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A Critical Review of Spiro Compounds in Anticancer Drug Discovery

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Abstract

The class of spiro compounds is important in the field of anticancer drug discovery because of the unique 3D structure and remarkable biological activities of these rigid heterocycles. They are useful as a template for the development of drugs because of the presence of a spiro center that allows them to be selectively targeted to the desired target with good pharmacological properties. The structural diversity, synthetic approaches, and anticancer activity of different spiro derivatives such as Spiro oxindole, Spiro pyrrolidine, Spiro pyrimidine, and Spiro indoles are discussed in this review critically. The mechanisms of action, such as induction of apoptosis, arrest of the cell cycle, inhibition of angiogenesis, modulation of signaling pathways, and overcoming drug resistance, are discussed in detail. The review also discusses the major molecular targets such as MDM2-p53, tubulin, protein kinases, and topoisomerases. Recent advances in computational methods like molecular docking, molecular dynamics simulation, QSAR modelling, prediction of ADMET properties, and artificial intelligence-based drug designing have also been discussed. Although some issues need to be addressed in translation, the evidence so far gained in the preclinical phase of drug development suggests that spiro-based compounds should be further developed as potentially useful targeted cancer therapeutics.

Keywords: *Spiro compounds; Spiro oxindoles; Anticancer agents; Heterocyclic compounds; Molecular docking; Drug discovery; MDM2–p53; Protein kinases; Apoptosis; Computational drug design.*

1. Introduction

In spite of the advances in the diagnosis, prevention, and treatment of cancer, it remains one of the leading causes of morbidity and mortality worldwide and is responsible for millions of deaths per year. Given the increasing prevalence of cancer globally, the emergence of multidrug resistance, toxicity effects, recurrence of cancer, and the lack of selectivity of current

chemotherapeutics, there is an urgent demand for novel, more effective anticancer agents. During the past few decades, the heterocyclic class of compounds has been indispensable for medicinal chemistry and has been shown to be very versatile in terms of structure, synthesis, and interaction with multiple biological targets. The heterocyclic moiety is vital for a lot of important drug discoveries, and a considerable proportion of marketed anticancer drugs contain one. But, of these privileged scaffolds, spiro compounds have generated considerable interest as a result of their unique three-dimensional structure featuring two or more cyclic structures connected by a quaternary carbon atom known as the "spiro centre". However, in this privileged class of scaffolds, spiro compounds have received considerable attention because of their challenging 3D structural features that involve two or more cyclic systems connected by a single quaternary carbon atom, which is called the “spiro centre”. This unique structural feature leads to conformational rigidity, enhanced receptor binding affinity, enhanced selectivity, and favourable pharmacokinetics compared to many planar heterocycles. A number of natural and synthetic derivatives of spiro compounds, particularly Spiro oxindoles, Spiro pyrrolidines, spiropyrimidines and spiroindoles have been reported to exhibit potent anticancer activity against various cancer cell lines, including those of leukemia, colon, brain, prostate, lung and ovarian origin, through various mechanisms such as induction of apoptosis, cell cycle arrest, inhibition of angiogenesis, suppression of metastasis and modulation of key signaling pathways.

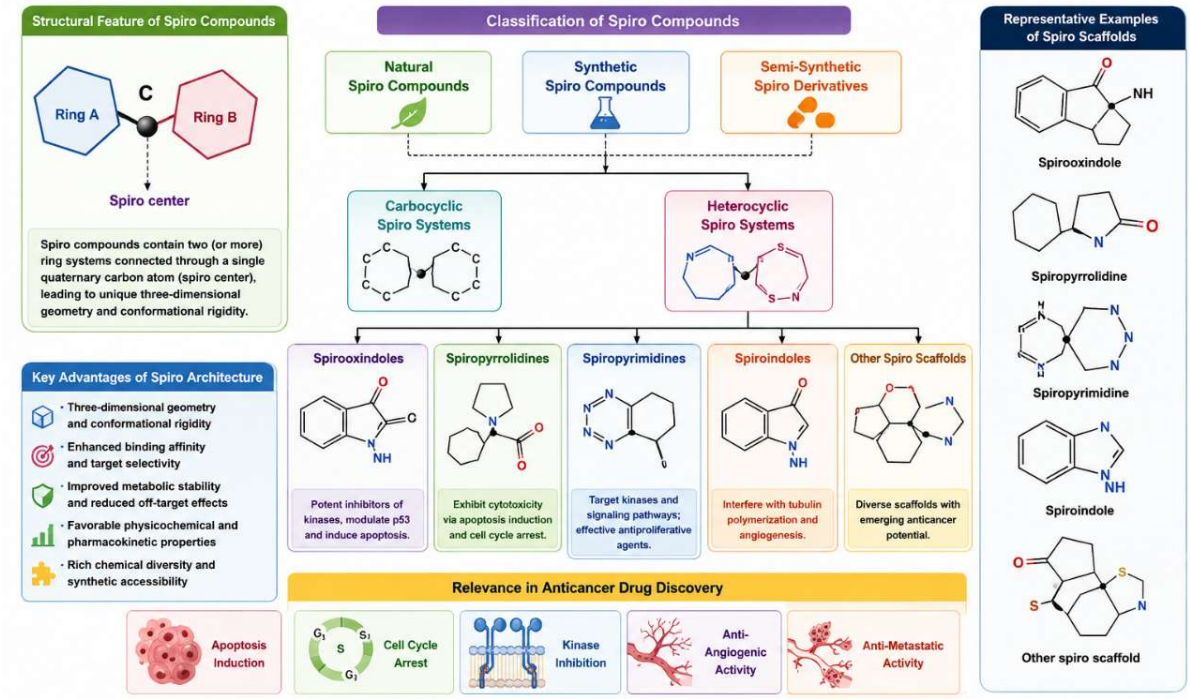


Figure 1. Chemical Architecture and Classification of Spiro Compounds: Overview of the structural framework, major classes, and anticancer applications of spiro-based molecules.

The molecules containing a spiro skeleton are an important source for anti-cancer drug development because of the increasing number of studies reporting promising biological activities and molecular target interactions of these molecules. In addition, the growing knowledge of synthetic approaches, computational drug design, molecular docking and structure–activity relationship (SAR) studies has sped up the discovery and optimization of new

spiro derivatives for improved therapeutic applications. This enables the representation of the chemical structure and general classification of the spiro compounds shown in Fig. 1. Therefore, in the present review, only recent research pertaining to the development of spiro compounds as anti-cancer agents has been discussed critically, highlighting their structural diversity, synthetic approaches, mechanism of action, molecular targets, computational studies, therapeutic potential and future prospects in drug development in the field of oncology.

2. Structural Features and Chemical Diversity of Spiro Compounds

The spiro compounds form a special and important family of organic compounds containing two or more cyclic systems with a single quaternary center, which is called the spiro center. According to IUPAC (International Union of Pure and Applied Chemistry), the spiro compounds are named with the prefix "spiro" followed by numbers in brackets, which indicate the number of atoms in each of the rings forming the spiro structure, excluding the spiro atom. This special class of structures yields a very restricted 3-D structure, making spiro compounds different from fused and bridged ring systems. Conformational stability, increased stereochemical complexity, and interaction with biological macromolecules are the reasons why spiro scaffolds are promising candidates in medicinal chemistry with the orthogonal arrangement of the rings. Spirotetramat is found in a large number of natural products and can be prepared by various synthetic methods. Spiromolecules occur naturally and have been isolated from plants, fungi, marine organisms, and microorganisms, and have a wide range of biological activities such as anticancer, antimicrobial, anti-inflammatory, and antiviral properties. Synthetic spiro compounds, on the contrary, have attracted much attention because of the developments of rapid and structurally variable synthetic spiro compounds by multicomponent reactions, cycloaddition reactions, organocatalysis, and green synthetic methods. This chemical variety of spiro compounds is due to the presence of many heterocyclic nuclei, leading to several subclasses of spiro compounds such as Spiro oxindoles, Spiro pyrrolidines, Spiro pyrimidines, Spiro indoles, spiropyrans, spirochromenes, and Spiro thiazolidines. Of these, Spiro oxindole derivatives are of particular interest as cancer therapeutic agents, as they are able to inhibit multiple cellular targets such as MDM2-p53 interactions, kinases, apoptotic pathways, etc. Biological activity has been shown to be highly dependent upon the nature of the heterocyclic ring, the pattern of substituents, the electronic nature, stereochemistry and spatial orientation around the spiro center through structure–activity relationship (SAR) studies. The introduction of electron-withdrawing groups, heteroatoms, and pharmacologically active substituents often results in an enhanced target affinity, target selectivity, and cytotoxic potency. In addition, it has been demonstrated that optimizing molecular flexibility, the degree of lipophilicity, and hydrogen-bonding ability can lead to better pharmacokinetic characteristics and therapeutic activity. A summary of the major classes of bioactive spiro compounds with typical biological applications is given in Table 1.

Table 1. Classification and Representative Examples of Bioactive Spiro Compounds

Class of Spiro Compound	Representative Scaffold	Key Structural Feature	Major Biological Activity	Anticancer Relevance
Spirooxindoles	Spiro[indoline-3,3′-pyrrolidine]	Oxindole is linked to a heterocycle through a spiro center	Anticancer, antimicrobial	MDM2–p53 inhibition, apoptosis induction
Spiropyrrolidines	Pyrrolidine-containing spiro systems	Five-membered nitrogen heterocycle	Cytotoxic, anti-inflammatory	Cell cycle arrest and tumor growth inhibition
Spiropyrimidines	Pyrimidine-based spiro derivatives	Nitrogen-rich heterocyclic framework	Anticancer, kinase inhibition	Targeting protein kinases and signaling pathways
Spiroindoles	Indole-containing spiro compounds	Indole nucleus attached to the spiro center	Antitumor, neuroprotective	Apoptosis and anti-metastatic activity
Spiropyrans	Pyran-based spiro systems	Photoresponsive spiro architecture	Antimicrobial, anticancer	DNA interaction and cytotoxic effects
Spirochromenes	Chromene-linked spiro compounds	Oxygen-containing fused heterocycle	Antioxidant, anticancer	Anti-proliferative activity against cancer cells
Spirothiazolidines	Thiazolidine-containing spiro derivatives	Sulfur- and nitrogen-containing ring	Anticancer, anti-inflammatory	Modulation of cancer-related enzymes
Spirobenzofuran Derivatives	Benzofuran-based spiro systems	Aromatic oxygen heterocycle	Cytotoxic and antioxidant	Potential lead compounds for solid tumors
Spiroquinazolines	Quinazoline-containing spiro compounds	Nitrogen-rich bicyclic scaffold	Kinase inhibition	EGFR and receptor-targeted anticancer activity
Other Emerging Spiro Scaffolds	Hybrid spiro heterocycles	Multiple pharmacophoric combinations	Broad-spectrum bioactivity	Development of next-generation anticancer agents

3. Synthetic Strategies for the Development of Spiro Compounds.

Spirogels have captured much interest in the medicinal and synthetic chemistry fields in recent years because of the realization of their potential for three-dimensional structures and wide-ranging biological activities. Traditional synthesis for the spiro center involves cyclization reactions, nucleophilic addition–cyclization sequences and intramolecular ring-forming reactions. Classical approaches such as the Pictet–Spengler reaction, Michael addition, Robinson annulation, and 1,3-dipolar cycloaddition have been used many times to prepare spirocycles and spirodoles. In particular, azomethine ylides have become one of the most effective methods for the preparation of structurally complex spiro heterocycles in one step with high regioselectivity and stereoselectivity, among these reactions. Among these reactions are 1,3 dipolar cycloaddition

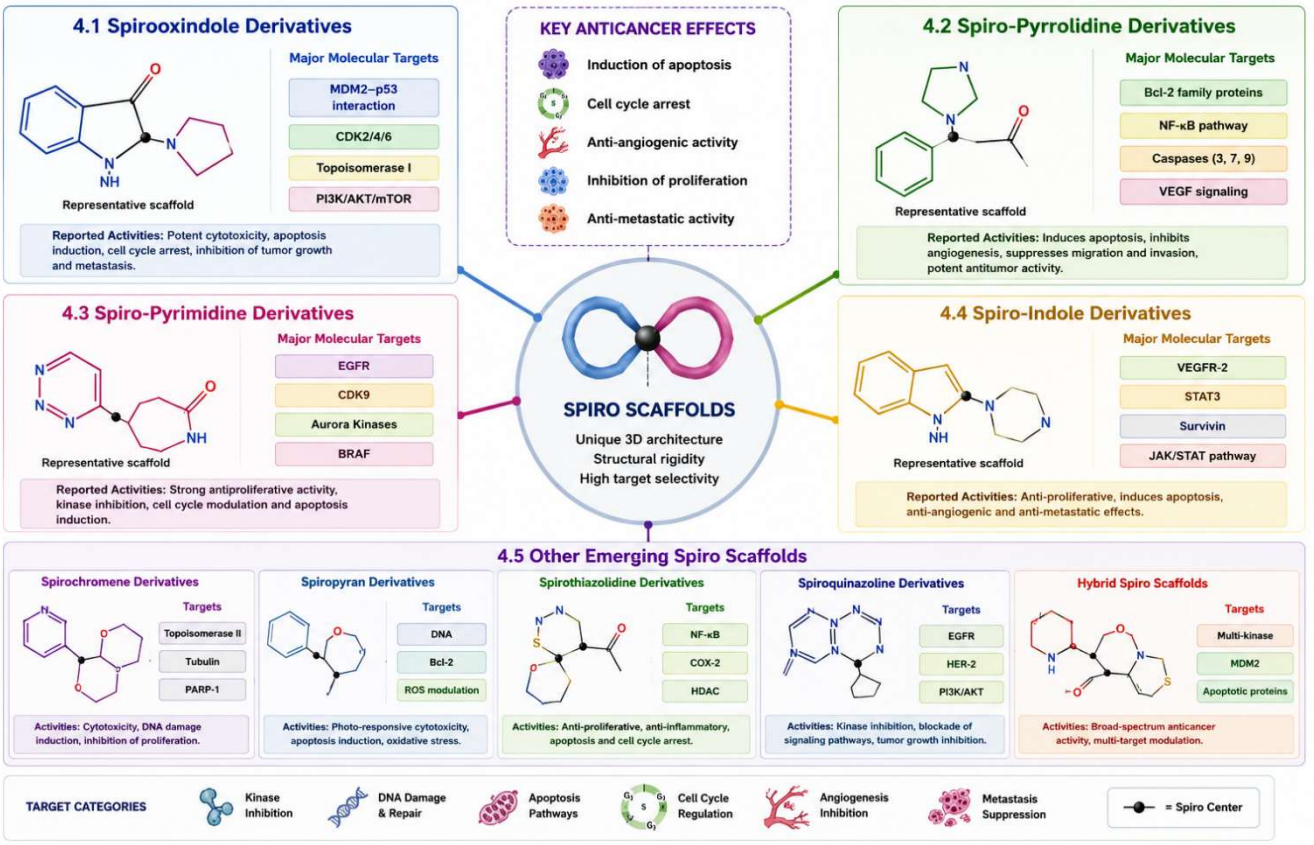
reactions of azomethine ylides, which has emerged as one of the most efficient methods for the synthesis of structurally complex spiro heterocycles with high regioselectivity and stereoselectivity. Multicomponent reactions (MCRs) have changed the face of spiro compound synthesis in recent years, allowing the efficient assembly with a single reaction vessel of complex molecular architectures from three or more readily available starting materials. The benefits of the MCR-based strategies are quite obvious and are highly attractive for a drug discovery program, as they are easy to operate, possess high atom economy, their reaction time is short, and the molecule diversity can be easily generated. At the same time, with the growing focus on environmental sustainability, green synthetic methods have been developed for the production of spiro compounds. Green approaches use environmentally friendly solvents, catalysts that can be recycled, use of microwaves for synthesis, use of ultrasound, use of a solvent-free process, and use of aqueous reaction systems to reduce the amount of waste produced and the amount of energy consumed whilst maintaining high yields and selectivity. The use of Green Chemistry principles has had a positive impact on the sustainability of the synthesis of spiro compounds without sacrificing complexity. Recent developments in synthetic technology have also allowed the extension of the development of spiro compounds by organ catalysis, photocatalysis, transition-metal-catalyzed transformations, asymmetric synthesis, and flow chemistry techniques. These new methods allow for more stereochemical control and more efficient reactions to more novel and difficult spiro architectures. Furthermore, reaction design using the computer and the synthesis of new anticancer spiro compounds using high-throughput synthetic techniques have helped in the discovery of new spiro compounds. These accomplishments have led to the development of a strong and synthetic toolbox for the efficient synthesis of structurally and chemically diverse spiro compounds and the continued studies of these compounds as potential anticancer agents and models in medicinal chemistry.

4. Anticancer Potential of Spiro Compounds

Spiro compounds are one of the most promising classes of heterocyclic molecules being investigated for anticancer drug discovery, due to their 3D characteristics and structural rigidity, which enable them to target multiple cancer-associated molecular targets. Spiroketals, in particular those of the spirooxindole class, have been the focus of special attention in the various subclasses because of their activity on multiple lines of human cancer cells. Several molecules are known to have a spirooxindole structure that inhibit the interaction between MDM2 and p53 and activate the p53 that results in apoptosis in tumour cells. It is also these compounds that have been found to inhibit the proliferation of tumours, to modulate protein kinases, and to disrupt cell cycle progression. Yet another class of compounds that show notable antiproliferative activity is the spiro-pyrrolidine derivatives that have a profound ability to trigger programmed cell death, inhibit DNA synthesis, and prevent metastasis. Similarly, spiro-pyrimidine derivatives are well explored in light of their structural resemblance to the biologically active nucleobases and the inhibition of kinase-mediated signaling pathways, known to be involved in cancer progression. Some of these compounds are highly inhibitory to epidermal growth factor receptors, cyclin-dependent kinases, and other enzymes with an important role in the survival of the tumor. Spiro-indole derivatives also exhibited outstanding anticancer activity by modulating

apoptosis-related proteins, inhibiting angiogenesis, and interfering with cellular signaling networks involved in the regulation of tumor growth and invasion.

Apart from these classes, a large number of novel spiro scaffolds with interesting cytotoxic and anti-metastatic properties like spirochromenes, spiropyrans, spirothiazolidines, and spiro hybrid heterocycles have been discovered. The important anti-cancer spiro scaffolds and their targets are shown in Figure 2. Structure–activity relationship analyses have demonstrated that the appropriate positioning of heterocyclic and pharmacophoric groups around the spiro center has been shown to enhance the biological activity, target specificity, and pharmacokinetic characteristics. This pleiotropic activity of spiro compounds, affecting multiple cancer-related pathways, such as apoptosis, angiogenesis, cell cycle regulation, and kinase signaling, makes them well suited to be further developed as a new generation of anticancer agents. As shown in Figure 2, the future development of targeted cancer therapy and oncology drug development is expected to be greatly affected by further investigation of the spiro structure as a molecular structure framework.



5. Mechanisms of Anticancer Action

The unprecedented anti-cancer properties of spiro compounds have been associated with their inhibition of several cellular and molecular pathways known to play a role in the initiation, progression, and metastasis of cancer. The induction of apoptosis, a programmed cell death process vital for the removal of damaged and/or malignant cells, is one of the most widely reported mechanisms. Multiple spirooxindole, spiropyrrolidine, and spiroindole derivatives have

been shown to both downregulate anti-apoptotic proteins, such as Bcl-2 and survivin, and upregulate pro-apoptotic proteins, including Bax, caspases, and p53, and consequently induce both intrinsic and extrinsic apoptotic pathways. Besides inducing apoptosis, numerous spiro compounds have anti-cancer properties by inhibiting cell cycle progression at various stages, including G0/G1, S, and G2/M checkpoints, stopping cells from proliferating out of control. A number of spiro molecules inhibit a variety of cyclins and checkpoint regulators and cyclin-dependent kinases (CDKs), which are vital for cell cycle progression. Another process that is significant is to inhibit the process of angiogenesis, or the provision of nutrients and oxygen to the growth of cells in a tumor. The anti-vascularization and anti-proliferative effects of spiro derivatives have been shown to inhibit signaling of the vascular endothelial growth factor (VEGF) and proliferation of endothelial cells, which helps to inhibit the vascularization and growth of tumors. Additionally, they regulate important intracellular pathways that are often altered in cancers such as PI3K/Akt/mTOR, MAPK/ERK, JAK/STAT, NF-κB, and Wnt/β-catenin. These signaling pathways have been demonstrated to promote cell survival, proliferation, migration, and invasion, and inhibition of these pathways is a key feature of the ability of spiro compounds to effectively suppress these cellular processes. Recent studies also show that there are a few spiro derivatives that specifically target cancer stem cells, a subset of cancer cells contributing to cancer recurrence, metastasis, and therapeutic resistance. They can inhibit the recurrence of tumors and improve the efficacy of extended treatment by interfering with a set of signaling pathways and self-renewal processes that have been linked to stemness. Moreover, spiro compounds have been reported to be effective in restoring the apoptotic sensitivity and to make the conventional chemotherapeutic agents more effective, and inhibiting drug efflux transporters to overcome the MDR. Given spiro scaffolds' capacity to modulate multiple oncogenic pathways, they certainly have potential as multifunctional anticancer agents and will continue to be developed as next-generation drugs to treat a variety of malignancies.

6. Molecular Targets of Spiro-Based Anticancer Agents

The anti-cancer activity of spiro compounds is mainly believed to be due to the interaction with a wide variety of molecular targets involved in tumor initiation, progression, and viability. The most widely studied target is the MDM2-p53 interaction, which is an important regulatory axis in cellular responses to oncogenic stress and DNA damage. It is now known that derivatives of spiroxindole are potent inhibitors of MDM2, the interaction of which with p53 results in the downregulation of the ability of p53 to induce cell cycle arrest and apoptosis in cancer cells. A number of spiro molecules have been reported to possess nanomolar inhibitory activity against MDM2, and it is one of the most promising targets for the development of anticancer drugs. Another important target is tubulin, which is the main structural protein of microtubules needed to form the mitotic spindle in cell division. Many spiro compounds are found to be inhibitors of tubulin polymerization, leading to arrest of cell division, inhibition of chromosome segregation, and induction of cell death by apoptosis. Protein kinases are other molecular targets involved with spiro-anticancer agents. Spirocycles have demonstrated strong CDK (cyclin-dependent kinases) inhibitory activity and inhibition of epidermal growth factor receptor (EGFR), Aurora kinases, BRAF, PI3K, and other signaling proteins that control cellular proliferation and survival. These inhibit the multiplication of tumors and the spread of cancer. There are other molecular

targets besides the ones mentioned, such as topoisomerases I and II, that are targeted by different spiro derivatives. These enzymes are inhibited, which stops the process of DNA replication, transcription, and repair, and leads to an increase in DNA damage and the death of cancer cells.

In addition to these known targets, there is growing evidence that spiro compounds can also target other pathways, such as NF-κB, STAT3, VEGFR, HDACs, PARP, survivin, and apoptosis-related proteins. This multi-target activity is even more advantageous in the fight against the cellular diversity of tumors and also the appearance of drug resistance. The different interactions shown with the spiro compounds demonstrate their versatility and the therapeutic relevance of these compounds as anticancer pharmacophores. The range of principal molecular targets and related anticancer activities of selected spiro compounds is summarized in Table 2, highlighting diverse biological pathways that are targeted by these unique heterocyclic compounds when it comes to anticancer activity.

Table 2. Selected Spiro Compounds, Molecular Targets, and Anticancer Activities

Spiro Compound Class	Representative Compound/Scaffold	Primary Molecular Target	Mechanism of Action	Reported Anticancer Activity
Spirooxindoles	MI-773 (SAR405838)	MDM2–p53	Restores p53 activity and induces apoptosis	Potent activity against leukemia and solid tumors
Spirooxindoles	Nutlin-inspired Spiro Derivatives	MDM2	Inhibition of MDM2–p53 interaction	Cell cycle arrest and apoptosis
Spiropyrrolidines	Spiro-pyrrolidine Analogues	Tubulin	Inhibition of tubulin polymerization	Mitotic arrest and cytotoxicity
Spiroindoles	Spiroindole Derivatives	VEGFR-2	Anti-angiogenic activity	Suppression of tumor vascularization
Spiropyrimidines	Spiro-pyrimidine Analogues	CDK2/CDK4	Cell cycle regulation	Inhibition of cancer cell proliferation
Spiroquinazolines	Spiroquinazoline Derivatives	EGFR	Tyrosine kinase inhibition	Activity against breast and lung cancers
Spirochromenes	Spirochromene Analogues	Topoisomerase I/II	DNA replication interference	Induction of DNA damage and apoptosis
Spirothiazolidines	Spiro-thiazolidine Derivatives	NF-κB	Suppression of inflammatory signaling	Antiproliferative activity
Spiropyrans	Spiropyran Analogues	PARP/DNA	DNA damage modulation	Enhanced cancer cell sensitivity
Hybrid Spiro Scaffolds	Multi-target Spiro Hybrids	PI3K/Akt/mTOR, STAT3	Simultaneous pathway inhibition	Broad-spectrum anticancer activity

Spirobenzofurans	Spirobenzofuran Derivatives	Survivin	Apoptosis regulation	Induction of programmed cell death
Emerging Spiro Hybrids	Novel Spiro Heterocycles	Multiple Targets	Multi-mechanistic anticancer effects	Potential next-generation anticancer agents

7. Computational Approaches in Spiro Compound Drug Discovery

As computational tools are very helpful in screening and identification of potential drug candidates, the search for identifying and optimizing the structure of a spiro anticancer agent now largely depends on computational tools, which have saved cost and time for the experimental screening process. One of the most widely utilized approaches for predicting the binding affinity and binding pattern of spiro compounds against molecular targets associated with cancer, like MDM2, p53, EGFR, CDKs, tubulin, topoisomerases, and PI3K/Akt signalling proteins, is molecular docking. Docking analyses can be used to gain information about hydrogen bonding, hydrophobic interactions, electrostatic contacts, and binding conformations that are important to the biological activity. Besides docking, molecular dynamics (MD) simulations are gaining popularity in order to investigate the stability and dynamics of a ligand–protein complex under physiological conditions. MD simulations help to analyze conformational flexibility, interaction persistence, binding stability, and their variation with time, providing more reliable computational predictions. The other significant advancement that facilitates drug design is the quantitative structure–activity relationship (QSAR) modelling that gives relationships between molecular descriptors and biological activity in quantitative terms. The anticancer activity of the spiro scaffolds has been predicted by physicochemical, electronic, steric, and topological descriptors used in the QSAR models, which can be used to rationally optimize their activity. Besides efficacy prediction, computational evaluation of pharmacokinetic and toxicological properties has become an essential part of contemporary drug discovery. Absorption, distribution, metabolism, excretion, and toxicity (ADMET) prediction tools are used routinely to assess the ADMET profiles of compounds, and drug-likeness evaluations using Lipinski's Rule of Five and related parameters help to identify compounds with desirable oral bioavailability and toxicity. AI and machine learning have also transformed the design of spiro compounds, enabling the exploration of the vast chemical space in databases, predictions of biological activities and virtual screening of compound libraries, and de novo molecule generation. AI-driven methods aid in the discovery of new spiro derivatives with enhanced target affinity and pharmacological properties, thereby accelerating lead discovery and optimization. The simultaneous integration of molecular docking, molecular dynamics simulation, QSAR modeling, ADMET prediction, and Artificial Intelligence into a single computational tool has enhanced the efficiency of developing anticancer drugs with a spiro structural motif. The whole computational procedure followed for the discovery and optimization of anticancer agents with the spiro topology is presented in Figure 3.

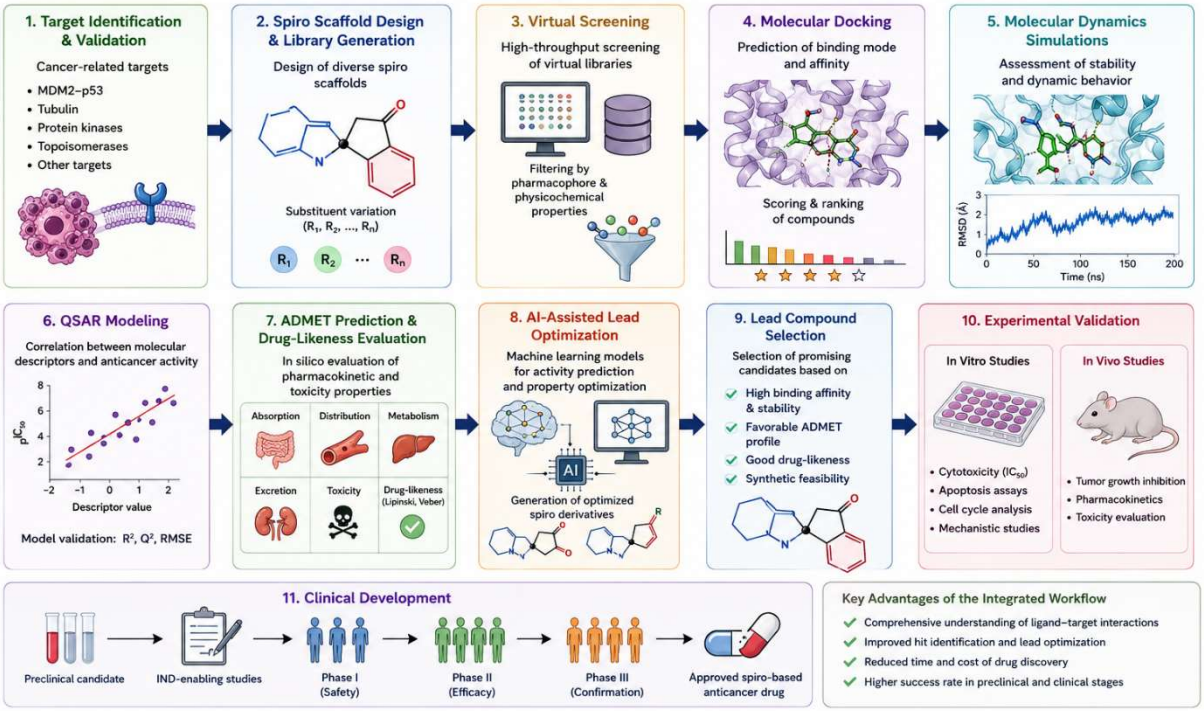


Figure 3. Integrated Drug Discovery Workflow for Spiro-Based Anticancer Agents

8. Clinical Prospects and Translational Challenges

The growing body of evidence of the anticancer activity of spiro compounds makes them promising compounds for further clinical studies. Spiros have been shown to have strong cytotoxic, antiproliferative, anti-angiogenic, and pro-apoptotic effects across a variety of preclinical cancer cell lines, such as breast, lung, colorectal, prostate, leukemia, and melanoma cell lines. A small number of spirooxindole derivatives were found to be exceptionally effective through selective inhibition of the main molecular targets MDM2–p53, tubulin, protein kinases and topoisomerases, and have exhibited very high degrees of tumor growth inhibition, in vitro and in vivo. Although these promising results have been achieved, the clinical translation of these compounds needs to be considered with caution, considering the pharmacokinetic and toxicological properties. Therapeutic performance can be influenced by factors such as solubility in water, metabolic stability, oral bioavailability, tissue distribution, and off-target toxicity. Some spiro compounds have been found to have good drug-likeness properties in preclinical assays and are safe in early developmental studies, but extensive toxicological testing needs to be performed to ensure long-term safety and clinical acceptability. A few translation problems still need to be addressed that are crucial for the progression of spiro-based compounds from the bench to the clinic. These include complicated synthetic steps, lack of scalability, lack of pharmacokinetic optimisation, poor understanding of resistance mechanisms, and lack of clinical validation. Moreover, the therapeutic efficacy is limited by tumor heterogeneity and the appearance of MDR, which requires the development of multitarget and personalized therapy options. However, there are some good prospects for the future development of drugs. The use of medicinal chemistry, structure-based drug design, precision oncology strategies, and artificial

intelligence-based lead optimization, combined with nanotechnology-based drug delivery systems, is likely to speed up the discovery of spiro derivatives with high specificity and clinical efficacy. Computational modelling together with experimental validation can also further improve the selection of candidates and reduce attrition in drug development. Therefore, the unique structural features, the pan-biological effects, and the multi-target therapeutic activities of spiro compounds warrant their further investigation as potential scaffolds to develop new anticancer drugs and possible future use as medicinal products in precision cancer medicine.

9. Future Perspectives

With the recent advances in medicinal chemistry, computational modelling, artificial intelligence, and precision medicine, the future of anticancer drug discovery by the spiro framework still looks promising. The emergence of new synthetic methodologies is expected to expand the scope of structurally diverse spiro scaffolds that can be synthesized and that have a higher degree of selectivity and potency. Identification and optimization of leads with molecular docking combined with machine learning and high-throughput screening will play a vital role. Furthermore, the drug delivery technologies involving nanotechnology and combination therapy could improve the pharmacokinetic properties and therapeutic effects of spiro compounds. Further studies of multitarget mechanisms and personalized treatment will further enhance the clinical usefulness of the spiro anticancer agents.

10. Conclusion

Spiros are a highly promising and intriguing class of heterocycle drugs for potential use in the field of anticancer drug discovery. Their unique three-dimensional structure, structural rigidity, and binding to a variety of targets make them highly effective against cancer cells, with several mechanisms of action including induction of apoptosis, cell cycle arrest, and inhibition of angiogenesis and modulation of signaling pathways. Due to the development of synthetic chemistry and computational drug design, new improved spiro derivatives are being developed at a faster rate. Although there are still translation hurdles to be overcome, increasing preclinical evidence shows that spiro scaffolds are excellent potential candidates in the quest for targeted and effective cancer therapeutics.

Declarations

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this review.

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No specific funding was received for this work.

Author Contributions

All authors contributed to the conceptualization, literature review, writing, and final approval of the manuscript.

Data Availability Statement

No new data were generated or analysed in this study. Data sharing is not applicable to this review article.

Ethical Approval

Ethical approval was not required as this study is based solely on published literature.

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