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Isolation and Characterization of Bioactive Compounds from Medicinal Plants for Anticancer Drug Development

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ABSTRACT: Cancer remains one of the leading causes of morbidity and mortality worldwide, and the search for safe, selective, and affordable anticancer agents continues to drive pharmaceutical research. Medicinal plants represent a vast and largely untapped reservoir of structurally diverse bioactive compounds, several of which have already been translated into clinically approved chemotherapeutics, including the vinca alkaloids, taxanes, camptothecin derivatives, and podophyllotoxin analogues. This review synthesizes current knowledge on the isolation and characterization of plant-derived bioactive compounds and their development as anticancer drug candidates. We summarize conventional and emerging extraction techniques, chromatographic isolation strategies, and spectroscopic methods used for structural elucidation; describe the major phytochemical classes, alkaloids, flavonoids, phenolics, terpenoids, and saponins, and their molecular mechanisms of cytotoxicity; discuss translational approaches including nanotechnology-based delivery, plant biotechnology for scalable production, and computational drug discovery; and outline the remaining challenges and future directions for moving plant-derived anticancer leads from bench to bedside. A divergent radial workflow diagram and four summary tables are provided to consolidate the extraction-to-clinic pipeline for natural anticancer drug development.

KEYWORDS: Medicinal plants; bioactive compounds; isolation; characterization; phytochemicals; anticancer drug development

1. Introduction

Cancer continues to impose an enormous global health burden. According to the most recent GLOBOCAN estimates, nearly 20 million new cancer cases and 9.7 million cancer-related deaths were recorded worldwide in 2022, with projections indicating a substantial further rise over the coming decades as populations age and grow [1]. Despite considerable advances in surgery, radiotherapy, immunotherapy, and targeted molecular therapy, conventional chemotherapeutic regimens remain limited by poor tumor selectivity, severe systemic toxicity, and the frequent emergence of multidrug resistance. These limitations have sustained an enduring interest in natural products, and particularly medicinal plants, as a source of novel chemical scaffolds with improved efficacy and safety profiles. More than 60% of currently

used anticancer drugs are natural products or derivatives thereof, and plant-derived agents such as vincristine, vinblastine, paclitaxel, etoposide, topotecan, and irinotecan continue to occupy a central place in oncology practice [2−5]. The chemical diversity of plant secondary metabolites, encompassing alkaloids, flavonoids, phenolic acids, terpenoids, saponins, and tannins, provides an exceptionally rich pool of multi-target scaffolds capable of modulating apoptosis, cell-cycle checkpoints, angiogenesis, and oncogenic signal transduction pathways such as MAPK/ERK, PI3K/Akt/mTOR, NF-κB, and Wnt/β-catenin [3−11].

Translating a crude plant extract into a well-defined anticancer drug candidate is, however, a long and technically demanding process. It requires systematic extraction, bioassay-guided fractionation, chromatographic purification, and unambiguous spectroscopic structural elucidation before any compound can be subjected to mechanistic, pharmacokinetic, and toxicological evaluation [4]. Furthermore, the low natural abundance of many bioactive metabolites, batch-to-batch chemical variability, and poor aqueous solubility of numerous phytochemicals necessitate complementary strategies such as nanocarrier-based delivery, plant biotechnological production, and computer-aided drug discovery to support clinical translation [12−17]. This review aims to provide an integrated overview of the isolation and characterization of medicinal plant-derived bioactive compounds for anticancer drug development. The discussion is organized into four main sections covering (1) extraction, isolation, and structural characterization methodologies; (2) the major phytochemical classes and their anticancer mechanisms of action; (3) translational strategies including nanotechnology, biotechnological production, and computational drug discovery; and (4) the clinical translation pipeline, current challenges, and future perspectives. A divergent radial flowchart summarizing the overall discovery workflow and four tables consolidating key techniques, compounds, delivery systems, and clinical-stage agents are presented to support a concise, practice-oriented synthesis of this rapidly evolving field.

2. Extraction, Isolation, and Structural Characterization of Plant Bioactive Compounds

The discovery of a plant-derived anticancer lead begins with careful selection and authentication of plant material, followed by a structured sequence of extraction, fractionation, purification, and structural elucidation. Each stage must preserve the chemical integrity of thermolabile or oxidation-prone metabolites while achieving sufficient yield and purity for downstream bioactivity testing [4].

2.1. Extraction Techniques.

Conventional solvent-based methods, maceration, Soxhlet extraction, and percolation, remain widely used because of their simplicity and broad applicability, although they are time- and solvent-intensive. Solvent polarity (from non-polar hexane to highly polar water, with intermediate solvents such as chloroform, ethyl acetate, and methanol) is selected according to the polarity of the target metabolite class. Increasingly, green and instrument-assisted techniques such as ultrasonic-assisted extraction (UAE) and microwave-assisted extraction (MAE) are favored because they disrupt plant cell walls more efficiently, shorten extraction time, reduce solvent consumption, and better preserve heat-labile phytochemicals such as flavonoids and certain alkaloids [4]. Supercritical fluid extraction and enzyme-assisted

extraction represent additional emerging approaches that further improve selectivity and environmental sustainability.

2.2. Fractionation and Chromatographic Isolation.

Following extraction, bioactivity-guided fractionation is typically used to track and concentrate the anticancer activity through successive purification steps. Thin-layer chromatography (TLC) and column chromatography (CC) over silica gel, alumina, or polyamide stationary phases remain the most accessible separation tools, while high-performance liquid chromatography (HPLC) and gas chromatography (GC) provide higher resolution for complex phytochemical mixtures [4]. Preparative and semi-preparative HPLC, medium-pressure liquid chromatography, and supercritical fluid chromatography are increasingly applied to isolate pure compounds in quantities sufficient for full structural characterization and in vitro cytotoxicity testing.

2.3. Spectroscopic Structural Characterization.

Once a pure compound is obtained, its chemical structure must be unambiguously established using complementary spectroscopic techniques. Ultraviolet–visible (UV-Vis) spectroscopy and Fourier-transform infrared (FTIR) spectroscopy provide preliminary information on chromophores and characteristic functional groups, respectively. One- and two-dimensional nuclear magnetic resonance (NMR) spectroscopy, including ^1H NMR, ^13C NMR, DEPT, COSY, HSQC, and HMBC, provides more detailed structural information by defining proton and carbon environments, connectivity, substitution patterns, and, when supported by appropriate experiments, stereochemical features. Mass spectrometry (MS), particularly when coupled with high-performance liquid chromatography (LC-MS/MS) or gas chromatography (GC-MS), enables determination of molecular mass, molecular formula, and diagnostic fragmentation patterns. These techniques are also important for dereplication, allowing previously reported metabolites to be rapidly distinguished from potentially novel compounds in complex plant extracts [4]. The combined application of these orthogonal analytical approaches therefore provides a robust basis for structural confirmation and reduces the possibility of incorrect compound identification.

As summarized in Table 1, structural characterization represents one component of a broader sequential process for discovering plant-derived anticancer compounds. The workflow begins with extraction of phytochemicals from plant material, followed by chromatographic fractionation and isolation of individual constituents. Spectroscopic characterization is subsequently used to establish the chemical identity and structure of purified compounds. Importantly, structural identification alone does not demonstrate therapeutic relevance; therefore, the identified compounds must subsequently undergo biological evaluation using approaches such as cytotoxicity assays, flow cytometry, and molecular docking. Table 1 thus highlights the complementary roles of extraction, purification, structural characterization, and bioactivity confirmation and demonstrates how each analytical stage contributes different information required for reliable identification of promising anticancer candidates.

Table 1. Common techniques used for extraction, isolation, and structural characterization of plant-derived bioactive compounds.

Stage	Representative Techniques	Principal Application / Output
Extraction	Maceration, Soxhlet, percolation, ultrasonic- and microwave-assisted extraction, supercritical fluid extraction	Recovery of crude phytochemical extract from dried plant material
Fractionation / Isolation	Thin-layer chromatography (TLC), column chromatography (CC), HPLC, GC, medium-pressure liquid chromatography	Bioactivity-guided purification of individual compounds from crude extracts
Structural Characterization	UV-Vis, FTIR, 1D/2D-NMR (1H, 13C, COSY, HSQC, HMBC), MS / LC-MS / GC-MS	Determination of functional groups, carbon skeleton, stereochemistry, and exact molecular mass
Bioactivity Confirmation	MTT/SRB cytotoxicity assays, flow cytometry, molecular docking	Verification of anticancer activity and probable molecular target of the isolated compound

The overall relationship among these experimental stages is illustrated separately in Figure 1. Rather than viewing phytochemical discovery as a single linear analytical procedure, the divergent radial workflow emphasizes the integrated nature of compound discovery, in which extraction, isolation, structural elucidation, and biological validation collectively contribute to the identification of promising plant-derived anticancer agents. The workflow also reflects the iterative character of natural-product research, because information obtained during bioactivity testing can guide subsequent fractionation and purification toward the most active constituents. In this context, Figure 1 provides a conceptual overview of how analytical chemistry and biological assessment are interconnected within the discovery pipeline, whereas Table 1 provides the specific techniques and analytical outputs associated with each stage.

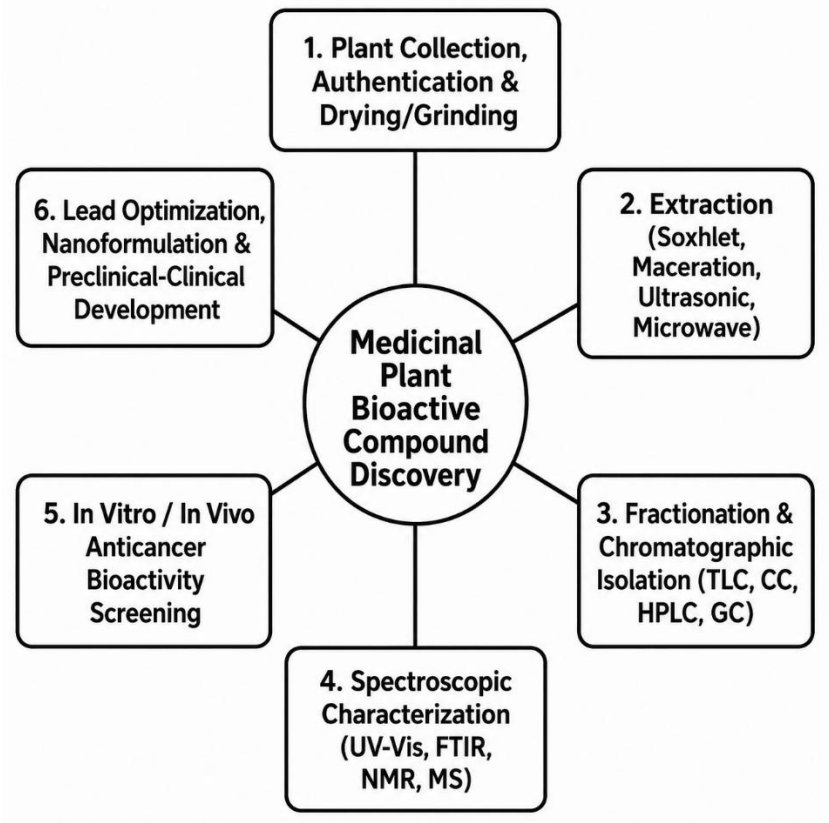

Figure 1. Divergent radial workflow summarizing the integrated discovery pathway.

3. Major Classes of Plant-Derived Bioactive Compounds and Their Anticancer Mechanisms

Plant secondary metabolites with anticancer activity span several major chemical classes, including alkaloids, flavonoids, phenolics, tannins, terpenoids, and saponins. Although these compounds differ considerably in their chemical structures and molecular targets, their biological effects frequently converge on several key anticancer processes, particularly induction of apoptosis, cell-cycle arrest, inhibition of tumor-cell proliferation, suppression of metastatic behavior, and disruption of tumor angiogenesis. The representative compounds, botanical sources, and principal molecular mechanisms discussed in the following subsections are summarized in Table 2, highlighting both the mechanistic diversity and overlapping anticancer activities of major plant-derived compounds.

Table 2. Selected plant-derived anticancer compounds, their botanical sources, and principal molecular mechanisms of action.

Chemical Class	Representative Compound(s) / Source Plant	Principal Mechanism of Action	Reference
Vinca alkaloids	Vincristine, vinblastine, vinorelbine (*Catharanthus roseus*)	Inhibition of tubulin polymerization; mitotic arrest and apoptosis	[5−7]
Camptothecin / podophyllotoxin derivatives	Irinotecan, topotecan (*Camptotheca acuminata*); etoposide (*Podophyllum peltatum*)	Inhibition of topoisomerase I/II; DNA damage-induced apoptosis	[2, 5]
Taxane diterpenoids	Paclitaxel (*Taxus brevifolia*), docetaxel	Microtubule stabilization; mitotic block [	[2, 5]
Flavonoids / stilbenes	Quercetin, curcumin (*Curcuma longa*), resveratrol (*Vitis vinifera*)	NF-κB/PI3K/MAPK modulation; ROS-mediated apoptosis and autophagy	[3, 8, 9, 11]
Saponins	Ginsenosides (*Panax ginseng*), saikosaponins, dioscin	Modulation of Wnt/β-catenin, JAK-STAT3, p53, EGFR pathways; anti-metastatic activity	[10]

3.1. Alkaloids.

Alkaloids constitute one of the most clinically successful classes of plant-derived anticancer agents. The vinca alkaloids vincristine and vinblastine, together with their semisynthetic derivatives vinorelbine, vinflunine, and vindesine, originally derived from *Catharanthus roseus*, bind to tubulin and inhibit microtubule polymerization. This disruption prevents normal mitotic spindle formation, resulting in metaphase arrest and subsequent induction of apoptosis [5–7]. Camptothecin, originally isolated from *Camptotheca acuminata*, and its clinically important derivatives irinotecan and topotecan inhibit topoisomerase I, whereas the podophyllotoxin-derived compounds etoposide and teniposide primarily target topoisomerase II. Inhibition of these enzymes interferes with DNA replication and repair, resulting in accumulation of DNA damage and ultimately cancer-cell death [2, 5]. Colchicine and vincamine further extend the spectrum of alkaloid-based compounds investigated for microtubule-targeting and antiproliferative properties [5]. The major alkaloid-derived anticancer drugs therefore act predominantly through two mechanisms: disruption of microtubule dynamics and inhibition of DNA topoisomerases.

3.2. Flavonoids, Phenolics, and Tannins.

Flavonoids and related phenolic compounds exhibit broader molecular activity than many conventional microtubule- or topoisomerase-targeting agents. Compounds such as quercetin, luteolin, hesperidin, and the curcuminoids of *Curcuma longa* exert antiproliferative and pro-apoptotic effects through modulation of NF-κB, PI3K/Akt, and MAPK/ERK signaling, regulation of reactive oxygen species (ROS), and alteration of the Bax/Bcl-2 balance toward apoptosis [3, 11]. The stilbene resveratrol, found in *Vitis vinifera*, similarly induces caspase-8/caspase-3-dependent apoptosis through ROS-associated autophagic mechanisms in colon cancer cells. Resveratrol may also act synergistically with curcumin by sensitizing transformed breast epithelial cells through suppression of Hedgehog–Gli and PI3K/AKT/mTOR signaling [8, 9]. Tannins contribute additional antioxidant, antiproliferative, and pro-apoptotic effects and are increasingly investigated as potential adjuncts in combination phytotherapy [3]. The representative flavonoids and stilbenes presented in Table 2 illustrate this multi-target behavior. Unlike alkaloids that frequently act on specific structural or enzymatic targets, these polyphenolic compounds can simultaneously regulate several intracellular signaling pathways involved in cancer-cell survival, oxidative stress, inflammation, apoptosis, and autophagy. Such pleiotropic activity may be particularly relevant for targeting heterogeneous tumors in which multiple signaling pathways contribute to treatment resistance.

3.3. Terpenoids and Saponins.

Terpenoids represent another important source of clinically established and experimentally promising anticancer compounds. Taxane diterpenoids, exemplified by paclitaxel from *Taxus brevifolia* and its semisynthetic analogue docetaxel, stabilize microtubules and prevent their normal depolymerization. This abnormal stabilization interferes with mitotic spindle dynamics, producing prolonged mitotic arrest and eventual cancer-cell death. Taxanes have consequently become important chemotherapeutic agents for several malignancies, including breast, ovarian, and non-small-cell lung cancers [2, 5]. Other terpenoids, such as betulinic acid and ingenol mebutate, have also demonstrated cytotoxic activity and remain of interest for the development of structurally diverse anticancer agents [2]. Saponins, including ginsenosides from *Panax ginseng*, saikosaponins, and dioscin, exhibit particularly broad molecular effects. Their reported anticancer mechanisms involve regulation of NF-κB, PI3K/Akt/mTOR, MAPK, Wnt/β-catenin, JAK/STAT3, AMPK, p53, and EGFR signaling pathways. Through these interconnected pathways, saponins can promote apoptosis while suppressing proliferation, invasion, metastasis, angiogenesis, and mechanisms associated with multidrug resistance [10].

Although numerous plant-derived compounds show promising in vitro and in vivo anticancer activity, their clinical translation is frequently hindered by poor aqueous solubility, low oral bioavailability, rapid metabolism, limited tumor selectivity, and low natural abundance. Three complementary translational strategies, nanotechnology-based delivery, biotechnological production, and computational drug discovery, are increasingly being applied to overcome these barriers. Representative nanocarrier systems and biotechnological production platforms, together with their principal translational benefits, are summarized in Table 3.

Table 3. Selected nanocarrier and biotechnological platforms used to enhance the delivery or production of plant-derived anticancer compounds.

Platform	Phytochemical Cargo / Target Metabolite	Reported Benefit	Reference
Plant-derived vesicle-like nanoparticles	Diverse plant bioactive cargo	Improved biocompatibility and non-immunogenic systemic delivery	[12]
Gold–silver core–shell nanoparticles	Protocatechuic acid (*Garcinia mangostana*)	Markedly lowered IC50 and improved colorectal cancer cell selectivity	[13]
Chitosan-based nanoparticles	Various cytotoxic phytochemicals/drugs	Enhanced bioavailability and sustained, targeted drug release	[14]
Lignocellulosic nanoparticles (lignin, xylan, cellulose nanocrystals)	Hydrophobic and hydrophilic anticancer agents	Amphiphilic, biodegradable carrier matrix improving drug loading	[15]
Co-delivery nanoplatforms	Phytochemicals with doxorubicin/etoposide	Synergistic cytotoxicity and reduced multidrug-resistance effect	[16]
Plant cell/tissue culture bioreactors	Paclitaxel, vinblastine, camptothecin	Sustainable, standardized, scalable metabolite biosynthesis	[17]

4.1. Nanoparticle and Nanocarrier Delivery Systems.

Encapsulation of phytochemicals in nanocarriers, including polymeric nanoparticles, liposomes, chitosan-based nanoparticles, lignocellulosic nanoparticles, plant-derived vesicle-like nanoparticles, and metal or metal-oxide nanoparticles, can improve aqueous solubility, protect compounds from premature degradation, prolong systemic circulation, and enhance delivery to tumor tissues [12–16]. Nanocarriers can also support controlled or sustained drug release and the simultaneous delivery of phytochemicals with conventional chemotherapeutic agents, providing a potential strategy for improving therapeutic efficacy and overcoming multidrug resistance. As summarized in Table 3, different nanocarrier materials provide distinct advantages depending on the physicochemical characteristics of the phytochemical cargo and the intended therapeutic application. For example, gold–silver core–shell nanoparticles loaded with the plant-derived phenolic acid protocatechuic acid have demonstrated enhanced cytotoxicity and improved selectivity toward colorectal cancer cells compared with the free compound [13]. Similarly, chitosan-based nanoparticles can enhance drug stability and bioavailability while facilitating sustained and targeted release [14]. Lignocellulosic nanomaterials, including lignin, xylan, and cellulose nanocrystals, offer biodegradable carrier matrices capable of accommodating compounds with different physicochemical characteristics [15]. Co-delivery platforms provide an additional advantage by incorporating phytochemicals alongside conventional cytotoxic agents such as doxorubicin or etoposide, potentially generating synergistic antitumor effects while reducing drug resistance and off-target toxicity [16]. These representative applications and their reported benefits are compared in Table 3.

4.2. Plant Biotechnology and Scalable Metabolite Production.

The clinical-scale supply of several plant-derived anticancer agents, most notably paclitaxel and the vinca alkaloids, has historically been constrained by their low natural abundance, variable accumulation in source plants, and the environmental consequences associated with extensive harvesting. Plant cell and tissue culture technologies, including undifferentiated

callus and suspension cultures, hairy root cultures, and elicitor- or precursor-fed bioreactor systems, provide an alternative approach for the controlled and potentially scalable biosynthesis of these high-value secondary metabolites. These systems can reduce dependence on field-grown plants while allowing greater control over culture conditions and metabolite production. Metabolic engineering and genetic transformation of in vitro culture systems may further enhance metabolite yield by modifying biosynthetic pathways, increasing precursor availability, or regulating rate-limiting enzymatic steps [17]. As indicated in Table 3, bioreactor-based plant cell and tissue culture therefore addresses a different translational barrier from nanocarrier technology: rather than improving drug delivery, it primarily addresses sustainable supply, production scalability, and batch-to-batch standardization of valuable metabolites such as paclitaxel, vinblastine, and camptothecin.

4.3. Network Pharmacology and Computational Drug Discovery.

Network pharmacology, molecular docking, and molecular dynamics simulations have become important tools for prioritizing candidate phytochemicals, predicting their interactions with oncogenic proteins, and providing molecular explanations for experimentally observed biological activity. By integrating compound–target–pathway networks with protein–protein interaction analysis, these in silico approaches can reveal the multi-target characteristics of plant-derived compounds and identify signaling pathways potentially responsible for their anticancer effects [18]. Computational approaches can additionally reduce the number of compounds requiring resource-intensive experimental screening by prioritizing candidates according to predicted binding affinity, molecular stability, target relevance, and pathway involvement. However, computational predictions should be regarded as hypothesis-generating tools rather than substitutes for experimental validation. Integration of computational screening with nanotechnology and scalable biotechnological production may therefore provide a more efficient pipeline in which promising compounds are first prioritized in silico, produced at sufficient scale, and subsequently formulated into optimized delivery systems for preclinical and clinical evaluation.

5. Clinical Translation, Challenges, and Future Perspectives

The path from an isolated and structurally characterized plant-derived anticancer lead to an approved clinical drug is long, highly selective, and shaped by recurring scientific, technological, regulatory, and logistical challenges. Despite these barriers, several plant-derived compounds have successfully progressed into established anticancer therapies, demonstrating the continued pharmaceutical importance of natural products. Representative compounds at different stages of clinical use and development are summarized in Table 4, illustrating the progression from naturally occurring lead structures to approved drugs and investigational semisynthetic derivatives.

Table 4. Selected plant-derived anticancer agents at different stages of clinical use or development.

Compound	Botanical Source	Clinical Status	Reference
Vincristine / vinblastine	*Catharanthus roseus*	Approved; used in leukemias, lymphomas, and solid tumors	[5]
Paclitaxel / docetaxel	*Taxus brevifolia*	Approved; breast, ovarian, and non-small-cell lung cancer	[2]
Irinotecan / topotecan	*Camptotheca acuminata* (camptothecin derivatives)	Approved; colorectal, ovarian, and lung cancers	[2]
Etoposide / teniposide	*Podophyllum peltatum* (podophyllotoxin derivatives)	Approved; testicular cancer, lymphomas, small-cell lung cancer	[2]
Gimatecan, elomotecan, diflomotecan	Camptothecin semisynthetic analogues	Phase I/II clinical trials for advanced solid tumors	[2]

5.1. Preclinical-to-Clinical Development Pipeline.

Following structural characterization and in vitro and in vivo proof-of-concept studies, promising compounds typically undergo pharmacological evaluation and, where necessary, structural or semisynthetic optimization to improve potency, selectivity, solubility, stability, or pharmacokinetic properties. Important examples include the development of camptothecin derivatives such as irinotecan and topotecan and the transformation of the podophyllotoxin scaffold into clinically useful derivatives such as etoposide and teniposide [2, 5]. Successful candidates subsequently progress through preclinical toxicological and pharmacokinetic assessment before entering phase I–III clinical trials. As shown in Table 4, several major classes of plant-derived compounds have successfully completed this translational pathway. Vincristine and vinblastine from *Catharanthus roseus*, paclitaxel and its semisynthetic derivative docetaxel, camptothecin-derived irinotecan and topotecan, and podophyllotoxin-derived etoposide and teniposide have become established anticancer drugs [2, 5]. Their clinical applications across leukemias, lymphomas, breast cancer, ovarian cancer, colorectal cancer, and lung cancer demonstrate that plant-derived molecular scaffolds can generate therapeutically valuable agents across diverse malignancies.However, clinical translation remains an active rather than completed process. Several semisynthetic camptothecin analogues, including gimatecan, elomotecan, and diflomotecan, have undergone clinical investigation for advanced solid tumors [2]. Their inclusion in Table 4 highlights an important distinction between compounds that have achieved regulatory approval and derivatives that remain investigational. This continuing development pipeline demonstrates how natural products can serve not only as therapeutic agents themselves but also as molecular scaffolds for subsequent medicinal-chemistry optimization.

5.2. Persistent Challenges.

Despite these successes, only a small proportion of promising plant-derived compounds ultimately achieve clinical application. Key obstacles include poor aqueous solubility and oral bioavailability, rapid metabolism, insufficient tumor selectivity, batch-to-batch variability in metabolite concentrations arising from genetic, geographic, and environmental factors, and the difficulty and cost associated with large-scale isolation from natural sources [2, 4]. Some compounds also exhibit a relatively narrow therapeutic window, where concentrations required

for anticancer activity may produce significant toxicity in normal tissues. The approved drugs presented in Table 4 demonstrate that these limitations are not necessarily insurmountable. In several cases, successful translation has depended on semisynthetic modification of a natural scaffold, optimization of formulation and dosing, and extensive pharmacological and toxicological evaluation. Nevertheless, comparable data remain insufficient for many newly identified phytochemicals. Comprehensive toxicological profiling, pharmacokinetic and pharmacodynamic characterization, reproducible formulation, and standardized Good Manufacturing Practice (GMP)-compliant production therefore remain essential prerequisites for regulatory approval. Another significant challenge is the transition from promising laboratory results to clinically meaningful efficacy. Cytotoxic activity observed in cancer cell lines does not necessarily predict therapeutic efficacy in humans because absorption, distribution, metabolism, excretion, tumor microenvironment, and systemic toxicity can substantially alter drug performance. Consequently, stronger integration of mechanistic studies, pharmacokinetic assessment, appropriate animal models, and well-designed clinical trials is required to reduce attrition during translation.

5.3. Future Directions.

Future progress will likely depend on the convergence of bioactivity-guided isolation with green extraction technologies, nanocarrier-enabled formulation, plant biotechnological scale-up, medicinal chemistry, and network pharmacology-guided mechanistic prioritization. These approaches can address different bottlenecks simultaneously, ranging from sustainable compound production and improved bioavailability to enhanced tumor targeting and identification of therapeutically relevant molecular pathways. Greater integration of artificial intelligence (AI) and machine learning into compound prioritization, structure–activity relationship prediction, toxicity screening, and target identification may further accelerate the discovery pipeline by identifying the most promising candidates before resource-intensive experimental testing [18]. Such computational approaches should nevertheless complement rather than replace experimental pharmacological and clinical validation. The progression from natural compounds such as vincristine, vinblastine, and paclitaxel to semisynthetically optimized agents such as irinotecan, topotecan, docetaxel, and etoposide provides strong evidence that plant-derived chemical diversity remains an important foundation for anticancer drug development. At the same time, the presence of investigational compounds such as gimatecan, elomotecan, and diflomotecan emphasizes the substantial attrition between promising molecular leads and approved therapies. Future advances will therefore require not only the discovery of additional bioactive phytochemicals but also coordinated efforts in formulation science, scalable production, computational screening, toxicology, pharmacokinetics, and rigorously designed clinical trials to translate promising natural products into safe and effective anticancer therapeutics.

6. Conclusion

Plant-derived bioactive compounds remain an important source of anticancer agents because of their chemical diversity and ability to target multiple mechanisms involved in cancer development and progression. Alkaloids, flavonoids, phenolics, terpenoids, and saponins exert anticancer effects through microtubule disruption, topoisomerase inhibition, apoptosis induction, oxidative stress regulation, and modulation of major signaling pathways, including

PI3K/Akt, MAPK, NF-κB, and JAK/STAT3. Several natural products and their semisynthetic derivatives, including vincristine, paclitaxel, irinotecan, and etoposide, have successfully reached clinical application, demonstrating the therapeutic value of plant-derived molecular scaffolds. Nevertheless, poor solubility, limited bioavailability, toxicity, variable metabolite production, and difficulties in large-scale production remain important translational barriers. Future development should integrate advanced nanocarrier systems, plant biotechnology, sustainable extraction, computational drug discovery, and artificial intelligence with rigorous pharmacological and clinical validation. Such multidisciplinary strategies could accelerate the translation of promising phytochemicals into safer, more selective, and clinically effective anticancer therapeutics.

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this review.

Author Contributions

Both authors contributed equally to the conceptualization, literature review, writing, and revision of this manuscript. Both authors have read and approved the final version of the manuscript.

Data Availability Statement

No new datasets were generated or analyzed during the preparation of this review. All data discussed are available within the cited published articles listed in the reference list.

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