: 0.35 HepG2: 1.98 BGC-823: 0.60 A549: 0.39 A2780: 0.67 - Tumor volume ↓ significantly after 18 days of treatment - Lower toxicity in normal cells (FHC, 293T)	Compound 10k induces ATG5-dependent autophagy and inhibits colorectal tumor growth both <i>In vitro</i> and <i>In vivo</i> . Strong candidate for anticancer drug development targeting autophagy.

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
[90]	- <i>In vitro</i> (EGFR kinase inhibition, A549 and A431 cancer cells) - <i>In silico</i> (molecular docking, FMO-RIMP2/PCM, MD simulations)	- Cell lines: A549 (lung cancer), A431 (epidermoid carcinoma, EGFR-overexpressing), Vero (normal)	Sulfonylated indeno[1,2-c]quinoline derivatives - Sulfonyl groups at 4-position - Best compound: SIQ17	Non-small cell lung cancer (NSCLC) focus (EGFR driven)	- EGFR-TK inhibition assay (ADP-Glo Kinase Assay) - MTT cytotoxicity assay (IC ₅₀) - Molecular docking - Fragment Molecular Orbital (FMO) calculations - 500 ns MD simulations (triplicate) - MM/PB(GB)SA free energy calculations	- ATP-competitive binding at EGFR-TK active site - Sulfonyl group stabilized by C797, L718, and E762 residues - Cation- π interaction with K745 - Autoinhibition of EGFR phosphorylation	- EGFR-TK IC ₅₀ (nM): SIQ17: 0.6–10.2 (more potent than erlotinib ~20 nM) - Cellular IC ₅₀ (μ M): A549: 32.98 A431: 19.17 - Stronger cytotoxicity against A431 vs A549 (higher EGFR expression)	SIQ17 shows potent EGFR kinase inhibition and selective cytotoxicity in EGFR-overexpressing cancer cells. Promising lead for developing new NSCLC therapies.
[91]	- <i>In vitro</i> (EC-109, PC-3, MGC-803 human cancer cells)	- Cell lines: EC-109 (esophageal cancer), PC-3 (prostate cancer), MGC-803 (gastric cancer)	Trimethoxyphenyl-quinoline hybrids - 8-aminoquinoline core - Linked to 3,4,5-trimethoxybenzoyl group - Best compound: 12j (N-(3-(chloromethyl)benzyl)-3,4,5-trimethoxy-N-(quinolin-8-yl)benzamide)	Esophageal, prostate, gastric cancers (focus on prostate, PC-3)	- MTT cytotoxicity assay (IC ₅₀) - Colony formation assay - Flow cytometry (cell cycle analysis, apoptosis) - Western blot (Cyclin B1, Bax, DR5, c-IAP1, PARP cleavage)	- Induces G2/M cell cycle arrest - Activates intrinsic (Bax \uparrow , PARP cleavage) and extrinsic (DR5 \uparrow) apoptosis pathways - Downregulates c-IAP1	- IC ₅₀ (μ M): PC-3: 9.23 MGC-803: 12.41 EC-109: 18.09 - 40% apoptosis at high dose - Strong colony formation inhibition in PC-3 cells	Compound 12j is a potent antitumor agent inducing G2/M arrest and apoptosis in PC-3 cells. Trimethoxyphenyl-quinoline hybrids are promising anticancer leads.
[92]	- <i>In vitro</i> (PC3-LN4, DU-145, MDA-MB-231, PANC1, A549 cancer cells) - <i>In vivo</i> (pharmacokinetics in mice)	- Cell lines: Prostate (PC3-LN4, DU-145), Breast (MDA-MB-231), Lung (A549), Pancreas (PANC1), T-ALL (DU528)	2-oxoquinoline derivatives (VBT-5445 analogs) - N-substituted 7-chloro-2-oxoquinoline core - Modifications at pyridine ring and phenoxy group - Best compounds: GRG-1-31, GRG-1-34, GRG-1-35, GRG-1-104	Prostate cancer, pancreatic cancer, breast cancer, lung cancer, leukemia	- Kinase inhibition assays (Pim, mTORC1/2, AKT phosphorylation) - Growth inhibition assays (dose-response curves) - Western blotting	- Dual inhibition of Pim and mTORC protein kinases - Decreased phosphorylation of S6, 4E-BP1, mTOR, c-Myc - Induces P-body formation (RNA decay sites)	- Most active compounds: GRG-1-31, GRG-1-34, GRG-1-35, GRG-1-104 - GRG-1-34 pharmacokinetics: Cmax = 1988 ng/mL (4 μ M), T1/2 = 2.1 h	2-Oxoquinoline derivatives potently inhibit Pim and mTORC kinases, reduce tumor cell growth, and are promising for multi-pathway anticancer therapy

Reference	Study type	Experimental model	Quinoline structure & modifications	Cancer type	Key methodology	Mechanism of action	Antitumor effect	Conclusion
					(substrates: S6, 4E-BP1, AKT, c-Myc) - RPPA proteomics analysis - P-body formation assay - Pharmacokinetics (mouse plasma levels)	- Combination effect with AKT inhibitors	- Strong growth inhibition in PC3-LN4, PANC1, DU-145 cells	
[93]	- <i>In vitro</i> (RPE-MYCBCL2 cells, multiple human cancer cell lines) - <i>In vivo</i> (HCT116 xenograft mouse model)	- Cell lines: RPE-MYCBCL2 (retinal pigment epithelial), HCT116 (colorectal cancer), MCF7, HeLa, A549, AGS, HCC827, PC-9 (various cancers)	4-phenoxy-quinoline derivatives - 6-methoxy, 7-methoxy, and acetylated analogs - Lead compound: 12a (N-(3-methoxy-5-((6-methoxyquinolin-4-yl)oxy)phenyl)acetamide)	Broad-spectrum cancer cell lines (lung, colon, breast, cervix, stomach)	- Mechanism-informed phenotypic screening (MIPS) - Cell cycle analysis (mitotic arrest, polyploidy) - Immunofluorescence (AURKB localization) - Kinome profiling (468 kinases) - Pharmacokinetics (rats) - Xenograft model (HCT116)	- Disrupts mitotic localization of AURKB - Does not inhibit AURKB kinase activity - Causes mitotic arrest and polyploidy - Prevents recruitment of PLK1 and MKLP1 - Inhibits midzone microtubule assembly	- IC ₅₀ (nM): Low nanomolar for most human cancer cells - Kinase selectivity: Very high (minimal off-targets at 2 μM) - <i>In vivo</i> : Good oral bioavailability (27–56%), tumor tissue accumulation, effective mitotic disruption without toxicity	Lead 12a disrupts AURKB localization without inhibiting kinase activity, showing potent anticancer effects and high specificity, paving the way for new strategies to bypass resistance to classic kinase inhibitors.
[94]	- <i>In vitro</i> (NCI-60 cell lines) - <i>In silico</i> (molecular docking, pharmacokinetics)	- Cell lines: NCI-60 cancer panel (Renal, CNS, Ovarian cancers mainly)	Triazolothiadiazepinyl-quinoline derivatives - Microwave-assisted synthesis - Best compounds: 10b, 10c, 10e, 10f	Renal cancer focus (UO-31), CNS and Ovarian Cancer	- NCI-60 growth inhibition screening (10 ⁻⁵ M single-dose assay) - MIC determination (antifungal assays) - Molecular docking to MetAP-2 and NMT enzymes - <i>In silico</i> pharmacokinetics	- Inhibits MetAP-2 and NMT enzymes - Disrupts myristoylation in cancer cells - Binds HIS231 and HIS382 residues (MetAP-2) and SER378, ASN434 (NMT) - Moderate inhibition of	- Best anticancer GI%: 10b: 35.71% inhibition (UO-31) 10c: 22.98% inhibition (UO-31) 10e: 17.99% inhibition (UO-31) 10f: 33.88% inhibition (UO-31) - Best antifungal MIC	10b and 10f act as potent NMT inhibitors, 10c and 10e as MetAP-2 inhibitors, showing moderate anticancer and strong antifungal potential. Promising multi-target lead molecules.

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					(Lipinski's rule, absorption %)	tumor cell growth (esp. UO-31)	(Aspergillus fumigatus): 0.20 mg/mL	
[95]	- <i>In vitro</i> (A2780, A2780/RCIS, MCF7, MCF7/MX, Huvec cells) - <i>In silico</i> (molecular docking, molecular dynamics simulations)	- Cell lines: A2780 (ovarian carcinoma), A2780/RCIS (cisplatin-resistant), MCF-7 (breast cancer), MCF-7/MX (mitoxantrone-resistant), Huvec (normal)	Quinoline-chalcone hybrids - Chalcone scaffold linked to substituted quinoline core - Best compounds: 5g, 5j (benzoyl substitution at C6 or C8)	Ovarian and breast cancers, including drug-resistant variants	- MTT cytotoxicity assay (IC ₅₀ determination) - Tubulin polymerization inhibition assay - Flow cytometry (cell cycle arrest analysis) - Molecular docking (colchicine-binding site) - 100 ns molecular dynamics simulations (MD)	- Inhibits tubulin polymerization (similar to CA-4) - Induces cell cycle arrest at G2/M phase - Triggers apoptosis - Binds colchicine-binding site (Tubulin, PDB 4O2B) with strong hydrophobic and H-bond interactions	- IC ₅₀ values (μM, compound 5j): A2780: 2.32 A2780/RCIS: 2.61 MCF7: 4.96 MCF7/MX: 2.32 - 5g also potent especially on MCF7/MX (IC ₅₀ 2.77 μM)	Compounds 5j and 5g are potent tubulin polymerization inhibitors and induce strong anticancer effects in sensitive and resistant cancer cell lines. Promising candidates for further development.
[96]	- <i>In vitro</i> (HT29, SW620 colorectal cancer cells) - <i>In silico</i> (molecular docking, pharmacokinetics)	- Cell lines: HT29 (colorectal adenocarcinoma), SW620 (metastatic colorectal carcinoma)	Substituted Indeno[1,2-b]quinoline amines - Mono-bromo (1-3), tri-bromo (4-6), and mono-phenyl (7-9) substitutions	Colorectal cancer (primary and metastatic)	- MTT assay (IC ₅₀ , GI50, TGI, LC50) - LDH cytotoxicity assay - DNA fragmentation assay (apoptosis) - Cell morphology (phase contrast microscopy) - Molecular docking (PDB: 1OLG for p53, 4LVT for Bcl-2)	- Induces apoptosis via DNA fragmentation - Inhibits proliferation of HT29 and SW620 - Targets mutated p53 and Bcl-2 proteins - Hydrophobic and H-bond interactions key for activity	- IC ₅₀ (μg/mL): HT29: 1.1-2.7 (compounds 1, 3, 7-9) SW620: 1.2-1.3 (compounds 1, 3, 7-9) - Moderate cytotoxicity (17-33% LDH release) - DNA fragmentation confirms apoptosis	Mono-substituted indenoquinoline amines 1, 3, and 7-9 showed strong antiproliferative and apoptotic activities against HT29 and SW620 cells, with low cytotoxicity, suggesting high potential as anticancer agents.

ABC-DLBCL: activated B-cell diffuse large B-cell lymphoma, ADME: absorption, distribution, metabolism, excretion, ADMET: absorption, distribution, metabolism, excretion, toxicity, AKT: protein kinase B, AML: acute myeloid leukemia, AMPK, AMP: activated protein kinase, AO/EB: acridine orange/ethidium bromide, ATP: adenosine triphosphate, AUC: area under the concentration-time curve, BBB: blood-brain barrier, BD1: bromodomain 1, BER: base excision repair, BET: bromodomain and extra-terminal, BRD4: bromodomain-containing protein 4, BSA: bovine serum albumin, CETSA: cellular thermal shift assay, CDK: cyclin-dependent kinase, Cmax: maximum plasma concentration, CNS: central nervous system, CYP: cytochrome P450, CYP1A2: cytochrome P450 1A2, DCFH-DA: 2',7'-dichlorodihydrofluorescein diacetate, DFT: density functional theory, DNMT1: DNA methyltransferase 1, DPPH: 2,2-diphenyl-1-picrylhydrazyl, EC50: half maximal effective concentration, EGFP: enhanced green fluorescent protein, EGFR: epidermal growth factor receptor, EPR: electron paramagnetic resonance, ER: endoplasmic reticulum, FMO: frontier molecular orbitals, FT-IR: Fourier-transform infrared spectroscopy, FTH: ferritin heavy

chain, G0/G1: cell-cycle phases G0/G1, G2/M: cell-cycle transition G2/M, GI: gastrointestinal, GI50: 50% growth inhibition, GPX4: glutathione peroxidase 4, GSH: reduced glutathione, H&E: hematoxylin and eosin, HDAC: histone deacetylase, HOMO-LUMO: highest occupied molecular orbital-lowest unoccupied molecular orbital, HSP90: heat shock protein 90, IC50: half maximal inhibitory concentration, ICP-MS: inductively coupled plasma mass spectrometry, IF: immunofluorescence, ITC: isothermal titration calorimetry, JC-1: 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazolylcarbocyanine iodide, Kd: equilibrium dissociation constant, LC50: median lethal concentration, LD50: median lethal dose, LAMP1: lysosomal associated membrane protein 1, LC3-II: microtubule-associated protein 1 light chain 3-II, LPO: lipid peroxidation, MDA: malondialdehyde, MDR: multidrug resistance, MEP: molecular electrostatic potential, MMP: mitochondrial membrane potential, mROS: mitochondrial reactive oxygen species, MD: molecular dynamics, mTOR: mechanistic target of rapamycin, MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, NCI: National Cancer Institute, NCI-60: NCI-60 human tumor cell line panel, NMR: nuclear magnetic resonance, NSCLC: non-small cell lung cancer, PARP: poly(ADP-ribose) polymerase, PBMCs: peripheral blood mononuclear cells, PDB: Protein Data Bank, PDAC: pancreatic ductal adenocarcinoma, P-gp: P-glycoprotein, PI: propidium iodide, PI3K: phosphoinositide 3-kinase, PK: pharmacokinetics, PK/PD: pharmacokinetics/pharmacodynamics, ProTox: ProTox (toxicity prediction tool), PBSA: Poisson-Boltzmann surface area, qPCR: quantitative polymerase chain reaction, QSAR: quantitative structure-activity relationship, RF: resistance factor, RMSD: root-mean-square deviation, RMSF: root-mean-square fluctuation, ROS: reactive oxygen species, RT-qPCR: reverse transcription quantitative polymerase chain reaction, SAR: structure-activity relationship, SHP-1: Src homology region 2 domain-containing phosphatase-1 (PTPN6), SI: selectivity index, SPR: surface plasmon resonance, STAT3: signal transducer and activator of transcription 3, TEM: transmission electron microscopy, TGI: tumor growth inhibition, TNBC: triple-negative breast cancer, Topo I/II: topoisomerase I/II, t1/2: elimination half-life, UV-Vis: ultraviolet-visible spectroscopy, WB: Western blot, XRD: X-ray diffraction, E/Z: geometric isomerism (E/Z configuration).