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Review Article

Plant-Derived Bioactive Compounds for Cancer Therapy: Mechanisms, Clinical Evidence, and Translational Challenges

Sonali Saste*, Shrikumar Vijaykumar Mahamuni

Department of Microbiology, Shardabai Pawar Mahila Arts, Commerce and Science College, Shardanagar, Malegaon Bk., Baramati, Pune, Maharashtra 413115, India

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ABSTRACT

Plant-derived bioactive compounds are widely investigated as sources of candidate molecules for cancer prevention and treatment. This narrative review summarizes major phytochemical classes—including polyphenols, flavonoids, alkaloids, terpenoids, brassinosteroids, and cardiac glycosides—and examines reported anticancer activities, molecular mechanisms, analytical approaches, and translational limitations. A selective literature search of PubMed and Google Scholar was used to identify English-language publications available through March 2023, using terms relating to medicinal plants, phytochemicals, cancer, apoptosis, cell-cycle arrest, angiogenesis, and cancer signalling. Evidence discussed in the literature includes preclinical observations of altered apoptosis, cell-cycle regulation, angiogenesis, oxidative stress responses, immune signalling, and pathways such as PI3K/AKT/mTOR, MAPK/ERK, NF- κ B, and Wnt/ β -catenin. Some plant-derived natural products have also informed approved anticancer medicines, but evidence for isolated phytochemicals and crude extracts varies substantially by compound, formulation, cancer type, and study design. Important barriers include limited bioavailability, inconsistent extract composition, uncertain dose–response relationships, toxicity, herb–drug interactions, and a shortage of robust clinical evidence for many candidates. This review is narrative rather than systematic and does not claim exhaustive retrieval or formal risk-of-bias assessment. Better chemical standardization, mechanistic validation, pharmacokinetic evaluation, and well-designed clinical studies are needed before most candidates can be considered reliable therapeutic options.

INTRODUCTION

According to estimates from the Global Cancer Observatory (GLOBOCAN), the number of new

***Corresponding Author:** Sonali Saste

Address: Department of Microbiology, Shardabai Pawar Mahila Arts, Commerce and Science College, Shardanagar, Malegaon Bk., Baramati, Pune, Maharashtra 413115, India

Email ✉: sonalisaste@adtaramati.com

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cancer cases worldwide in 2020 was 19.3 million (Sung, Hyuna et al. 2021). India was ranked as the third-highest country in terms of incident cancer cases, following China and the United States of America. GLOBOCAN has projected that the number of cancer cases in India will reach 2.08 million by 2040, representing a significant increase of 57.5 percent compared to 2020. (Ferlay, Jacques et al. 2020). The search for effective and safe treatments for cancer remains a global priority, as this devastating disease continues to impact millions of lives worldwide. In recent years, there has been a growing interest in exploring natural sources, such as medicinal plants, for potential anticancer agents. Medicinal plants have a long history of use in traditional medicine systems and are known to contain a wide array of bioactive compounds with diverse therapeutic properties. The scientific and research community is increasingly focusing on naturally-derived compounds due to their perceived lower toxic side effects in comparison to current treatments like chemotherapy. The Plant Kingdom produces naturally occurring secondary metabolites which are being investigated for their anticancer activities leading to the development of new clinical drugs. (Greenwell et al., 2015).

Among the bioactive compounds derived from medicinal plants, botanical derivatives have gained significant attention due to their potential anticancer properties. These derivatives, including alkaloids, flavonoids, terpenoids, polyphenols, and lectins, have demonstrated promising effects against various types of cancers (Nasim et al. 2022). Understanding the mechanisms underlying their anticancer activities is crucial for harnessing their therapeutic potential. Critical regulatory pathways, including the MAPK pathway, PI3K/AKT/mTOR signaling, and the Wnt/ β -catenin signaling pathway, hold vital significance in governing signal transduction and fundamental

biological processes such as cell proliferation, apoptosis, and metabolism, among others. The intricate regulatory mechanisms and biological functions of these signaling pathways are pivotal in numerous human cancers. Despite promising outcomes from combining various therapeutic approaches, several challenges persist in devising an effective antitumoral treatment that specifically targets tumoral cells (Fu et al., 2022). Natural plant extracts and derivatives have been reported to impact multiple oncological pathways that are related to apoptosis, angiogenesis, MAPK, cell cycle progression/proliferation, reprogrammed metabolisms, and epigenetics. Identification of these botanic derivative-impacted oncological pathways will help design or modify botanical lead compounds to generate potent anticancer drugs with minimal side-effects.

Botanical derivatives exhibit multifaceted mechanisms of action against cancer cells. Some compounds induce apoptosis, a programmed cell death mechanism that eliminates damaged or abnormal cells. Others disrupt cell cycle progression, leading to cell cycle arrest and inhibition of uncontrolled cell growth. Additionally, certain botanical derivatives inhibit angiogenesis, the process by which tumors develop their blood supply, thereby impeding tumor growth and metastasis (Banerjee et al 2022). Moreover, botanical derivatives can modulate signalling pathways involved in cancer development and progression. By targeting these pathways, they can interfere with key cellular processes, such as cell proliferation, migration, and invasion. Furthermore, botanical derivatives have been shown to enhance the immune system's response to cancer cells, promoting immune-mediated cytotoxicity and suppressing tumor growth.



Plant-derived drugs offer desirable attributes for cancer treatment owing to their natural origin and easy availability. These compounds have played a crucial role in addressing various types of cancer effectively. Notable examples of such agents include Vinblastine, Vincristine, Docetaxel, Etoposide (derived from Epipodophyllotoxin), Paclitaxel (Taxol), Flavonoids from Ginkgo biloba, Curcuma longa, Berberine, among others. Additionally, marine and microbiological organisms have also provided a diverse array of bioactive agents with significant therapeutic potential for anticancer treatments, complementing the efficacy of herbal natural products. Prominent examples of these drugs include trabectedin, dolastin, halichondrin, anthracyclines, and enediynes (Deep *et al.*, 2023). The wide range of anticancer mechanisms exhibited by botanical derivatives makes them an intriguing area of research and holds promise for the development of novel therapeutic interventions. Furthermore, their natural origin offers potential advantages, such as reduced toxicity and better tolerability compared to synthetic drugs. However, extensive scientific investigations, including preclinical and clinical studies, are essential to fully understand their efficacy, safety, and potential interactions with conventional cancer treatments. (Saklani & Kutty, 2008)

In this article, we aim to provide a narrative overview of the anticancer properties and mechanisms of action of botanical derivatives derived from medicinal plants. By examining the current body of scientific literature, we will delve into the diverse classes of compounds and their specific effects on cancer cells. Understanding the mechanisms by which botanical derivatives exert their anticancer activities will not only contribute to our knowledge of natural therapeutics but also

pave the way for the development of targeted and personalized cancer treatments.

By exploring the potential of botanical derivatives as anticancer agents, we hope to contribute to the growing body of evidence supporting the use of natural compounds in cancer therapy. Ultimately, the integration of traditional medicine and modern scientific approaches can provide new avenues for improving cancer treatment outcomes and enhancing the quality of life for patients.

2. LITERATURE SEARCH STRATEGY

This article is a narrative review, not a systematic review or meta-analysis. A selective literature search was conducted using PubMed and Google Scholar to identify publications relevant to plant-derived bioactive compounds and cancer. Search concepts included medicinal plants, plant extracts, phytochemicals, anticancer activity, apoptosis, cell-cycle arrest, angiogenesis, tumour growth, signalling pathways, phytochemical isolation, and clinical trials. English-language publications available up to March 2023 were considered.

Publications were considered relevant when they addressed phytochemical composition, extraction or characterization, anticancer activity in cellular or animal models, mechanisms of action, clinical development, safety, or limitations affecting translation. The review also considered selected established anticancer medicines derived from natural products to provide context for natural-product drug discovery. This selective approach was intended to provide a broad overview of key themes rather than a reproducible exhaustive search.

Because a complete database-specific search strategy, duplicate-removal log, formal screening flow, and structured risk-of-bias assessment were not documented, the article should not be



interpreted as a systematic or scoping review. Statements about clinical evidence should be checked against primary trial records and publications before submission.

3. PLANT-DERIVED BIOACTIVE COMPOUNDS AS ANTICANCER AGENTS

Bioactive principles found in medicinal plants are of significant interest due to their potential therapeutic applications. These bioactive compounds, also known as secondary metabolites, are derived from primary metabolites and play essential roles in the survival and defense mechanisms of plants against pathogens and herbivores. (Newman & Cragg, 2016). Additionally, they exhibit diverse pharmacological effects in mammalian systems, making them valuable sources for drug discovery and development.

Several classes of bioactive principles have been identified in medicinal plants, including alkaloids, flavonoids, terpenoids, phenolic compounds, and glycosides, among others. These compounds have demonstrated various biological activities, such as antioxidant, anti-inflammatory, antimicrobial, anticancer, and neuroprotective properties. In recent decades, researchers have directed their efforts towards drug discovery using herbal medicines or botanical sources, which are an essential part of complementary and alternative medicine (CAM) therapy (Pan *et al.*, 2013).

3.1. Polyphenols

Polyphenols are a group of organic compounds with over 10,000 members that share a three-membered flavan ring system. These natural compounds are known for their advantageous properties, including scavenging free radicals, reducing oxidative stress, and modulating inflammation. In this context, the role of

polyphenols, particularly curcumin, resveratrol, and epigallocatechin gallate (EGCG), in addressing various aspects of cancer drug resistance is discussed (Maleki *et al.*, 2022). Resveratrol, found in peanuts, grapes, and red wine, and gallacatechins from green tea, exhibit antioxidative effects, contributing to overall health improvement and reducing the risk of cancer. Moreover, polyphenols trigger apoptosis in cancer cells by regulating copper ion mobilization, causing DNA fragmentation, and interfering with cancer-related proteins, such as Tumour Necrosis Factor (TNF) (Niedzwiecki *et al.*, 2016).

3.2. Flavonoids

Flavonoids, which are a subclass of polyphenolic compounds, constitute a wide family of plant secondary metabolites with diverse structures and physiological activities. They can be categorized into several classes, such as flavones (e.g., flavone, apigenin, and luteolin), flavonols (e.g., quercetin, kaempferol, myricetin, and fisetin), flavanones (e.g., flavanone, hesperetin, and naringenin), and others. Flavonoids share a benzo- γ -pyrone structure and are widely distributed in plants (Kumar *et al.*, 2013). Extracted from various plants, flavonoids display potent anticancer effects against different types of cancer, including hepatoma, cervical carcinoma, and breast cancer. These compounds induce apoptosis through intrinsic and extrinsic signaling pathways, disrupt mitochondrial function, and interfere with proteins involved in cancer cell survival, proliferation, and angiogenesis (Kopustinskiene *et al.*, 2020).

3.3. Alkaloids

Alkaloids are a remarkably diverse group of compounds characterized by cyclic structures containing at least one basic nitrogen atom. These compounds are widely distributed in the plant kingdom, with significant presence in plants



belonging to families like Leguminosae, Menispermaceae, Ranunculaceae, Loganiaceae, and Papaveraceae (Benyhe, 1994; Li *et al.*, 2007; Huang *et al.*, 2007). Many well-known chemotherapeutic agents, such as camptothecin, vincristine, vinblastine, berberine, sanguinarine, evodiamine, piperine, matrine, and tetrandrine, are classified as alkaloids. They have garnered considerable attention for their ability to regulate various mechanistic pathways involved in proliferation, cell cycle, and metastasis. Notably, vincristine and vinblastine have a historical significance in cancer treatment and are actively used in managing acute lymphoblastic leukemia (Mondal *et al.*, 2019). Some antitumor drugs used clinically, including vincristine, vinblastine, and paclitaxel, have natural origins as alkaloids.

3.4. Terpenoids

Terpenoids, the largest and most diverse group of naturally occurring phytoconstituents, are responsible for imparting fragrance, taste, and pigmentation to plants. Their classification is based on the number of isoprene units they contain, which serve as the building blocks for terpenoids. Isoprene is a gaseous hydrocarbon with a molecular formula of C₅H₈ (Kamran *et al.*, 2022). Terpenoids, composed of these isoprenoid units, represent one of the most extensive groups of natural products, with over 40,000 individual compounds discovered so far, and new ones continue to be identified each year (Sacchettini *et al.*, 1997; Peñuelas *et al.*, 2005; Withers *et al.*, 2007). While most terpenoids originate from plants, they are also synthesized by other organisms, such as bacteria and yeast, as part of their primary or secondary metabolism. The classification of terpenoids includes various classes, such as monoterpenes (e.g., carvone, geraniol, d-limonene, and perillyl alcohol), diterpenes (e.g., retinol and trans-retinoic acid),

triterpenes (e.g., betulinic acid, lupeol, oleanic acid, and ursolic acid), and tetraterpenes (e.g., α -carotene, β -carotene, lutein, and lycopene) (Rabi *et al.*, 2009).

3.5. Brassinosteroids

Brassinosteroids (BRs), which are naturally occurring compounds in plants, play vital roles in hormonal signaling, growth regulation, and stress responses. Among them, 28-homocastasterone and 24-epibrassinolide have shown remarkable anticancer effects against multiple cancer cell lines, including T-lymphoblastic leukemia, multiple myeloma, and various carcinoma cell lines. These BRs interact with crucial proteins involved in breast and prostate cancers, such as estrogen receptor, epidermal growth factor receptor, and androgen receptor, leading to growth inhibition and induction of apoptosis. Notably, BRs exhibit distinct responses in normal and cancer cells, making them promising selective agents against cancer cells (Ma *et al.*, 2022).

3.6. Cardiac Glycosides

Cardiac glycosides (CGs) are natural compounds widely utilized to treat various cardiac conditions and have more recently gained recognition as potential antitumor agents. They act as ligands for Na/K-ATPase, which is a promising drug target in cancer treatment (Schneider *et al.*, 2017). Additionally, there is growing evidence suggesting that CGs can activate tumor-specific immune responses. CGs are of particular interest for drug repurposing, as they can be derived from both plant and animal sources and have been used to address various human ailments (Kara's *et al.*, 2020). While CGs are primarily known for their role in inhibiting the Na⁺/K⁺ ATPase pump during heart failure, leading to their clinical approval for cardiovascular disease treatment (El-Mallakh *et al.*, 2020), their potential application in



diverse cancers has been explored. CGs demonstrate selective cytotoxic effects on tumor cells, elevating their potential as promising anticancer molecules (Reddy *et al.*, 2020).

4. ISOLATION, PURIFICATION AND CHARACTERIZATION OF PHYTOMEDICINAL COMPOUNDS

In ancient times, the isolation, extraction, and purification of drugs from medicinal plants led to the discovery of miraculous compounds that have been instrumental in alleviating human ailments. However, in modern drug discovery, successfully isolating, purifying, characterizing, and evaluating these compounds for their *in vitro* or *in vivo* activities remains a formidable challenge (Wijngaard *et al.*, 2022). To overcome this challenge, researchers have turned to ethnopharmacological knowledge, using it to identify specific plant species, their relevant parts, and appropriate extracts for validating the potential of phytomedicines (Paliwal *et al.*, 2020).

Various methodologies have been developed for the isolation, purification, and characterization of phytomedicinal compounds. The process typically begins with phytoextraction, involving prewashing, shade drying, and grinding the plant sample to obtain a fine powder. Crude extracts are then prepared using different solvent systems

based on the polarity of the targeted compound (Cos *et al.*, 2006). Several extraction techniques are employed, such as soxhlet extraction, sonication, heating under reflux, maceration, solid-solid extraction, microwave-assisted extraction, and others (Huie *et al.*, 2020). Once extracted, the purification of specific bioactive compounds becomes a critical step and poses significant challenges. Purification is essential for subsequent characterization. Commonly used techniques include thin-layer chromatography (TLC), column chromatography, size exclusion chromatography (SEC), and high-performance liquid chromatography (HPLC).

Further structural elucidation of pure phytocompounds is achieved through analytical techniques such as Liquid Chromatographic Mass Spectrometry (LC-MS), Gas Chromatographic-Mass Spectrometry (GC-MS), Nuclear Magnetic Resonance spectroscopy (NMR), and Fourier-Transform Infrared Spectroscopy (FTIR) (Altemimi *et al.*, 2017). These analytical techniques are vital for identifying bioactive compounds before subjecting them to *in vitro* or *in vivo* biological assays. The continuous advancement in these methodologies contributes significantly to the exploration and potential utilization of phytomedicinal compounds in drug development.



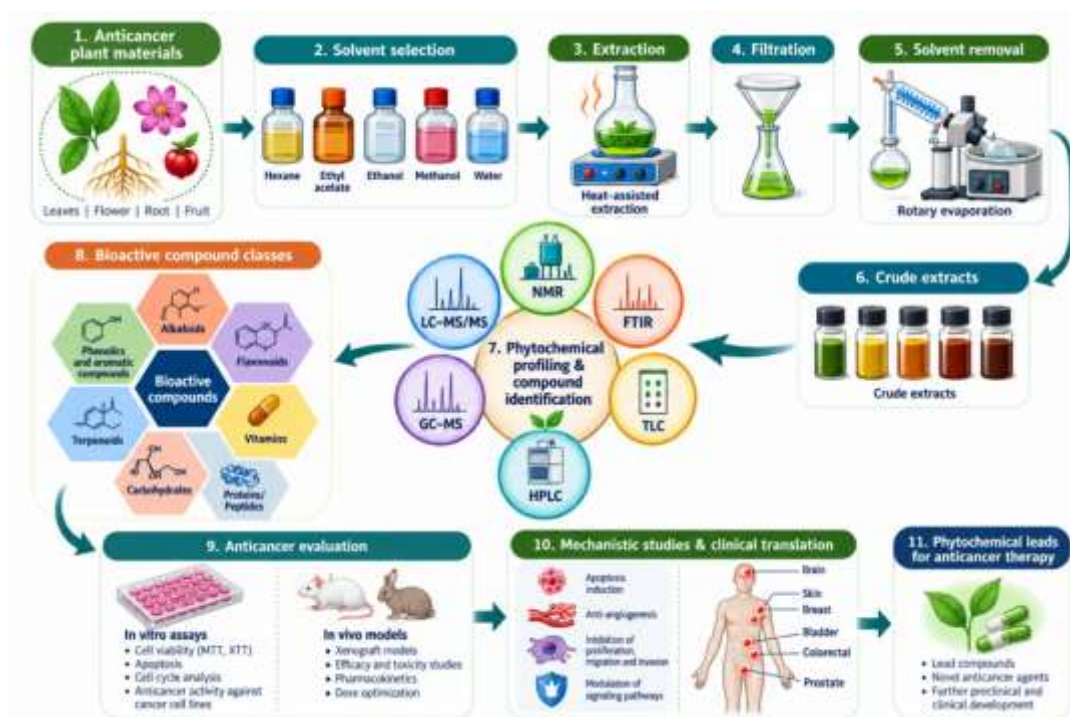


Figure 1. Workflow for the discovery and evaluation of plant-derived anticancer compounds.

The process includes plant selection based on ethnomedicinal knowledge, authentication and sample preparation, solvent extraction, fractionation and purification, structural characterization, in vitro and in vivo biological evaluation, toxicity assessment, formulation or bioavailability enhancement, and clinical translation. Artwork/diagram: author-prepared with AI-assisted illustration using ChatGPT and reviewed by the authors. No third-party figure was intentionally reproduced; underlying scientific claims should be supported by cited sources.

5. CHEMICAL AND BIOCHEMICAL PROPERTIES OF ANTICANCER PLANT DERIVATIVES

Chemical and biochemical properties play a vital role in the effectiveness of plant derivatives against cancer. These properties govern how bioactive compounds interact with cancer cells, the mechanisms they employ, and their potential as therapeutic agents. In this discussion, we delve into some crucial chemical and biochemical

properties that characterize anticancer plant derivatives.

Molecular Structure: The molecular structure of plant derivatives significantly influences their ability to interact with cellular targets involved in cancer progression. It determines their size, shape, and functional groups, which are crucial for binding to specific receptors, enzymes, or signaling molecules. For example, certain functional groups like hydroxyl (-OH) or carbonyl (C=O) groups present in polyphenolic compounds enable them to scavenge free radicals, exhibit antioxidant activity, and regulate cellular signaling pathways implicated in cancer development (Du *et al.*, 2018; Newman & Cragg, 2020).

Bioavailability: Bioavailability refers to how effectively a bioactive compound can be absorbed, distributed, metabolized, and excreted within the body. Anticancer plant derivatives with good bioavailability have a higher chance of reaching target tissues and exerting their therapeutic effects. Factors affecting bioavailability include the

compound's solubility, stability, membrane permeability, and metabolism. To enhance the bioavailability of anticancer plant derivatives, strategies like formulation development or combination with other compounds can be employed (Panahi *et al.*, 2019; Hwang *et al.*, 2017).

Cytotoxicity and Apoptosis Induction: Anticancer plant derivatives often display cytotoxic effects on cancer cells, leading to cell cycle arrest, inhibition of cell proliferation, and promotion of apoptosis (programmed cell death). These effects can be mediated through various mechanisms, such as DNA damage, inhibition of key enzymes or signaling pathways, and modulation of apoptotic regulators. For example, vinca alkaloids derived from *Catharanthus roseus* disrupt microtubule assembly, resulting in cell cycle arrest and apoptosis induction (Zhang & Han, 2017; Siveen *et al.*, 2014).

Anti-Angiogenesis: Angiogenesis, the formation of new blood vessels, is critical for tumor growth and metastasis. Anticancer plant derivatives with anti-angiogenic properties can inhibit the formation of new blood vessels, thereby suppressing tumor progression. Compounds like resveratrol from *Vitis vinifera* and curcumin from *Curcuma longa* have demonstrated anti-angiogenic effects by targeting various molecular pathways involved in angiogenesis (Chen *et al.*, 2017; Yallapu *et al.*, 2015).

Immunomodulation: The immune system plays a crucial role in cancer surveillance and elimination. Plant derivatives can modulate immune responses, enhancing the body's ability to recognize and eliminate cancer cells. They can stimulate immune cells such as natural killer (NK) cells and cytotoxic T lymphocytes, as well as regulate the production of immune mediators, including cytokines and chemokines. This immunomodulatory activity

contributes to the anticancer effects of plant derivatives (Guo *et al.*, 2017; Lin *et al.*, 2019).

Synergistic Interactions: Anticancer plant derivatives often contain multiple bioactive compounds that can act synergistically, enhancing their overall effectiveness. Synergistic interactions occur when the combined effect of two or more compounds is greater than the sum of their individual effects. For instance, combining curcumin and piperine from *Piper nigrum* has been shown to increase the bioavailability and anticancer activity of curcumin (Li *et al.*, 2010; Choi & Berhow, 2018).

6. REPRESENTATIVE ANTICANCER PLANTS AND THEIR PHYTOCHEMICALS

These are those plants that have been extensively studied and shown to possess notable anticancer effects. These plants contain bioactive compounds that exhibit specific mechanisms of action against cancer cells, making them potential sources of new anticancer therapies. The following is an overview of some well-known plants with documented anticancer properties and their natural origins/habitats:

Catharanthus roseus (Madagascar periwinkle): Native to Madagascar, this plant is known for producing vinca alkaloids, including vinblastine and vincristine. Vinca alkaloids disrupt microtubule formation, inhibiting cell division and inducing apoptosis. They have been used in the treatment of various cancers, including leukemia and lymphomas.

Curcuma longa (Turmeric): Turmeric, a member of the ginger family, is native to Southeast Asia. Its active compound, curcumin, has been extensively studied for its anticancer properties. Curcumin exhibits multiple mechanisms of action, including inhibition of inflammation, modulation



of cell signaling pathways, and induction of apoptosis.

Viscum album (European mistletoe): European mistletoe is a parasitic plant found in various parts of Europe and Asia. Extracts from mistletoe have been used in complementary cancer treatments, particularly in Europe. They are believed to modulate the immune system and have cytotoxic effects on cancer cells.

Camellia sinensis (Tea): Tea, derived from the leaves of *Camellia sinensis*, is widely consumed worldwide. It contains various polyphenols, including epigallocatechin gallate (EGCG). EGCG exhibits antioxidant and anticancer properties, and numerous studies have reported its potential in preventing and treating cancer.

Panax ginseng (Asian ginseng): Ginseng is a popular medicinal plant native to Asia. It contains ginsenosides, which have been shown to possess anticancer effects. Ginsenosides modulate various signaling pathways involved in cell proliferation, apoptosis, and angiogenesis.

Podophyllotoxin derivatives from Podophyllum peltatum (Mayapple): Podophyllotoxin and its derivatives, including etoposide and teniposide, obtained from the roots and rhizomes of *Podophyllum peltatum*, exhibit anti-neoplastic activities. They inhibit topoisomerase II, leading to DNA damage and cell death. Etoposide and teniposide are commonly used in the treatment of various cancers, such as testicular cancer, lung cancer, and lymphomas.

Resveratrol from Vitis vinifera (Grapes): Resveratrol, a polyphenol found in grapes and other plants, has demonstrated anti-neoplastic effects. It exhibits antioxidant, anti-inflammatory, and anti-proliferative activities. Resveratrol modulates multiple signalling pathways involved in cell cycle regulation, apoptosis, angiogenesis, and metastasis. It has shown promising results in various preclinical and clinical studies for the prevention and treatment of cancers, including breast, colorectal, and prostate cancer.

Table 1. Plant-derived bioactive compounds, cancer types, study models, and proposed modes of action.

Plant Source	Bioactive Compound/ Phytochemical	Cancer Cells Type	Study Type	Mode of Action	Ref
<i>Catharanthus roseus</i>	Vinblastine	Leukemias, lymphomas, and solid tumors	<i>In vitro</i>	Inhibits microtubule formation	Wall <i>et al.</i> , (1966).
	Irinotecan	Colorectal	Clinical	Topoisomerase I inhibitor	
	Vinblastine	Hodgkin's lymphoma, Testicular cancer	<i>In vivo</i>	Inhibits microtubule formation, leading to cell cycle arrest and apoptosis	Jordan & Thrower (1991)
<i>Camptotheca acuminata</i>	Camptothecin	Various	<i>In vitro</i>	Topoisomerase I inhibitor	Tewey <i>et.</i> , (1984).
	Etoposide	Various	<i>In vitro</i>	Topoisomerase II inhibitor	Hande <i>et al.</i> , (1998).
<i>Podophyllum peltatum</i>	Podophyllotoxin	Various	<i>In vitro</i>	Inhibits microtubule formation	Sultana <i>et al.</i> , (2008).

	Paclitaxel	Various	<i>In vitro</i>	Stabilizes microtubules	Gopalakrishnan <i>et al.</i> , (2018).
<i>Ginkgo biloba</i>	Ginkgolides	Hepatocarcinoma, ovary, prostate, colon and liver cancer Brain cancer	<i>In vitro</i> Preclinical study	Anti-inflammatory, antioxidant Inhibits cell proliferation and induces apoptosis	Ahlemeyer <i>et al.</i> , (2003). Mahadevan and Park, 2008; Yao <i>et al.</i> , 2017
<i>Curcuma longa</i>	Curcumin	Leukemia, glioblastoma, Colon adenocarcinoma, prostate esophagus, liver and skin cancer (<i>In vitro</i>)	<i>In vitro</i>	Inhibits cell proliferation Anti-inflammatory, antioxidant, and pro-apoptotic effects	Aggarwal <i>et al.</i> , (2009). Anand <i>et al.</i> (2008); Kunnumakkara <i>et al.</i> (2017)
<i>Viscum album</i>	Viscotoxin	Breast cancer, Colorectal cancer	Preclinical studies	Induces apoptosis and inhibits tumor growth	Büssing <i>et al.</i> , (1996). Steiner <i>et al.</i> (2003); Semmler-Behnke <i>et al.</i> (2013)
<i>Vitis vinifera</i>	Resveratrol	Breast Osteosarcoma Colorectal	<i>In vitro</i> <i>In vitro</i> , <i>in vivo</i> <i>In vitro</i> ,	Cell cycle inhibition, apoptosis STAT3 pathway and cell cycle inhibition <i>In vitro</i> NF-kB pathway inhibition, apoptosis	Wu, H. <i>et al</i> 2019, Peng, L. <i>et al</i> 2018 Buhrmann, C. <i>et al</i> 2017.
<i>Zingiber officinale</i>	Gingerol	Lung Breast	<i>In vitro</i> , <i>in vivo</i> <i>In vitro</i>	A549 cells death by iron accumulation, USP14 expression inhibition ROS generation, activation of p53 expression mediated apoptosis,	Tsai <i>et al.</i> , 2020 Sp <i>et al.</i> , 2021
<i>Carica papaya</i>	Benzyl isothiocyanate	Pancreatic	<i>In vitro</i> , <i>in vivo</i>	FOXO/PI3K/AKT pathways-mediated tumor apoptosis	Boreddy <i>et al</i> 2011
<i>Piper longum</i>	Piperlongumine	Prostate	<i>In vitro</i>	DNA damage-mediated proliferation inhibition	Zhang <i>et al.</i> , 2021
		Lung	<i>In vitro</i> , <i>in vivo</i>	mTOR/AKT/PI3K pathway inhibition-induced apoptosis	Wang <i>et al.</i> , 2015
<i>Gossypium hirsutum</i>	Gossypol	Skin	<i>In vitro</i>	Mitochondrial apoptosis	Haasler <i>et al.</i> , 2021
		Cervical	<i>In vitro</i> , <i>in vivo</i>	FAK pathway inhibition and	Hsieh <i>et al.</i> , 2021

				TGF- β 1-mediated EMT reversal	
		Colon	<i>In vitro</i>	Downregulation of FAS, CLAUDIN1, GAPDH, ELK1, ZFAND5, IL2, and IL8 expression	Cao <i>et al.</i> , 2021
<i>Taxus brevifolia</i>	Paclitaxel	Breast cancer	<i>in vivo</i>	Stabilizes microtubules, leading to cell cycle arrest	Schiff <i>et al.</i> , 1979; Rowinsky and Donehower, 1995
<i>Camellia sinensis</i>	Epigallocatechin gallate (EGCG)	Prostate cancer	Preclinical study	Inhibits tumor growth and metastasis	Khan and Mukhtar, 2007; Butt <i>et al.</i> , 2009
<i>Panax ginseng</i>	Ginsenosides	Lung cancer	Preclinical study	Modulates cell signaling pathways and induces apoptosis	Helms and Miller, 2004; Jia <i>et al.</i> , 2021
<i>Allium sativum</i>	Allicin	Stomach cancer	Preclinical study	Induces apoptosis and inhibits cell proliferation	Zhang and Tang, 2007; Banerjee and Sethi, 2013
	Diallyl trisulfide	Prostate cancer	Preclinical study	Induces apoptosis, inhibits cell proliferation, and angiogenesis	Yang <i>et al.</i> , 2019
<i>Berberis vulgaris</i>	Berberine	Liver cancer	Preclinical study	Induces cell cycle arrest and apoptosis	Mantena <i>et al.</i> , 2006; Mantena <i>et al.</i> , 2011
<i>Tripterygium wilfordii</i>	Celastrol	Prostate cancer	Preclinical study	Inhibits cell proliferation and induces cell cycle arrest	Chen <i>et al.</i> , 2016
<i>Aloe vera</i>	Aloin	Colorectal cancer	Preclinical study	Induces cell death and inhibits angiogenesis	Tseng <i>et al.</i> , 2016
<i>Annona muricata</i>	Annonacin	Liver cancer	Preclinical study	Inhibits cancer cell growth and induces apoptosis	Liaw <i>et al.</i> , 2020
	Acetogenins	Breast cancer	Preclinical study	Inhibits mitochondrial complex I, inducing apoptosis	George <i>et al.</i> , 2021
<i>Curcuma zedoaria</i>	Zerumbone	Pancreatic cancer	Preclinical study	Induces apoptosis and inhibits cell migration	Matsuo <i>et al.</i> , 2020
<i>Euphorbia neriifolia</i>	Diterpene compound	Cervical cancer	Preclinical study	Disrupts cell cycle, triggers apoptosis, and inhibits invasion	Abubakar <i>et al.</i> , 2020

<i>Podophyllum peltatum</i>	Etoposide	Testicular, lung, and others	Clinical trial	Inhibits DNA topoisomerase II, causing DNA damage	Hande <i>et al.</i> , 1998; Moxley <i>et al.</i> , 2020
<i>Maytenus senegalensis</i>	Maytansine	Breast, lung, and others	Preclinical study	Disrupts microtubule function, leading to cell cycle arrest	Pourgholami <i>et al.</i> , 2011; Bai <i>et al.</i> , 2015

7. ANTICANCER MECHANISMS OF BOTANICAL DERIVATIVES

Anticancer mechanisms of botanical derivatives encompass a wide array of intricate cellular processes that target cancer cells and impede tumor growth. These mechanisms involve multiple pathways and molecular targets. For instance, many botanical derivatives induce apoptosis in cancer cells, triggering programmed cell death and eliminating abnormal or damaged cells (Elmore, 2007). Additionally, these compounds can disrupt cell cycle progression, leading to cell cycle arrest and inhibition of uncontrolled cell growth (Kastan and Bartek, 2004). Some botanical derivatives inhibit angiogenesis, the formation of new blood vessels that nourish tumors, thereby depriving tumors of essential nutrients and oxygen (Folkman, 2007). Furthermore, these derivatives can modulate various signaling pathways involved in cancer development and progression, such as those related to cell proliferation, survival, migration, and invasion (Huang *et al.*, 2020). Moreover, botanical derivatives have demonstrated the ability to enhance the immune response against cancer cells, stimulating immune-mediated cytotoxicity and suppressing tumor growth (Wang *et al.*, 2014). By targeting these intricate mechanisms, botanical derivatives derived from medicinal plants offer a promising approach for combating cancer and may pave the way for the development of novel and effective anticancer therapies.

7.1. Induction of Apoptosis

Apoptosis, or programmed cell death, plays a crucial role in maintaining tissue homeostasis and eliminating abnormal cells, including cancer cells. Many botanical derivatives have been shown to induce apoptosis in cancer cells through various mechanisms. For instance, resveratrol, a polyphenol found in grapes and berries, activates apoptotic pathways by modulating Bcl-2 family proteins, caspases, and the tumor suppressor p53 (Nguyen *et al.*, 2003). Curcumin, derived from turmeric, induces apoptosis in cancer cells by targeting multiple signalling pathways, including NF- κ B, Akt, and MAPK pathways (Aggarwal *et al.*, 2003). These botanical derivatives promote cell death and inhibit cancer cell survival, thereby impeding tumor progression.

7.2. Cell-Cycle Arrest

Botanical derivatives can disrupt the cell cycle progression of cancer cells, leading to cell cycle arrest and inhibition of uncontrolled cell growth. One example is paclitaxel, a terpenoid derived from the Pacific yew tree. Paclitaxel stabilizes microtubules, preventing their depolymerization during cell division and causing cell cycle arrest at the G2/M phase (Schiff *et al.*, 1979). Another botanical derivative, quercetin, a flavonoid present in various fruits and vegetables, induces cell cycle arrest at different phases, depending on the cancer cell type, by modulating cyclins, cyclin-dependent kinases (CDKs), and their inhibitors (Serrano *et*



al., 2007). By interfering with cell cycle progression, these botanical derivatives limit cancer cell proliferation and promote their elimination.

7.3. Inhibition of Angiogenesis

Angiogenesis, the formation of new blood vessels, is essential for tumor growth and metastasis. Several botanical derivatives have been found to possess anti-angiogenic properties, inhibiting the formation of new blood vessels and limiting the blood supply to tumors. For example, epigallocatechin gallate (EGCG), a polyphenol abundant in green tea, inhibits angiogenesis by targeting multiple angiogenic factors, such as vascular endothelial growth factor (VEGF) and its receptors (Yang *et al.*, 2003). Another botanical derivative, curcumin, suppresses angiogenesis through inhibition of VEGF expression and signalling pathways (Arbiser *et al.*, 1998). These compounds effectively block the development of new blood vessels, impairing the tumor's ability to obtain necessary nutrients and promoting its regression.

7.4. Modulation of Signalling Pathways

Botanical derivatives can modulate various signalling pathways that play crucial roles in cancer development and progression. For instance, genistein, an isoflavone found in soybeans, exerts its anticancer effects by inhibiting protein tyrosine kinases, thereby disrupting signalling pathways involved in cell proliferation, survival, and angiogenesis (Sarkar *et al.*, 2008). Resveratrol, through its interaction with multiple molecular targets, including AMP-activated protein kinase (AMPK), SIRT1, and PI3K/Akt, modulates various signalling pathways to inhibit cell

proliferation, induce apoptosis, and inhibit tumor growth (Bishayee, 2009). These botanical derivatives act as potent regulators of critical signalling pathways, thereby interfering with cancer cell survival and growth.

7.5. Enhancement of Immune Response

Several botanical derivatives have been shown to enhance the immune response against cancer cells, promoting immune-mediated cytotoxicity and suppressing tumor growth. For example, polysaccharides derived from medicinal mushrooms, such as *Ganoderma lucidum* (reishi mushroom) (Gao *et al.*, 2005)

Drugs derived from botanical derivatives that are currently in clinical trials or whose clinical trials were completed. Summary of all clinical trials that have been designed due to previous knowledge of the anti-cancer activity recognized in botanical derivatives. (Bhatia *et al.*, 2011)

8. SIGNALLING PATHWAYS INVOLVED IN PLANT-DERIVED PREVENTION OF TUMOUR GROWTH

Plant derivatives have been found to exhibit preventive effects on tumor growth by modulating various signalling pathways involved in cancer development and progression. These compounds interact with key molecular targets within these pathways, leading to the inhibition of cell proliferation, induction of apoptosis, suppression of angiogenesis, and modulation of immune responses. The following sections provide a detailed exploration of the signalling pathways targeted by plant derivatives and their role in tumor growth prevention.



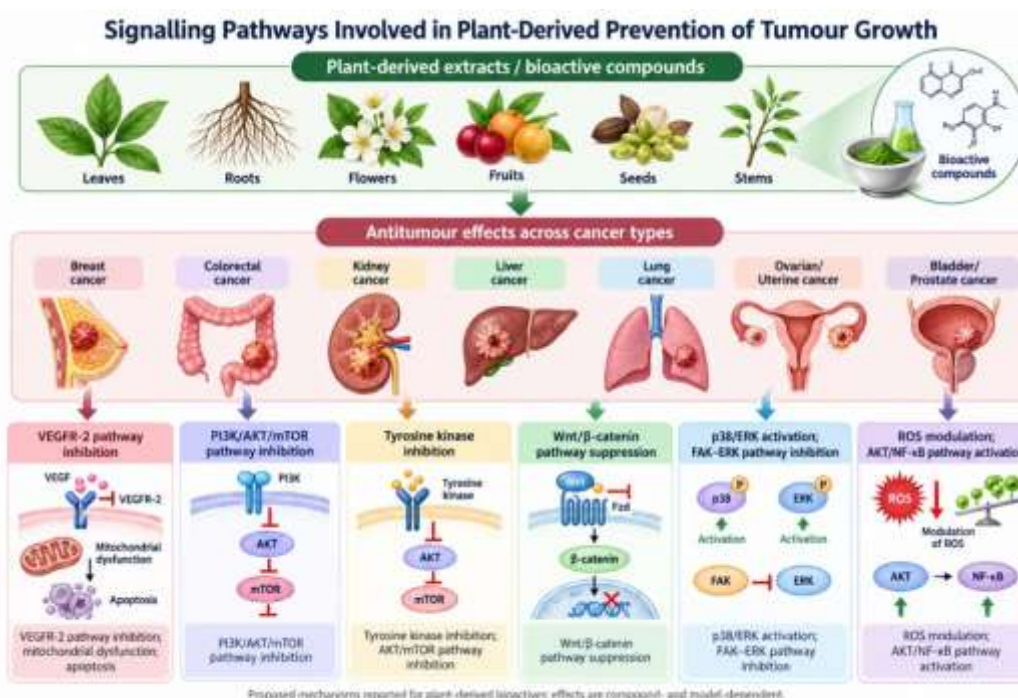


Figure 2. Principal signalling pathways associated with the anticancer effects of plant-derived compounds.

Plant-derived molecules may influence PI3K/Akt/mTOR, MAPK/ERK, NF-kappaB, Wnt/beta-catenin, JAK/STAT, p53, and apoptotic pathways, thereby affecting cell survival, proliferation, differentiation, migration, angiogenesis, and programmed cell death. Artwork/diagram: author-prepared with AI-assisted illustration using ChatGPT and reviewed by the authors. No third-party figure was intentionally reproduced; underlying scientific claims should be supported by cited sources.

8.1. PI3K/AKT/mTOR Pathway

The PI3K/Akt/mTOR pathway plays a critical role in regulating cell growth, survival, and metabolism. Dysregulation of this pathway is commonly observed in cancer cells, leading to increased cell proliferation and survival. Plant derivatives have been shown to inhibit this pathway, thereby exerting preventive effects on tumor growth. For instance, resveratrol inhibits Akt phosphorylation and downstream mTOR signaling, leading to cell cycle arrest and apoptosis

in various cancer cell types (Panda, 2019). Curcumin suppresses Akt activation and mTOR signaling, resulting in the inhibition of cell proliferation and induction of apoptosis (Ko *et al.*, 2019). By targeting the PI3K/Akt/mTOR pathway, plant derivatives can impede tumor growth and prevent cancer progression.

8.2. NF-κB Pathway

The NF-κB pathway is involved in regulating immune responses, inflammation, cell survival, and proliferation. Aberrant activation of NF-κB has been implicated in various cancers. Plant derivatives can inhibit NF-κB activation, thereby preventing tumor growth. Curcumin, for example, inhibits NF-κB signaling by suppressing the degradation of IκBα, an inhibitor of NF-κB (Huang *et al.*, 2020). This leads to the suppression of NF-κB target genes involved in cell survival, angiogenesis, and metastasis. By targeting the NF-κB pathway, plant derivatives can attenuate the inflammatory response and inhibit tumor growth.

8.3. Wnt/ β -Catenin Pathway

The Wnt/ β -catenin pathway plays a crucial role in regulating cell proliferation and differentiation. Dysregulation of this pathway is commonly observed in cancer, leading to uncontrolled cell growth. Plant derivatives have been found to modulate this pathway, inhibiting tumor growth. For instance, curcumin inhibits the Wnt/ β -catenin pathway by downregulating β -catenin levels and suppressing its nuclear translocation (Sun *et al.*, 2019). This disrupts the transcription of Wnt target genes involved in cell proliferation and survival. By targeting the Wnt/ β -catenin pathway, plant derivatives can hinder tumor growth and inhibit cancer progression.

8.4. MAPK/ERK Pathway

The MAPK/ERK pathway regulates various cellular processes, including cell proliferation, survival, and differentiation. Dysregulation of this pathway is commonly associated with cancer development. Plant derivatives have been shown to modulate this pathway, resulting in the inhibition of tumor growth. For example, resveratrol inhibits the activation of ERK1/2, downstream effectors of the MAPK pathway, leading to cell cycle arrest and apoptosis in cancer cells (Li *et al.*, 2019). By targeting the MAPK/ERK pathway, plant derivatives can impede cell proliferation and promote tumor growth inhibition.

8.5. Notch Signalling Pathway

The Notch signalling pathway plays a critical role in cell fate determination, differentiation, and proliferation. Dysregulation of Notch signalling has been implicated in various cancers. Plant derivatives can modulate this pathway, contributing to the prevention of tumor growth. For instance, genistein inhibits Notch signaling by

suppressing the expression of Notch receptors and downstream target genes (Girardi *et al.*, 2021). This disrupts Notch-mediated cell proliferation and survival. By targeting the Notch signaling pathway, plant derivatives can impede tumor growth and inhibit cancer progression.

8.6. Hedgehog Signalling Pathway

The Hedgehog pathway regulates cell growth and differentiation during embryonic development and is also involved in cancer development. Plant derivatives like curcumin and resveratrol have been found to inhibit the Hedgehog pathway, leading to antitumor effects (Li *et al.*, 2019).

8.7. JAK/STAT Pathway

The JAK/STAT pathway plays a critical role in cell proliferation, survival, and immune responses. Dysregulation of this pathway is associated with various cancers. Plant-derived compounds, including resveratrol and curcumin, have been shown to modulate JAK/STAT signaling, resulting in antitumor effects (Li *et al.*, 2019).

9. THERAPEUTIC APPLICATIONS OF PLANT-DERIVED ANTICANCER COMPOUNDS

Anticancer botanic derivatives have shown immense potential as therapeutic agents in the field of oncology. These natural compounds, derived from various medicinal plants, possess bioactive properties that can effectively target cancer cells and inhibit tumour growth. The therapeutic applications of these anticancer botanic derivatives encompass a wide range of areas, including cancer prevention, treatment, and supportive care. Here, we explore some of the key therapeutic applications of these natural compounds:



Table 2. Clinical-trial status of selected plant-derived anticancer compounds.

Active Ingredient Name	Mode of Action	Cancer Type	Current Status	References (ClinicalTrials.gov)
Apigenin	Cell cycle arrest, inhibiting cancer cell migration and invasion	Colorectal Cancer	Suspended	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Apigenin&cntry=&state=&city=&dist=
Curcumin	Induce apoptosis	Prostate Cancer, Breast Cancer, Colorectal Cancer, Metastatic Colon Cancer	Completed; Recruiting	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Curcumin&cntry=&state=&city=&dist=
Allicin	Inhibit cancer cell growth	Follicular Lymphoma	Unknown	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Allicin&cntry=&state=&city=&dist=&Search=Search
Andrographolide / Andrographis paniculata	Cell-cycle arrest	Squamous Cell Carcinoma of Esophagus	Terminated ; Completed	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Andrographolide&cntry=&state=&city=&dist=&Search=Search
Epigallocatechin	Induce cell cycle arrest and apoptosis	Colon Cancer, Esophageal Cancer, Lung Cancer, Nonmetastatic Bladder Cancer, Colorectal Cancer, Prostate Cancer, Small Cell Lung Cancer	Recruiting; Completed	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Epigallocatechin&cntry=&state=&city=&dist=&Search=Search
Emodin	Suppress tumor growth by inhibiting AKT, MAPK, PI3K pathway	Breast Cancer	Unknown	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Emodin&cntry=&state=&city=&dist=&Search=Search
Genistein	Angiogenesis inhibitors, inhibit uncontrolled cancer cell growth	Breast Cancer, Non-Small Cell Lung Cancer, Colon Cancer, Rectal Cancer, Colorectal	Completed, Terminated , Suspended, Withdrawn	https://clinicaltrials.gov/ct2/results?cond=Cancer&term=Genistein&cntry=&state=&city=&dist=&Search=Search

		Cancer, Breast Cancer, Endometrial Cancer		
Gingerol	Inhibit PI3K, upregulate pro- apoptotic protein p21, induce apoptosis	Colorectal Cancer, Colorectal Adenoma	Completed	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Gingerol& cntry=&state=&city=&dist=& Search=Search
Glycyrrhizin	Induces apoptosis	Lung Cancer, Liver Cancer, Hepatocellular Carcinoma	Completed, Recruiting, Unknown	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Glycyrrhizin& cntry=&state=&city=&dist=& Search=Search
Licochalcone A	Inhibits PI3K/AKT/mTO R signaling pathway	Squamous Cell Carcinoma	Unknown	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Licochalcone& cntry=&state=&city=&dist=& Search=Search
Pterostilbene	Inhibit cancer cell growth through apoptotic- dependent and - independent pathway	Endometrial Carcinoma	Recruiting	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Pterostilbene& cntry=&state=&city=&dist=& Search=Search
Resveratrol	Induce apoptosis and cell cycle arrest through p53-dependent pathway	Colon Cancer, Neuroendocrine Tumor, Neoplasms, Colorectal, Adenocarcinoma of the Colon, Breast Cancer, Stage III & IV Melanoma	Completed, Terminated , Suspended, Withdrawn	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Resveratrol& cntry=&state=&city=&dist=& Search=Search
Sulforaphane	Induce apoptosis	Adenocarcinoma of the Prostate, Prostate Cancer, Breast Cancer, Colon Cancer	Completed, Terminated , Withdrawn	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Sulforaphane& cntry=&state=&city=&dist=& Search=Search
Thymoquinone	Induces apoptosis; regulate pro- and anti-apoptotic genes; reduce metastasis	Premalignant Lesion	Completed	https://clinicaltrials.gov/ct2/results? cond=Cancer&term=Thymoquinone & cntry=&state=&city=&dist=& Search=Search

Camptothecin	S-phase-specific killing through potentially lethal collisions between advancing replication forks and topo-I cleavable complexes	Human breast carcinoma and normal endothelial cells	Completed	https://clinicaltrials.gov/search?term=Camptothecin&cond=Cancer
Podophyllotoxin	Destabilize microtubules and prevent cell division	Testicular, breast, pancreatic, lung, stomach, and ovarian cancers	Completed	https://clinicaltrials.gov/search?term=podophyllotoxin&cond=Cancer
Ingenol Mebutate	PKC/MEK/ERK signaling pathway	Actinic keratosis	Completed	https://clinicaltrials.gov/search?term=ingenol%20mebutate&cond=Cancer
Quercetin and Genistein	Acting as a scavenger of free radicals	Prostate Cancer	Unknown Status	https://clinicaltrials.gov/search?term=Flavonoids&cond=Cancer
Berberine	Strong lipogenic activity ROS/AMPK pathway	Lung cancer with EGFR mutation	Unknown Status	https://clinicaltrials.gov/search?term=berberine&cond=Cancer

10. CHALLENGES AND LIMITATIONS

One of the significant challenges in harnessing the potential of anticancer bioactive compounds from medicinal plants is the standardization and quality control of herbal products.

Standardization and Quality Control:

Harnessing the potential of anticancer bioactive compounds from medicinal plants faces a significant obstacle in the form of standardization and quality control of herbal products. Since the composition of plant extracts can vary based on factors like geographical origin, season of harvest, and extraction methods used, ensuring consistency and reproducibility in research and clinical applications becomes crucial. Standardization

protocols need to be established to accurately quantify the active compounds in herbal extracts, which would not only aid in the development of effective therapies but also facilitate regulatory approval for their clinical use. Additionally, stringent quality control measures are essential to identify and eliminate contaminants and adulterants that could compromise the safety and efficacy of these bioactive compounds. Implementing robust quality control procedures will instil confidence in the reliability and safety of medicinal plant-based treatments, inspiring greater adoption in the medical community and patient populations. The composition of these plant extracts can vary depending on various factors such as the geographical origin of the plant,



the season of harvest, and the extraction methods used. Standardization is crucial to ensure consistent and reproducible results in research and clinical applications. Moreover, quality control measures are essential to identify and eliminate contaminants and adulterants that may affect the safety and efficacy of these bioactive compounds (Molyneux, 2018; Posadzki *et al.*, 2013).

Sustainability and Conservation: The increasing global demand for herbal medicines and phytochemicals presents a challenging dilemma of sustainable sourcing and conservation of medicinal plant species. Overharvesting and habitat destruction pose significant threats to many plant species, some of which might hold crucial anticancer properties. It is essential to strike a balance between utilizing medicinal plants for therapeutic purposes and ensuring their long-term availability in their natural habitats. Sustainable practices such as responsible harvesting, cultivation, and conservation of endangered species can help prevent species depletion and protect biodiversity. Collaborative efforts between stakeholders, including local communities, researchers, policymakers, and conservation organizations, are vital in designing and implementing strategies that promote the sustainable use of medicinal plants. Additionally, awareness campaigns about the importance of conservation and sustainable practices can encourage responsible consumption and contribute to the preservation of these valuable botanical resources for future generations. With increasing global demand for herbal medicines and phytochemicals, overharvesting and habitat destruction pose significant threats to many plant species. Sustainable practices must be adopted to ensure the long-term availability of these valuable resources while preserving biodiversity and protecting the ecosystems in which these plants thrive (Cunningham, 2001; Verma, 2012).

Addressing these challenges will require a multi-faceted approach that involves the cooperation and coordination of various stakeholders, including researchers, healthcare professionals, regulatory bodies, policymakers, and local communities. Emphasizing the importance of quality control and standardization will ensure that the potential therapeutic benefits of medicinal plants are realized consistently and reliably. Simultaneously, promoting sustainable practices and conservation efforts will safeguard the natural reservoirs of bioactive compounds, fostering a harmonious relationship between human health and ecological well-being.

Despite the challenges, exploring the anticancer potential of bioactive compounds from medicinal plants remains an area of immense promise and hope. As scientific understanding and technological advancements progress, it is likely that we will overcome these hurdles and unlock the full therapeutic potential of these natural treasures in the fight against cancer. The fusion of traditional medicinal knowledge with modern scientific rigor will undoubtedly pave the way for innovative and effective anticancer therapies, enhancing healthcare outcomes and contributing to the betterment of human health worldwide.

11. FUTURE DIRECTIONS

To overcome the challenges faced in harnessing the potential of anticancer bioactive compounds from medicinal plants, future research should prioritize the integration of traditional knowledge and modern scientific approaches. Collaborative efforts that bring together traditional healers, local communities, and scientific researchers can create a synergistic platform for knowledge exchange and exploration. Traditional healers possess valuable knowledge about the historical use of medicinal plants for various ailments, including cancer. By working hand-in-hand with scientific



researchers, they can provide critical insights into the traditional use and therapeutic properties of specific plant species. This integrative approach is crucial in identifying promising plant candidates for further investigation and understanding their mechanisms of action, thereby facilitating evidence-based phytotherapy (Heinrich *et al.*, 2020; Moerman, 1996).

Moreover, to solidify the position of bioactive compounds from medicinal plants as viable anticancer agents, more extensive clinical studies are necessary. Rigorous clinical trials, designed with well-controlled methodologies and large sample sizes, are essential to validate the safety, efficacy, and optimal dosages of these compounds in cancer treatment (Pan *et al.*, 2013; Semple *et al.*, 2015). By adhering to the gold standard of clinical research, the potential of phytotherapy can be substantiated, gaining the trust of the medical community and regulatory authorities.

In addition to clinical trials, there is a need for further exploration of the synergistic effects of combinations of bioactive compounds. In traditional medicine systems, plant extracts are often used in combination to enhance therapeutic effects and reduce side effects. This phenomenon, known as the "entourage effect," is gaining attention in modern research as well. Studying the interactions between different bioactive compounds and their combined effects on cancer cells could lead to the development of more potent and selective therapies (Sharma *et al.*, 2021).

Furthermore, advances in technology, such as high-throughput screening methods and computational modeling, can accelerate the discovery of new bioactive compounds from medicinal plants. These techniques can efficiently analyze large numbers of plant extracts and identify potential lead compounds with anticancer properties, streamlining the drug discovery

process (Chen *et al.*, 2021). In silico approaches, such as molecular docking and virtual screening, can also provide valuable insights into the interactions between bioactive compounds and specific cancer targets, guiding the design of more effective and targeted therapies.

As research in this field progresses, it is crucial to emphasize the importance of conservation and sustainability. Collaborative efforts between researchers, policymakers, and local communities are vital to promote responsible harvesting practices, protect endangered plant species, and preserve biodiversity (Cunningham, 2001; Verma, 2012). Ethical considerations in bioprospecting and fair benefit-sharing mechanisms with local communities can ensure that medicinal plant resources are used responsibly and sustainably.

By addressing the challenges related to standardization, sustainability, and integration of knowledge through collaborative research endeavors and rigorous clinical studies, the field of phytotherapy can advance significantly. This integration of traditional knowledge and modern science will not only enhance our understanding of the therapeutic potential of medicinal plants but also contribute to the fight against cancer in the future. With continued dedication and interdisciplinary efforts, natural compounds from medicinal plants could become valuable additions to the arsenal of cancer treatments, offering safer and more targeted therapeutic options for patients.

12. CONCLUSION

In conclusion, the search for potent and effective anticancer agents remains a critical priority as cancer continues to pose a significant global health challenge. Natural sources, particularly medicinal plants, have emerged as promising reservoirs of bioactive compounds with diverse therapeutic properties. These botanical derivatives have



demonstrated remarkable potential in the fight against cancer, offering multifaceted mechanisms of action, including apoptosis induction, cell cycle arrest, angiogenesis inhibition, and modulation of key signalling pathways involved in cancer development and progression.

The extensive research on botanical derivatives has already yielded several successful anticancer drugs, such as vincristine, vinblastine, paclitaxel, and docetaxel, which have proven their efficacy in various cancer types. Moreover, ongoing investigations on other plant-derived compounds, such as gimatecan and elomotecan, show promise and demonstrate the potential for continued discovery of novel anticancer agents from natural sources.

The natural origin of these botanical derivatives offers advantages, including reduced toxicity and better tolerability compared to synthetic drugs, making them attractive candidates for cancer treatment. Additionally, the integration of traditional medicine knowledge with modern scientific approaches opens up new avenues for developing targeted and personalized cancer therapies.

However, to fully harness the potential of botanical derivatives for cancer treatment, extensive preclinical and clinical studies are imperative to understand their safety, efficacy, and possible interactions with conventional treatments. Rigorous scientific investigations will pave the way for the development of optimized formulations and targeted delivery systems, ensuring that these natural compounds can be effectively used in clinical settings.

As we advance in our understanding of botanical derivatives' anticancer properties and mechanisms, collaboration between traditional medicine practitioners, pharmaceutical researchers, and

healthcare professionals becomes essential. By combining their expertise, we can accelerate the translation of promising natural compounds into viable cancer treatments, providing patients with improved therapeutic options and better quality of life.

In conclusion, this narrative review highlights the tremendous potential of botanical derivatives from medicinal plants as a promising approach for anticancer therapy. The pursuit of natural compounds as anticancer agents offers a potential source of leads for drug discovery, although safety and efficacy must be established experimentally in the battle against cancer, bringing hope for a future where natural sources play a significant role in improving cancer treatment outcomes worldwide.

INSTITUTIONAL REVIEW BOARD STATEMENT

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AUTHOR CONTRIBUTIONS

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CONFLICTS OF INTEREST

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 paper.



INFORMED CONSENT STATEMENT

Not Applicable.

DATA AVAILABILITY STATEMENT

No new data were created or analyzed in this review. Data sharing is not applicable.

GENERATIVE ARTIFICIAL INTELLIGENCE (GENAI) DISCLOSURE

Generative AI disclosure: ChatGPT (OpenAI; model/version as displayed by the service at the time of use) was used to assist with drafting and formatting portions of the manuscript and generating illustrative graphical abstracts/figures. The authors are responsible for reviewing the output, checking scientific accuracy and references, and ensuring that the final manuscript reflects their own scholarly assessment. Any AI-assisted text or figure content should be reviewed and revised by the authors before submission.

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ABBREVIATIONS

Sr. No.	Abbreviation	Full form
1	AKT	Protein kinase B
2	AMPK	AMP-activated protein kinase
3	BRs	Brassinosteroids
4	CAM	Complementary and alternative medicine
5	CDKs	Cyclin-dependent kinases
6	CGs	Cardiac glycosides
7	DNA	Deoxyribonucleic acid
8	EGCG	Epigallocatechin gallate

9	EGFR	Epidermal growth factor receptor
10	ERK	Extracellular signal-regulated kinase
11	FDA	Food and Drug Administration
12	FTIR	Fourier-transform infrared spectroscopy
13	GC-MS	Gas chromatography-mass spectrometry
14	GLOBOCAN	Global Cancer Observatory
15	HPLC	High-performance liquid chromatography
16	JAK/STAT	Janus kinase/signal transducer and activator of transcription
17	LC-MS	Liquid chromatography-mass spectrometry
18	MAPK	Mitogen-activated protein kinase
19	MEK	Mitogen-activated protein kinase kinase
20	mTOR	Mechanistic target of rapamycin
21	NF-κB	Nuclear factor kappa B
22	NMR	Nuclear magnetic resonance spectroscopy
23	Na ⁺ /K ⁺ -ATPase	Sodium-potassium adenosine triphosphatase
24	PI3K	Phosphoinositide 3-kinase
25	PKC	Protein kinase C
26	ROS	Reactive oxygen species
27	SEC	Size-exclusion chromatography
28	SIRT1	Sirtuin 1
29	TLC	Thin-layer chromatography
30	TNF	Tumour necrosis factor
31	VEGF	Vascular endothelial growth factor
32	Wnt	Wingless-related integration site signalling pathway

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