

Role of Plant-Based Phytochemicals in Cancer Therapy: A Review

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Date of Submission: 15-04-2026

Date of Acceptance: 25-04-2026

ABSTRACT:

Cancer continues to pose a significant global health problem and remains one of the primary causes of death across the world. It is defined by uncontrolled cell proliferation and the capacity of these cells to invade and spread to other areas of the body. Although treatments like chemotherapy and radiotherapy have enhanced survival rates, they still have notable drawbacks, including toxicity, resistance to drugs, and limited specificity for cancer cells. These limitations have driven the search for safer and more efficient therapeutic alternatives.

In this regard, phytochemicals derived from plants have attracted growing interest due to their potential in cancer treatment. These natural compounds display a broad spectrum of biological activities and are typically linked with lower toxicity. This review examines their classification, sources, and mechanisms of action. Numerous phytochemicals demonstrate anticancer properties by triggering apoptosis, modulating important cellular pathways, and affecting gene expression.

Their possible applications cover various cancers, such as breast, lung, and colorectal cancer. Nevertheless, challenges including low bioavailability, safety issues, and insufficient clinical evidence continue to limit their widespread application. Consequently, additional research, especially well-structured clinical trials, is necessary to confirm their effectiveness and promote their use in cancer therapy.

KEYWORDS: Phytochemicals; Cancer therapy; Apoptosis; Cell signaling pathways; Gene regulation; Anticancer activity; Natural compounds; Breast cancer; Lung cancer; Colorectal cancer.

I. INTRODUCTION

Cancer continues to pose a serious global health challenge and remains one of the primary causes of illness and mortality worldwide. It is characterized by uncontrolled cell division, genetic mutations, and the capacity of abnormal cells to invade surrounding tissues and spread to distant organs. Despite significant advancements in treatments such as chemotherapy, radiotherapy, and surgery, these approaches are still constrained by notable drawbacks, including severe side effects, drug resistance, and limited specificity for cancer cells [1].

Recently, growing attention has been directed toward plant-derived compounds as potential alternatives or complementary therapies. Phytochemicals naturally occurring bioactive compounds found in plants have demonstrated a broad spectrum of beneficial biological effects, including anticancer, anti-inflammatory, and immune-modulating properties. One of their key advantages is their ability to target multiple molecular pathways, enabling them to influence various processes involved in cancer initiation and progression [2].

Substances such as flavonoids, alkaloids, terpenoids, and different phenolic compounds have shown encouraging anticancer activity. These compounds can inhibit tumor growth, induce programmed cell death (apoptosis), and modulate critical signalling pathways in cancer cells. Compared to traditional chemotherapy agents, many phytochemicals exhibit lower toxicity, making them more suitable for prolonged use and supportive treatment [3].

There is also increasing interest in using phytochemicals alongside conventional cancer therapies. In certain cases, they may enhance therapeutic outcomes while reducing adverse side effects. Their natural origin and multi-targeted

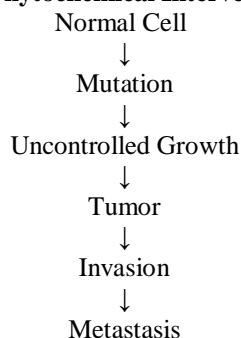
mechanisms make them promising candidates in the development of more effective and balanced cancer treatment strategies [4].

This review aims to present a comprehensive overview of plant-based phytochemicals in cancer therapy, focusing on their classification, mechanisms of action, and potential applications across various cancer types.

Table 1: Global Cancer Statistics

Parameter	Corrected Value
Annual global cancer cases	~19.3 million (2020); projected ~28.4 million by 2040
Annual cancer deaths	~10.0 million
Most common cancer (incidence)	Breast cancer (~2.3 million cases)
Leading cause of cancer death	Lung cancer (~1.8 million deaths)
Major risk factors	Tobacco use, unhealthy diet, physical inactivity, alcohol, infections, genetic predisposition

Flowchart 1: Overview of Cancer Development and Phytochemical Intervention



II. CLASSIFICATION AND SOURCES OF PHYTOCHEMICALS

Types of Phytochemicals

Phytochemicals comprise a wide range of naturally occurring compounds synthesized by plants as part of their secondary metabolism. Unlike primary metabolites, which are vital for growth and development, these compounds primarily function in defense, helping plants cope with environmental stress, pathogens, and herbivores. Due to their chemical diversity and varied biological roles, phytochemicals are typically classified into several

major groups based on their structures and biosynthetic pathways [5].

Among these groups, flavonoids are one of the most abundant and extensively researched classes. They possess a characteristic C6–C3–C6 framework, consisting of two aromatic rings linked by a three-carbon bridge. Minor structural differences give rise to subclasses such as flavonols, flavones, flavanones, isoflavones, and anthocyanins, each associated with specific biological activities, including antioxidant, anti-inflammatory, and anticancer effects [6].

Alkaloids represent another significant class, identified by the presence of nitrogen atoms within their structure. Often derived from amino acids, these compounds are commonly found in medicinal plants and are known for their strong pharmacological effects. For example, alkaloids such as vincristine and vinblastine are widely used in cancer therapy due to their ability to interfere with microtubule formation and block cell division [7].

Terpenoids, also known as isoprenoids, constitute the largest group of phytochemicals. They are composed of repeating isoprene units (C₅ H₈) and are categorized into monoterpenes, sesquiterpenes, diterpenes, and triterpenes based on the number of these units. Terpenoids exhibit a broad range of biological activities, including anticancer, antimicrobial, and anti-inflammatory effects [8].

Phenolic compounds form another important category, defined by one or more hydroxyl groups attached to aromatic rings. This group includes simple phenols, phenolic acids, as well as more complex molecules such as tannins and other polyphenols. They are particularly valued for their antioxidant properties and their involvement in modulating oxidative stress and cellular signalling pathways associated with cancer progression [9].

In addition to these major classes, other phytochemicals such as saponins, glycosides, and lignans also contribute significantly to plant defence mechanisms and human health. Their extensive structural diversity and functional versatility enable them to interact with multiple molecular targets, highlighting their increasing relevance in disease prevention and therapeutic research [10].

Natural Sources of Phytochemicals

Phytochemicals are abundantly present in natural sources, especially in plant-based foods and medicinal plants. Their composition and

concentration can vary significantly depending on factors such as plant species, environmental conditions, and methods of processing and storage. These differences contribute to the diverse biological activities of phytochemicals, many of which are associated with their potential roles in cancer prevention and management [11].

Fruits are key sources of these compounds, particularly flavonoids and other phenolic substances. Berries, apples, grapes, and citrus fruits are especially rich in polyphenols, which are recognized for their antioxidant properties and potential anticancer benefits. Vegetables also provide a wide range of phytochemicals. Leafy greens, cruciferous vegetables such as broccoli and cabbage, and root vegetables like carrots contain important compounds including carotenoids, glucosinolates, and flavonoids that contribute to their health-promoting effects [12].

Additional dietary sources include whole grains, legumes, nuts, and seeds. These foods supply phytochemicals such as phenolic acids, lignans, and saponins, which enhance their nutritional value and may help reduce the risk of chronic diseases, including cancer. Furthermore, medicinal plants and herbs have long been valued for their high phytochemical content, and many traditional medical systems continue to utilize them for their therapeutic potential [13].

Beverages such as green tea, black tea, coffee, and various herbal drinks are also significant sources of phytochemicals, particularly polyphenols and catechins. These compounds have been widely studied for their ability to affect important biological processes and may contribute to lowering cancer risk. Overall, the broad presence of phytochemicals in plant-based foods underscores the importance of diets rich in fruits, vegetables, and other plant-derived products for promoting health and reducing disease risk [14].

III. MOLECULAR MECHANISMS OF ANTICANCER ACTIVITY

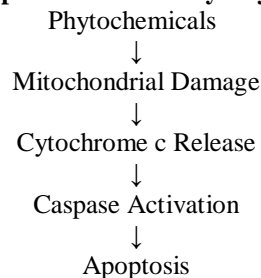
Apoptosis Induction

Apoptosis, also known as programmed cell death, is a highly regulated process essential for maintaining normal cellular homeostasis. In cancer, this mechanism is frequently impaired, enabling abnormal cells to survive and proliferate uncontrollably. For this reason, reactivating or inducing apoptosis has become a key objective in cancer treatment. Plant-derived phytochemicals have gained attention in this area due to their capacity to target multiple cellular pathways [15].

These compounds can modulate both principal apoptotic pathways: the intrinsic (mitochondrial) pathway and the extrinsic (death receptor) pathway. Within the intrinsic pathway, phytochemicals can disrupt mitochondrial membrane integrity, causing the release of cytochrome c into the cytoplasm. This triggers a cascade of caspase activation, particularly involving caspase-9 and caspase-3, ultimately leading to cell death. They also regulate important proteins such as Bax and Bcl-2, shifting the balance toward apoptosis [16].

Moreover, phytochemicals can stimulate the extrinsic pathway by enhancing the activity of death receptors, including Fas and tumor necrosis factor (TNF) receptors. This activation initiates downstream signalling events that also result in caspase activation and apoptosis. Some phytochemicals additionally modulate tumor suppressor proteins like p53, which plays a crucial role in responding to DNA damage and cellular stress by promoting apoptotic processes [17].

Figure: Apoptosis Induction by Phytochemicals



Cell Signalling Pathways

Cell signalling pathways play a crucial role in regulating essential cellular processes such as growth, differentiation, survival, and programmed cell death. In cancer, these pathways are often disrupted, enabling cells to grow uncontrollably and evade apoptosis. Due to their ability to interact with multiple molecular targets, plant-derived phytochemicals have gained significant interest for their capacity to modulate these signalling networks and help inhibit cancer progression [18].

One of the key pathways affected by phytochemicals is the nuclear factor kappa B (NF- κ B) pathway. This pathway is strongly associated with inflammation, cell survival, and tumor development, and its abnormal activation is commonly observed in various cancers. Compounds like curcumin and resveratrol have been found to inhibit NF- κ B activity, thereby decreasing

the expression of genes involved in cell proliferation and survival [19].

Another important target is the phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) pathway, which plays a vital role in controlling cell survival and metabolism. Its overactivation is frequently linked to tumor growth and resistance to apoptosis. Phytochemicals can disrupt this pathway, resulting in reduced cell proliferation and increased programmed cell death in cancer cells [20].

The mitogen-activated protein kinase (MAPK) pathway is also critical in regulating cell division and differentiation. Depending on the cellular context, phytochemicals can either inhibit or activate specific components of this pathway, ultimately affecting cancer cell behaviour [21].

Additionally, phytochemicals can influence other signalling pathways such as the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, which is involved in cell proliferation and immune responses. By targeting multiple signaling mechanisms simultaneously, phytochemicals exhibit a multifaceted mode of action, enhancing their potential as complementary or alternative options in cancer treatment [22].

Gene Regulation

Gene regulation is essential for preserving normal cellular activities such as growth, differentiation, and programmed cell death. In cancer, however, genetic mutations and epigenetic alterations disrupt normal gene expression, resulting in uncontrolled cell proliferation and tumor development. In recent years, plant-derived phytochemicals have gained attention for their ability to modulate gene expression at multiple levels, contributing to their anticancer effects [23].

These compounds can help rebalance the activity of oncogenes and tumor suppressor genes, which are critical for controlling the cell cycle and apoptosis. For instance, phytochemicals have been found to inhibit oncogenes like c-Myc and Ras—both linked to increased cell division—while enhancing the function of tumor suppressor genes such as p53. This shift can reduce tumor growth and promote the removal of damaged or abnormal cells [24].

In addition to direct effects on gene expression, phytochemicals also act through epigenetic mechanisms. They can influence processes like DNA methylation, histone modification, and microRNA (miRNA) regulation,

all of which determine how genes are activated or silenced without changing the DNA sequence itself. Certain compounds, including curcumin and epigallocatechin gallate (EGCG), have been shown to reverse abnormal methylation patterns and alter histone activity, helping to restore more normal gene expression profiles [25].

Furthermore, phytochemicals can regulate genes involved in key cellular pathways related to inflammation, oxidative stress, and signal transduction. Through these combined actions, they exert broad control over cancer cell behavior, affecting proliferation, apoptosis, and even metastasis.

IV. ROLE OF PHYTOCHEMICALS IN CANCER THERAPY

Breast Cancer

Breast cancer continues to be one of the most commonly diagnosed cancers and a leading cause of cancer-related mortality among women worldwide. It is a complex and heterogeneous disorder that originates from the abnormal proliferation of breast epithelial cells and is influenced by a mix of hormonal, genetic, and environmental factors. Although treatment strategies such as chemotherapy, radiotherapy, and hormone therapy have improved clinical outcomes, challenges like drug resistance, cancer recurrence, and treatment-associated side effects remain significant [26].

In recent years, plant-derived phytochemicals have gained considerable attention for their potential roles in both preventing and treating breast cancer. These naturally occurring compounds exert their effects through various mechanisms, including inducing apoptosis, inhibiting uncontrolled cell growth, and regulating key signaling pathways involved in tumor progression.

A variety of phytochemicals have been extensively investigated for their effects on breast cancer cells. For example, curcumin has been shown to suppress tumor growth by inhibiting NF- κ B signaling and activating apoptotic pathways. Resveratrol exhibits antiproliferative properties by modulating estrogen receptor signaling and promoting cell cycle arrest. Similarly, genistein—an isoflavone present in soy—can influence hormone-dependent pathways and contribute to reducing tumor growth [27].

Phytochemicals are especially relevant in hormone-responsive breast cancer, where they can regulate estrogen receptor activity and disrupt

hormone-driven tumor progression. Additionally, many of these compounds have demonstrated the ability to inhibit angiogenesis and metastasis, thereby restricting cancer spread. When used in combination with conventional therapies, they may enhance therapeutic efficacy while minimizing toxicity, offering a more balanced treatment strategy.

Overall, the capacity of phytochemicals to target multiple molecular pathways underscores their potential as safer and more effective agents in the management of breast cancer.

Lung Cancer

Lung cancer continues to be one of the primary causes of cancer-related mortality worldwide. It is closely associated with risk factors such as tobacco use, exposure to air pollution, and genetic predisposition. Clinically, lung cancer is categorized into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), both of which are characterized by aggressive progression and a high likelihood of metastasis. Although advancements in targeted therapies and immunotherapy have expanded treatment options, overall outcomes remain limited due to late diagnosis, the emergence of drug resistance, and treatment-related side effects [28].

In this setting, plant-derived phytochemicals have attracted interest as potential agents for both prevention and therapy. These compounds can interact with multiple molecular targets involved in cancer development and progression. Their anticancer properties are largely linked to their ability to induce apoptosis, inhibit uncontrolled cell proliferation, and modulate key signaling pathways such as PI3K/Akt and MAPK.

Several phytochemicals have demonstrated promising effects against lung cancer cells. Epigallocatechin gallate (EGCG), a polyphenol in green tea, has been shown to suppress tumor growth by inhibiting angiogenesis and promoting apoptosis. Curcumin, known for its wide-ranging biological activities, can target multiple signaling pathways, thereby reducing cancer cell survival and proliferation. Quercetin also exhibits significant anticancer activity by inducing cell cycle arrest and triggering apoptotic cell death [29].

In addition to these effects, phytochemicals may help prevent metastasis and enhance the sensitivity of cancer cells to conventional chemotherapy. Their capacity to reduce oxidative stress and inflammation further supports their

protective role. Overall, the multi-targeted actions of phytochemicals underscore their potential as safer and more effective approaches in the management of lung cancer.

Colorectal Cancer

Colorectal cancer is one of the most prevalent cancers globally, affecting both the colon and rectum, and remains a significant cause of cancer-related morbidity and mortality. Its development is commonly associated with factors such as poor dietary habits, physical inactivity, genetic predisposition, and chronic inflammation. The disease typically progresses through multiple stages, starting from normal epithelial cells that gradually evolve into adenomatous polyps and eventually malignant tumors. Colorectal cancer is one of the most prevalent cancers globally, affecting both the colon and rectum, and remains a significant cause of cancer-related morbidity and mortality. Its development is commonly associated with factors such as poor dietary habits, physical inactivity, genetic predisposition, and chronic inflammation. The disease typically progresses through multiple stages, starting from normal epithelial cells that gradually evolve into adenomatous polyps and eventually malignant tumors.

In recent years, plant-derived phytochemicals have gained considerable attention for their potential roles in the prevention and treatment of colorectal cancer. These compounds exert their effects through various mechanisms, including inducing apoptosis, inhibiting uncontrolled cell proliferation, and modulating inflammatory processes involved in tumor progression.

Several extensively studied phytochemicals have demonstrated promising activity against colorectal cancer cells. For instance, curcumin has been shown to suppress tumor growth by targeting inflammatory mediators and interfering with signaling pathways such as NF- κ B and Wnt/ β -catenin. Epigallocatechin gallate (EGCG) is recognized for its potent antioxidant properties and its ability to inhibit cell proliferation, while resveratrol has been reported to induce apoptosis and decrease cancer cell survival.

Another important aspect of phytochemical activity is their impact on gut microbiota, which plays a crucial role in the development of colorectal cancer. By promoting a balanced microbial environment and reducing inflammation, these compounds support intestinal health and may help slow disease progression. Additionally, they have been found to enhance the effectiveness of

conventional therapies while potentially minimizing their side effects.

Overall, the diverse biological activities and relatively low toxicity of phytochemicals make them promising candidates for both the prevention and treatment of colorectal cancer.

V. CHALLENGES AND LIMITATIONS

Bioavailability

Bioavailability is a crucial factor in determining the effectiveness of plant-derived phytochemicals in cancer therapy. It refers to the proportion of a compound that enters the bloodstream in an active form and reaches its target site.

Although many phytochemicals demonstrate strong anticancer activity in experimental settings, their clinical application is often restricted due to poor bioavailability [30].

A major limitation is their low water solubility, which hinders absorption in the gastrointestinal tract. Compounds such as curcumin and resveratrol are well-known for this issue, as their poor solubility results in inefficient uptake. Even when absorption occurs, these compounds often undergo extensive first-pass metabolism in the liver, significantly reducing the amount of active substance available in circulation.

Stability also presents a challenge. Many phytochemicals are sensitive to physiological conditions and may degrade due to changes in pH, temperature, or enzymatic activity. Additionally, they are rapidly eliminated from the body and typically have short plasma half-lives, further limiting their therapeutic effectiveness.

To overcome these challenges, various strategies have been developed to enhance delivery and efficacy. Techniques such as the use of nanoparticles, liposomes, and nanoemulsions have shown promise in improving solubility, protecting compounds from degradation, and enabling more targeted delivery to cancer cells.

In summary, improving bioavailability remains a significant hurdle in translating the potential of phytochemicals into effective cancer treatments. Ongoing research in advanced formulation and drug delivery systems will be essential to bridge the gap between laboratory research and clinical application.

Toxicity and Safety

Although plant-derived phytochemicals are often considered safe due to their natural origin, their safety and toxicity profiles still need careful

assessment before therapeutic use. The assumption that “natural” automatically means “harmless” can be misleading, as the effects of these compounds depend on factors such as dosage, duration of exposure, and interactions with other substances.

One key concern is dose-dependent toxicity. While many phytochemicals are beneficial at low concentrations, higher doses may produce harmful effects. For instance, excessive consumption of certain alkaloids or phenolic compounds has been linked to cellular damage and even organ toxicity, emphasizing the need for controlled and appropriate dosing.

Another issue involves interactions with conventional drugs. Phytochemicals can alter the absorption, metabolism, or elimination of medications, potentially reducing their efficacy or increasing the likelihood of adverse effects. Additionally, variability in plant composition arising from differences in environmental conditions, harvesting methods, or processing techniques can result in inconsistencies in both safety and biological activity.

A further challenge is the lack of standardized dosing guidelines and comprehensive clinical data. Much of the existing knowledge is derived from *in vitro* or animal studies, with limited clinical evidence available to confirm long-term safety in humans.

Therefore, thorough toxicity assessments including acute, sub-chronic, and chronic studies are essential before phytochemicals can be broadly applied in cancer therapy. At the same time, well-defined regulatory frameworks and strict quality control measures are necessary to ensure their safe and reliable use in clinical practice.

VI. CONCLUSION

Plant-derived phytochemicals have attracted significant interest as potential agents in cancer therapy, largely because of their diverse biological activities and ability to target multiple molecular pathways. By modulating processes such as apoptosis, cell signaling, and gene expression, these compounds can interfere with various stages of cancer progression. This multi-targeted mode of action offers an advantage over many conventional treatments that typically focus on a single pathway.

Research findings indicate that phytochemicals may contribute to the management of cancers such as breast, lung, and colorectal cancer. They have been shown to inhibit tumor growth, limit metastasis, and in some cases enhance the effectiveness of existing

therapies. Additionally, their comparatively low toxicity makes them appealing for supportive care and long-term use.

Despite these promising aspects, several challenges remain before their full therapeutic potential can be achieved. Limitations such as poor bioavailability, potential toxicity at higher doses, and insufficient clinical evidence continue to hinder their broader application. Overcoming these issues will be essential for translating experimental results into clinical practice.

In conclusion, phytochemicals represent a promising avenue for future cancer treatment strategies. Ongoing research particularly well-structured clinical trials and advances in drug delivery systems will be crucial to fully understand their benefits and support their integration into modern oncology.

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