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Beyond Single-Target Drugs: The Emergence of Dual-Acting Anticancer Molecules

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ABSTRACT

Dual-acting anticancer agents represent an innovative and promising strategy in the field of oncology, aiming to overcome the limitations of conventional monotherapies. These compounds are designed to simultaneously target two or more distinct molecular pathways involved in cancer progression, thereby enhancing therapeutic efficacy and reducing the development of drug resistance. By integrating multiple pharmacophores into a single chemical entity, dual-acting agents can exert synergistic effects on crucial biological processes such as cell proliferation, apoptosis, angiogenesis, DNA repair, and immune modulation. In recent years, considerable efforts have been made to design and optimize such agents using rational drug design, structure–activity relationship (SAR) studies, and computational modeling. This review highlights the key mechanisms targeted by dual-acting agents and provides representative examples based on diverse chemical scaffolds, including quinoline, quinazoline, coumarin, triazole, hydantoin, and metal complexes. Furthermore, we discuss the therapeutic potential of these compounds in preclinical and clinical settings, as well as emerging trends in the development of multifunctional drugs. Dual-targeted therapies may represent a transformative approach for improving cancer treatment outcomes and overcoming resistance mechanisms.

Introduction

Cancer remains one of the most pressing global health challenges, representing a leading cause of morbidity and mortality worldwide. According to the latest GLOBOCAN statistics, an estimated 20 million new cancer cases and 9.7 million cancer-related deaths were reported in 2022, highlighting the urgent need for more effective therapeutic strategies[1]. Despite considerable advances in early diagnosis and therapeutic modalities, conventional cancer treatments such as surgery, radiotherapy, and chemotherapy often exhibit substantial limitations. These include non-specific cytotoxicity, severe side effects, development of drug resistance, and suboptimal therapeutic outcomes, especially in advanced or metastatic settings[2, 3]. A particularly formidable barrier in cancer therapy is the development of multidrug resistance (MDR), which is driven by diverse mechanisms such as overexpression of ATP-binding cassette (ABC) transporters like P-glycoprotein (P-gp), mutations in drug targets,

enhanced DNA repair capabilities, and activation of compensatory survival pathways[4]. Moreover, tumor heterogeneity, both at the inter- and intra-patient levels, further complicates the success of monotherapy approaches and calls for multi-targeted therapeutic designs. In this context, dual-acting anticancer agents have emerged as a promising strategy in modern drug discovery. These agents are designed to exert therapeutic effects through two distinct mechanisms, either by combining two pharmacophores within a single molecular scaffold or by interacting with multiple biological targets. Such an approach offers several advantages: enhanced efficacy due to synergistic or additive effects, reduced likelihood of resistance development, simplified pharmacokinetics compared to combination therapy, and improved selectivity toward malignant cells[5]. Recent studies have shown that dual-acting agents can concurrently inhibit key cancer hallmarks such as uncontrolled proliferation, evasion of apoptosis, angiogenesis, metastasis, and impaired DNA repair. Notable examples include compounds that simultaneously inhibit kinases and anti-apoptotic proteins, hybrid molecules targeting epigenetic regulators and DNA repair enzymes, and metal-based complexes with multi-target activity[6, 7] (Fig.1).

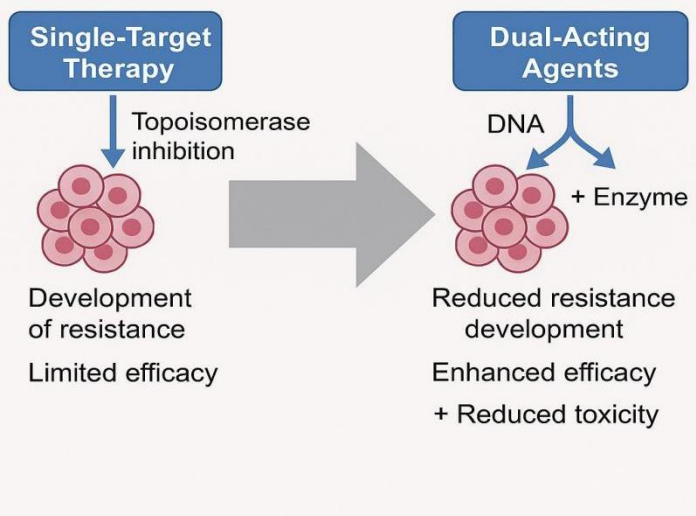

Figure. 1 Advantages of Dual-Acting Agents Over Single-Target Therapy

2. Mechanisms of Action of Dual-Acting Anticancer Agents

Dual-acting anticancer agents are designed to interfere with multiple hallmarks of cancer, providing a multifaceted attack on tumor growth and progression. By targeting distinct molecular pathways simultaneously, these agents can enhance therapeutic efficacy and reduce the likelihood of resistance. Key mechanisms of action include modulation of the cell cycle and apoptosis, inhibition of angiogenesis, and disruption of DNA repair systems [6, 7].

2.1 Modulation of Cell Cycle and Induction of Apoptosis

One of the most common dual-targeting strategies involves inducing apoptosis while simultaneously arresting the cell cycle. Cancer cells often evade apoptosis through upregulation of anti-apoptotic proteins (e.g., Bcl-2, Mcl-1) and downregulation of pro-apoptotic factors (e.g., Bax, p53)[8]. Dual-acting compounds may inhibit cyclin-dependent kinases (CDKs), such as CDK1 and CDK4/6, while also activating the intrinsic apoptotic pathway via mitochondrial membrane permeabilization[9]. For instance, CDK inhibitors coupled with Bcl-2 antagonists have demonstrated synergistic effects by preventing cell cycle progression and simultaneously triggering programmed cell death[10]. A clinically relevant example includes the combination of abemaciclib, an FDA-approved CDK4/6 inhibitor, with venetoclax, a Bcl-2 inhibitor approved for chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML). These agents have shown synergistic pro-apoptotic and anti-proliferative effects in preclinical and clinical studies[11].

2.2 Inhibition of Angiogenesis

Angiogenesis is a critical process for tumor growth and metastasis, primarily mediated by vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) signaling pathways. Dual-acting agents that inhibit angiogenesis while targeting tumor proliferation have shown significant efficacy in preclinical models [12]. For instance, FDA-approved drugs such as Lenvatinib, a dual inhibitor of VEGFR and FGFR, exemplify the success of this approach, demonstrating anti-angiogenic and anti-proliferative effects in several cancer types [13]. Targeting angiogenesis disrupts nutrient and oxygen supply, creating a hypoxic environment that limits tumor expansion.

2.3 Disruption of DNA Repair and Genomic Stability

Cancer cells often rely on robust DNA repair mechanisms to survive genotoxic stress caused by chemotherapy or radiation. Dual-acting agents that inhibit DNA repair enzymes, such as poly(ADP-ribose) polymerase (PARP), in combination with other cytotoxic or signaling inhibitors, can enhance therapeutic outcomes [14]. For example, PARP inhibitors combined with PI3K/mTOR inhibitors or HDAC inhibitors can lead to synthetic lethality in tumors with homologous recombination deficiencies (e.g., BRCA1/2 mutations)[15]. Such combinations not only prevent repair

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of DNA damage but also sensitize cancer cells to subsequent treatments. A notable FDA-approved example is Olaparib, a PARP inhibitor used in the treatment of BRCA-mutated ovarian and breast cancers. When combined with alpelisib, a PI3Kα-selective inhibitor, this regimen demonstrates synthetic lethality and enhanced efficacy[16]. Moreover, investigational compounds like CEP-9722 exhibit dual activity by inhibiting PARP and exerting additional cytotoxic effects, offering further validation of this dual-targeting approach [17].

2.4 Targeting Immune Checkpoints and Epigenetic Regulators

Recent advances in immunotherapy have driven the development of dual-acting agents that modulate immune responses while also inhibiting oncogenic pathways. For instance, HDAC inhibitors can up regulate tumor antigen expression and improve immune recognition, while concurrently inhibiting proliferation and inducing apoptosis [18]

Agents like entinostat illustrate this dual action by enhancing the efficacy of immune checkpoint inhibitors through modulation of the tumor microenvironment [19]

3. Examples of Dual-Acting Anticancer Agents

Over the past decade, several dual-acting anticancer agents have progressed from preclinical evaluation to clinical trials and even market approval. These agents exemplify how simultaneous modulation of multiple pathways can overcome resistance mechanisms and improve clinical efficacy. Below are representative examples: (Fig. 2)

3.1 Dactolisib (BEZ235)

Mechanism: Dual inhibition of PI3K and mTOR

Targeted Pathways: Cell proliferation, metabolism, and survival

Cancer Types: Breast, lung, and head & neck cancers.

Dactolisib is an orally bioavailable imidazoquinoline derivative that targets both PI3K and mTOR, two key nodes in the PI3K/Akt/mTOR signaling pathway. This dual blockade impairs tumor cell metabolism and survival, making dactolisib particularly effective in cancers with activated PI3K mutations or PTEN loss [20].

3.2 Lenvatinib

Mechanism: Dual VEGFR and FGFR inhibition

Targeted Pathways: Angiogenesis, tumor proliferation

Cancer Types: Thyroid, liver, and renal cell carcinoma.

Lenvatinib is a multi-targeted tyrosine kinase inhibitor that simultaneously blocks VEGFR1-3, FGFR1-4, PDGFRα, and RET. This dual inhibition of angiogenic and proliferative signals contributes to its clinical success in radioiodine-refractory thyroid cancer and advanced hepatocellular carcinoma [21].

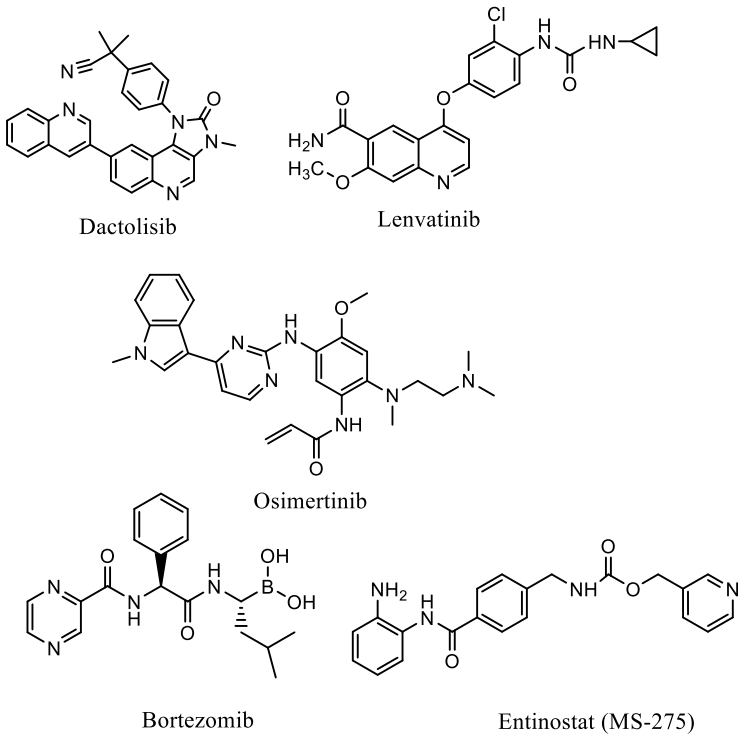

Figure. 2 structure of Dual-Acting Anticancer Agents

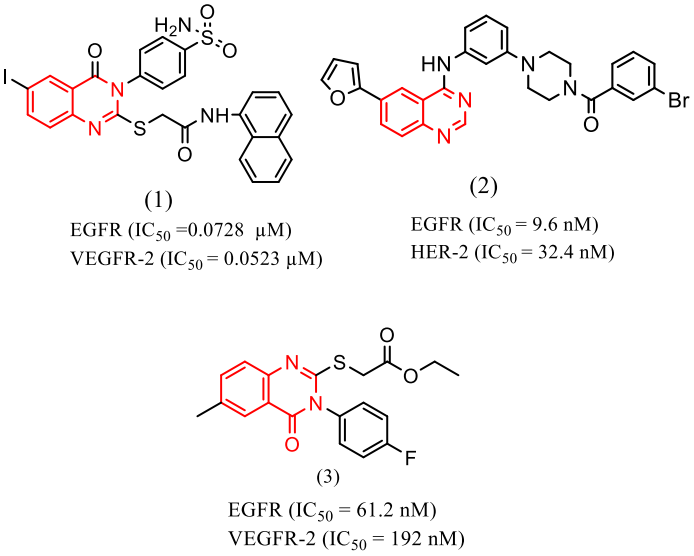

Figure. 3 quinazoline derivatives have dual anti-cancer activity

3.3 Osimertinib (AZD9291)

Mechanism: EGFR T790M mutation inhibition and EGFR pathway blockade.

Targeted Pathways: EGFR signaling.

Cancer Types: Non-small cell lung cancer (NSCLC)

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Osimertinib is a third-generation EGFR inhibitor that irreversibly binds mutant EGFR (T790M), while sparing wild-type EGFR. This dual mechanism overcomes resistance to earlier EGFR inhibitors and is now a first-line treatment for EGFR-mutant NSCLC [22].

3.4 Bortezomib

Mechanism: Proteasome inhibition and NF-κB pathway suppression.

Targeted Pathways: Protein degradation and inflammation

Cancer Types: Multiple myeloma, mantle cell lymphoma

Bortezomib inhibits the 26S proteasome, leading to the accumulation of pro-apoptotic proteins and suppression of the NF-κB pathway. This dual action induces apoptosis and reduces inflammatory signaling, making it a backbone therapy in hematologic cancers [23].

3.5 Entinostat (MS-275)

Mechanism: Class I HDAC inhibition and immune modulation.

Targeted Pathways: Epigenetic control and immune checkpoint regulation.

Cancer Types: Breast cancer, melanoma, lung cancer

Entinostat selectively inhibits histone deacetylases (HDAC1 and HDAC3), leading to chromatin relaxation and transcriptional reactivation of tumor suppressor genes. It also enhances MHC expression and T-cell infiltration, showing synergy with immune checkpoint inhibitors in solid tumors [24].

4. Modified compounds serving as agents with dual anticancer activities

Several chemical scaffolds have been modified to generate dual-acting agents capable of targeting multiple cancer pathways. These scaffolds not only serve as core structures for drug development but also provide flexibility for pharmacophore hybridization. Below is an overview of the major classes of derivatives studied for their dual-acting anticancer potential.

4.1 Quinazoline Derivatives

A series of quinazoline–sulfonamide conjugates was synthesized and investigated for their potential as dual-targeting anticancer agents against both EGFR^T790M and VEGFR-2. The molecular design of these derivatives was guided by the structural requirements of the target kinases, and their chemical structures were confirmed through spectroscopic analyses. Cytotoxicity screening against HepG2, MCF-7, HCT116, and A549 cancer cell lines using the MTT assay demonstrated promising antiproliferative effects. Among them, compound 1 exhibited the highest activity, with an IC_{50} of 0.0977 μM against MCF-7 cells. Further enzymatic evaluation showed potent inhibition of EGFR^T790M and VEGFR-2, with IC_{50} values of 0.0728 μM and 0.0523 μM, respectively. Mechanistic studies revealed that compound 1 induces apoptosis and causes cell cycle arrest at the G2/M phase. Its relative safety was confirmed using normal HEK-293 cells, along with favorable ADMET properties. Additionally, radiosensitization analysis indicated its ability to enhance the efficacy of gamma irradiation (8 Gy) in cancer cells. Molecular docking suggested effective binding of compound 1 to the ATP-binding pockets of both EGFR and VEGFR-2, supporting its dual inhibitory activity [25]. Among recent quinazoline derivatives, Compound 2 (Fig.3) represents a promising candidate among synthesized quinazoline derivatives, designed as a dual-target inhibitor for EGFR and HER-2. This compound incorporates a quinazoline core linked to a heterocyclic tail, which was specifically engineered to enhance selectivity and binding affinity to both kinase targets. Biological evaluations revealed that compound 2 exhibited strong inhibitory activity with IC_{50} values of 9.6 nM against EGFR and 32.4 nM against HER-2, showing its potential as a potent dual-target agent. Structure-activity relationship (SAR) analysis indicated that the presence of the heterocyclic tail played a crucial role in improving the antitumor efficacy by enhancing interaction with the kinase active sites. These results highlight the potential of compound 2 as an effective lead compound for the development of anticancer therapies targeting both EGFR and HER-2 pathways, which are key drivers in many cancers [26]. Further advancing this scaffold, Riadi *et al*. designed a thioacetate quinazolinone derivative compound 3 (Fig.3), ethyl 2-((3-(4-fluorophenyl)-6-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetate, which demonstrated potent cytotoxicity against various cancer cell lines (A549 IC_{50} = 0.57 μM, MDA-MB-231 IC_{50} = 1.19 μM, HeLa IC_{50} = 1.26 μM). The compound effectively inhibited EGFR (IC_{50} = 61.2 nM) and VEGFR-2 (IC_{50} = 192 nM), with docking studies revealing strong binding affinity toward EGFR via two hydrogen bonds (Met793, Cys797) and a halogen bond (Pro794), correlating with a more favorable binding energy (−6.63 kcal/mol) compared to VEGFR-2 (−5.97 kcal/mol). These results emphasize the potential of fluorinated quinazolinone-thioacetate hybrids as efficient dual-acting anticancer agents [27].

4.2 Coumarin Derivatives

Among the various coumarin-based hybrids with promising anticancer potential, two notable examples stand

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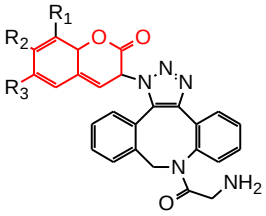
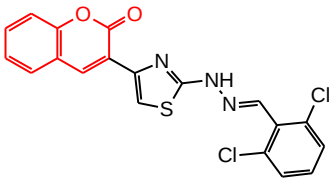
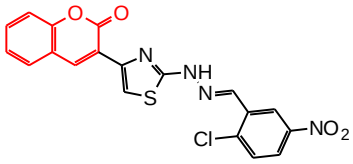


(4a) R_1=H, R_2=OH, R_3=H
(4b) R_1=Cl, R_2=H,R_3=Cl
4a;HeLa ($IC_{50=}$ 21.12µM), MCF-7($IC_{50=}$ 18.4 µM)
4b:HeLa ($IC_{50=}$ 17.5 µM), MCF-7($IC_{50=}$ 9.83µM)



(5)
Hela (IC_{50}= 1.90µM)
COS-7(IC_{50}=>50 µM)



(6)
Hela (IC_{50}= 1.42µM)
COS-7 (IC_{50}=1.96µM)

Figure 4 coumarin derivatives have dual anti-cancer activity

out for their potent activity and well-studied structure–activity relationships. The first is the coumarin-triazole hybrid, particularly compounds 4a and 4b (Fig.4), which demonstrated significant cytotoxicity against MCF-7 and HeLa cancer cell lines as evaluated by MTT assay. These compounds benefited from electron-withdrawing groups (EWGs) such as nitro and chloro at the phenyl ring, enhancing their anticancer efficacy. Docking studies revealed strong interactions with key cancer-related enzymes, suggesting improved binding affinity and bioavailability due to the triazole moiety. These hybrids showed activity comparable to standard chemotherapeutics like cisplatin [28]. In a study by Gabr *et al*. (2017), a series of novel thiazolyl-coumarin derivatives were synthesized using a microwave-assisted method and evaluated for their anticancer activity. Among the synthesized compounds, 5 and 6 (Fig.4) exhibited the most potent cytotoxic effects against various human cancer cell lines, including HeLa, MCF-7, and HepG2. These compounds demonstrated significant inhibitory activities with relatively low IC_{50} values, outperforming several reference drugs. Structure–activity relationship (SAR) analysis highlighted the critical role of halogen substituents and nitrogen-containing groups in enhancing anticancer potency. Additionally, molecular docking studies revealed that these active compounds had strong binding affinities toward the epidermal growth factor receptor (EGFR) active site, supporting their potential mechanism of action. Overall, the promising cytotoxic profiles and favorable docking scores suggest that thiazolyl-coumarin hybrids, particularly compounds 5 and 6, are attractive candidates for further development as anticancer agents [29].

4.3 Quinoline Derivatives

In the study conducted by Li *et al*. (2019), a new series of quinoline-indole derivatives were designed and synthesized as anti-tubulin agents by targeting the colchicine binding site. Biological evaluations demonstrated that several compounds exhibited potent antiproliferative activity against human cancer cell lines, including A549 (lung cancer), HepG2 (liver cancer), and MCF-7 (breast cancer). Among them, compounds 7 and 8 showed the most significant cytotoxic effects, with IC50 values ranging from 2 to 11 nM, respectively, outperforming the reference drug combretastatin A-4 (CA-4) in certain assays. Structure–activity relationship (SAR) analysis revealed that the introduction of electron-withdrawing groups (such as halogens) on the quinoline ring significantly enhanced antiproliferative activity. Additionally, modifications to the indole moiety further optimized the binding affinity and improved the overall efficacy of these compounds. Molecular docking studies confirmed that compounds 7 and 8 are effectively bound to the colchicine binding site of tubulin, showing strong interactions through hydrogen bonding and hydrophobic contacts. The promising cytotoxic profiles and favorable docking scores indicate that quinoline-indole hybrids, particularly compounds7 and 8 (Fig.5), are promising candidates for further development as anticancer agents [30]. In the study by Lu *et al*. (2025), a series of quinoline-based dihydrazone derivatives was synthesized and evaluated for their anticancer activity. Compounds 9 and 10 (Fig.5) exhibited notable cytotoxic effects against MCF-7 breast cancer cells, with IC_{50} values in the micromolar range. Structure–activity relationship (SAR) analysis indicated that modifications to the quinoline core and the nature of substituents on the aromatic ring significantly influenced biological activity. Although detailed trends regarding electron-withdrawing groups were not extensively discussed, it was evident that structural changes impacted potency. Furthermore, molecular docking studies demonstrated that compounds 9 and 10 could interact with DNA through intercalation and

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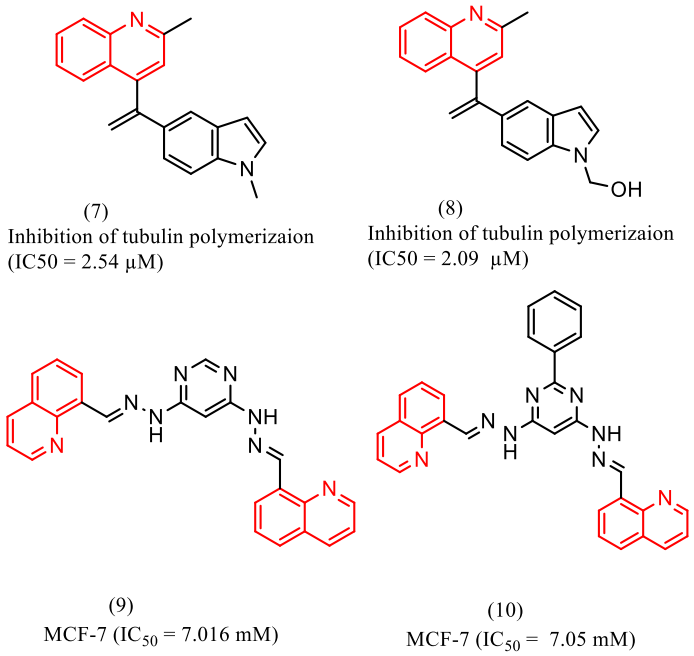

Figure. 4 quinoline derivatives have dual anti-cancer activity

potentially inhibit CDK2 kinase, suggesting a dual mechanism of anticancer action involving both DNA interaction and kinase inhibition [31].

4.4 Hydantoin Derivatives

In the study by Aqeel *et al*. (2023), Compound 11and Compound 12 (Fig.6) emerged as the most potent hydantoin derivatives with significant anticancer activity. Both compounds exhibited strong cytotoxic effects against cancer cell lines such as MCF-7 (breast cancer) and A549 (lung cancer), showing superior potency compared to other

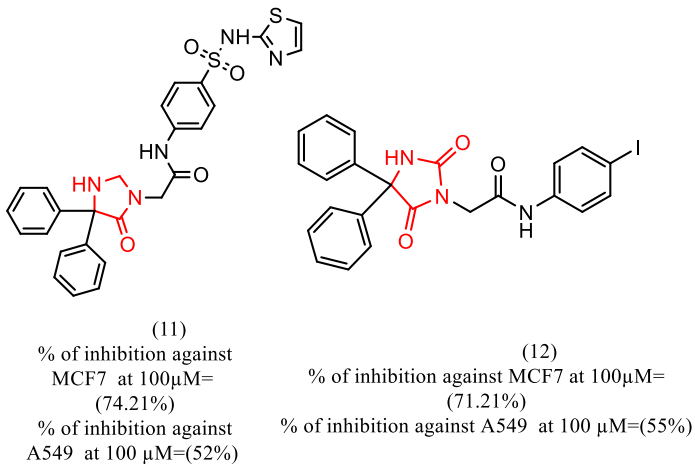

Figure. 5 Hydantoin derivatives have dual anti-cancer activity

derivatives in the study. Structure–activity relationship (SAR) analysis revealed that the presence of electronegative substituents, such as halogens, on the hydantoin scaffold significantly enhanced their anticancer efficacy. Modifications made to the hydantoin core, particularly at the R1 and R2 positions, contributed to the increased binding affinity and improved bioavailability of these compounds. Molecular docking studies confirmed that Compound 11and 12 effectively bind to key cancer-related targets, showing strong interactions with the tubulin binding site. The docking results indicated favorable hydrogen bonding and hydrophobic interactions, which were essential for their enhanced anticancer activity. These findings, combined with their promising biological profiles, make Compound 11 and Compound 12 strong candidates for further development as anticancer agents [32].

5.4 Triazole Derivatives

Triazoles are widely studied for their ability to enhance bioavailability and target DNA repair mechanisms. Recently, a series of dual-acting anticancer agents, incorporating a 1, 2, 3-triazole-chromene-glucose scaffold, was reported. These compounds were synthesized via copper-catalyzed click chemistry, forming hybrid molecules that demonstrated potent antiproliferative activity against MCF-7, HepG2, and HeLa cancer cell lines, while exhibiting low toxicity toward normal WI-37 cells. Among them, compound 13 (Fig.7), chemically named 2-Amino-4-(2,4-dihydroxyphenyl)-7-((1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1H-1,2,3-triazol-4-yl)methoxy)-4H-chromene-3-carbonitrile, showed remarkable dual inhibitory activity against both EGFR and VEGFR-2, supported by docking studies and molecular dynamics simulations. This dual-target approach enhances therapeutic potential by simultaneously blocking key pathways involved in tumor progression and angiogenesis [33]. In this study, compound 14 (Fig.7), a bifunctional naphtho[2,3-d][1,2,3]triazole-4,9-dione derivative, was synthesized to target human dihydroorotate dehydrogenase (hDHODH) and induce the production of reactive oxygen species (ROS). Compound 14 exhibited potent inhibitory activity against hDHODH, highlighting its effectiveness in enzyme inhibition. Docking studies revealed that compound 14 forms key hydrogen bonds and hydrophobic interactions with hDHODH, elucidating its mechanism of action. In vitro assays demonstrated that compound 14 effectively inhibited the proliferation of leukemia and solid tumor cells, while also inducing ROS production, mitochondrial dysfunction, apoptosis, and cell cycle arrest [34]. The study focuses on the design and synthesis of benzimidazole/1, 2, 3-triazole hybrid molecules, specifically compounds 15 and 16 (Fig.7), which

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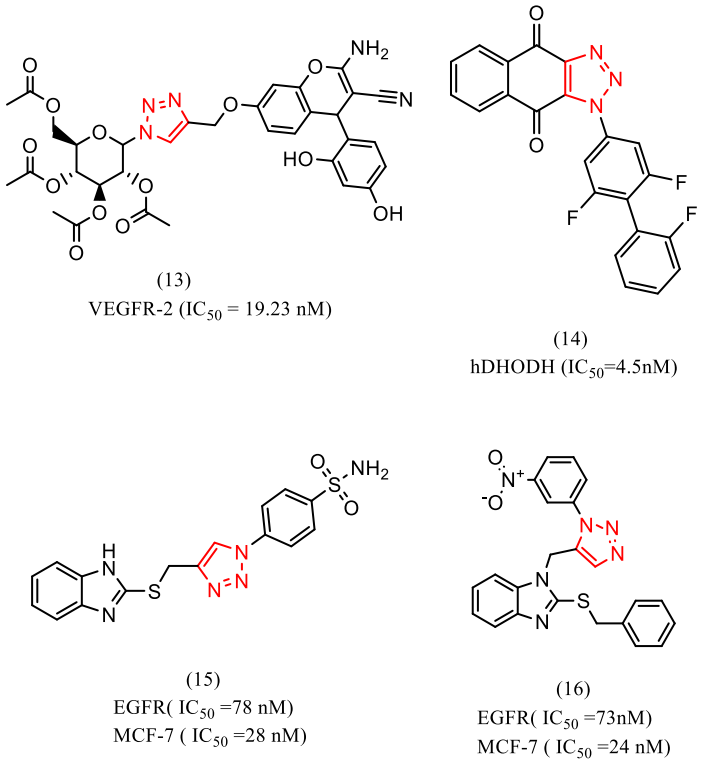

Figure. 6 triazole derivatives have dual anti-cancer activity

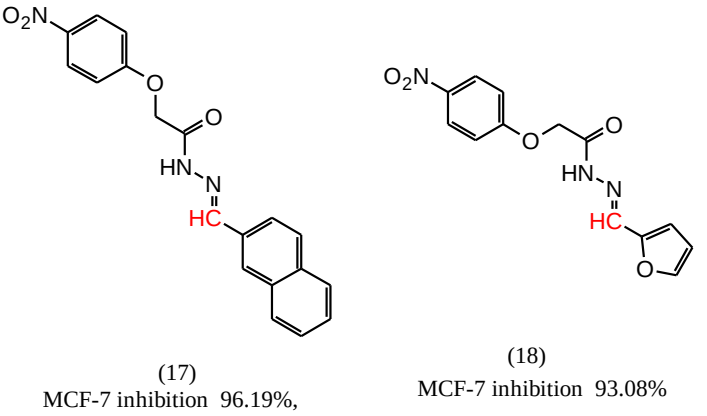

Figure. 7 Hydrazone derivatives have dual anti-cancer activity

demonstrate significant biological activity as selective epidermal growth factor receptor (EGFR) inhibitors. These compounds exhibited potent inhibitory effects on EGFR with IC_{50} values of 78 nM and 73 nM, respectively, surpassing the activity of the commonly used EGFR inhibitor erlotinib. Additionally, compounds 15 and 16 exhibited strong apoptotic potential, inducing apoptosis through the activation of caspases-3, -8, and Bax, while simultaneously downregulating the anti-apoptotic protein Bcl-2. Their antiproliferative activity was further confirmed against the MCF-7 breast cancer cell line, with IC_{50} values of 28 nM and 24 nM, respectively, while showing selective toxicity, as no significant effects were observed on non-tumor MCF-10A cells at a dose of 50 μM, indicating a promising tumor-cell selectivity profile. Molecular docking studies were employed to explore the binding interactions of 15and 16 with the EGFR active site, revealing crucial insights into their mechanism of action as EGFR inhibitors. Furthermore, the absorption, distribution, metabolism, and excretion (ADME) properties of these compounds were carefully evaluated, demonstrating their potential as therapeutic agents with favorable pharmacokinetic profiles

5.5. Hydrazone Derivatives with Dual-Acting Anticancer Activity

A series of sugar hydrazones, oxadiazoline derivatives, and arylidene analogues were synthesized. Among the synthesized compounds, 17 and 18 (Fig.8) exhibited significant antiproliferative activity against the MCF-7 breast cancer cell line. Compound 17 demonstrated a remarkable inhibitory effect, with an inhibitory percentage of 96.19%, while 18 exhibited an inhibition of 93.08%, both surpassing the activity of the reference drug 5-fluorouracil (96.02%). These findings underscore the potential of compound 17 and 18 as highly effective anticancer agents. Molecular docking studies were performed to identify the binding interactions at the active sites, providing valuable insights into their mechanisms of action. Additionally, the interaction of these compounds with DNA in cancer cells further supports their potential to inhibit cancer cell proliferation [36].

5.6. Metal Complexes with Dual-Acting Anticancer Activity

Metal-based compounds have emerged as a promising class of dual-acting anticancer agents due to their unique coordination chemistry and versatile mechanisms of action. These complexes can simultaneously exert cytotoxic effects through DNA interaction, oxidative stress induction, and enzyme inhibition, while also being engineered to target specific tumor microenvironments or cellular pathways. Platinum-based complexes (Pt), such as cisplatin derivatives, represent the earliest examples of metal-based anticancer agents, functioning primarily through DNA crosslinking. Notably, platinum (IV) prodrugs conjugated with bioactive ligands such as non-steroidal anti-inflammatory drugs (NSAIDs) have been developed to enhance tumor selectivity and exert a synergistic inhibitory effect on cyclooxygenase-2 (COX-2), thereby combining cytotoxic and anti-inflammatory mechanisms (Figure.9) [37, 38]. Ruthenium complexes (Ru) offer unique properties including photoreactivity and lower systemic toxicity.

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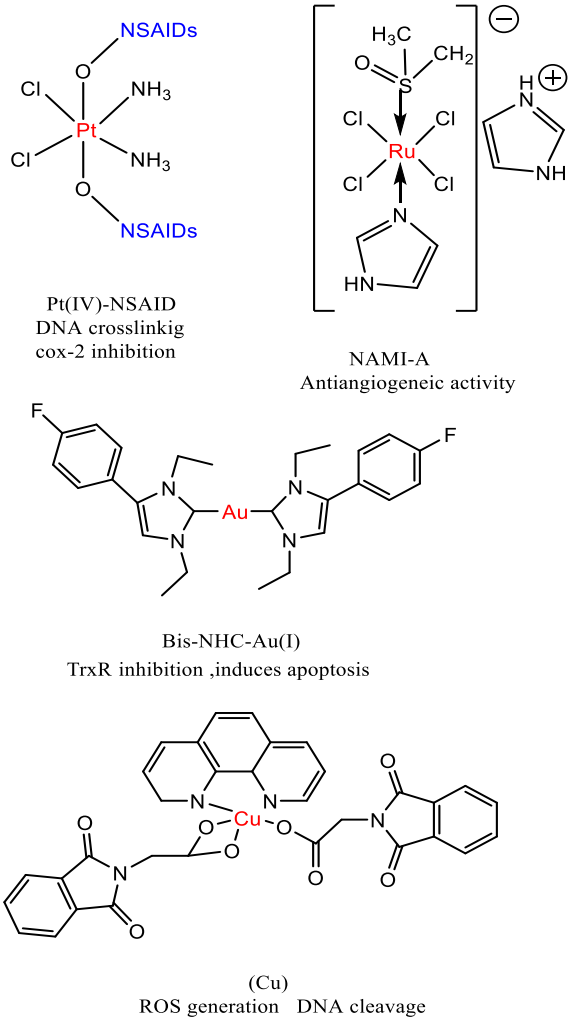

Figure. 8 Metal Complexes with Dual-Acting Anticancer Activity

NAMI-A has demonstrated both anti-metastatic and antiangiogenic effects [39] (Figure .9). Among metal-based dual-acting agents, Cu (II) complexes have demonstrated remarkable ROS-dependent anticancer activity. A recent study investigated Cu(II) and Zn(II) phthaloylglycinate(phen) complexes against triple-negative breast cancer cells (MDA-MB-231), revealing that the Cu (II) complex exhibited significantly higher cytotoxicity. This effect was attributed to its enhanced ability to generate reactive oxygen species (ROS), leading to DNA cleavage and apoptosis induction. The Cu(II) complex showed stronger DNA-binding affinity compared to its Zn(II) counterpart, further contributing to its pro-oxidant and anticancer mechanisms (Figure.9) [40]. Gold (I) complexes, particularly those containing N-heterocyclic carbene (NHC) ligands, inhibit thioredoxin reductase (TrxR), thereby promoting oxidative stress and apoptosis in cancer cells. These complexes exhibit improved selectivity and pharmacological stability compared to earlier gold-based compounds(Figure.9) [41].

Conclusion

Dual-acting anticancer agents represent a transformative approach in oncology by offering the potential to modulate multiple cancer-related pathways within a single molecular framework. These agents address key limitations of conventional therapies, such as non-specific toxicity and acquired resistance, through mechanisms that involve simultaneous inhibition of proliferative signaling, angiogenesis, DNA repair, immune evasion, and epigenetic dysregulation. Structural frameworks such as quinazoline, coumarin, quinoline, hydantoin, triazole, and metal complexes have been utilized as the basis for creating hybrid compounds that exhibit enhanced selectivity and potency. Clinically advanced agents such as dactolisib, lenvatinib, and osimertinib highlight the practical success of dual-target strategies in treating solid and hematological malignancies. Despite the promise, challenges remain in optimizing pharmacokinetics, reducing off-target toxicity, and validating dual mechanisms in heterogeneous tumor environments. The future of dual-acting agents will likely depend on rational drug design, biomarker-guided therapy, and the integration of systems biology to tailor combinations based on patient-specific tumor profiles. As our understanding of cancer complexity deepens, dual-acting therapeutics are poised to become a cornerstone in precision oncology, offering enhanced efficacy, reduced resistance, and better patient outcomes.

Ethical consideration

All the participants in this study gave their informed permission.

Conflicts of Interest

No conflicts of interest are disclosed.

The authors reported no potential conflict of interest.

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