

The Role of Medicinal Herbs and Phytochemicals in Cancer Management: A Review

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Abstract

Bioactive compounds have demonstrated notable potential in the management of cancer and are recognized for their diverse therapeutic applications. Among these, phytochemicals have garnered significant attention for their capacity to modulate key cellular mechanisms involved in cancer development, particularly autophagy and apoptosis. The current body of evidence indicates that these naturally derived compounds may influence cancer pathogenesis by regulating interconnected pathways. Consequently, the targeting of the autophagy-apoptosis signaling axis using phytochemicals emerges as a promising adjunct strategy alongside conventional chemotherapeutic regimens. In order to enhance comprehension of the autophagy-apoptosis pathway's role in cancer pathobiology and its potential as a therapeutic target for the development of anticancer drugs, this review will attempt to delve into its molecular dynamics. A variety of credible scientific databases were systematically searched to retrieve data for this review. The effectiveness of phytochemicals as cancer treatments was assessed using a holistic method that took into account the compounds' molecular signaling connections, pharmacological profiles, and action mechanisms. From a cancer biology perspective, significant factors such as caspase activity, Nrf2, NF-κB, and the autophagy-apoptosis pathway are studied.

Keywords: Herbs; Phytochemicals; Anticancer; Autophagy; Apoptosis.

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Introduction

Among all causes of death, cancer ranks second. According to recent epidemiological data, both cancer incidence and mortality rates have increased. In 2018, it is estimated that 9.6 million people died from cancer, while an additional 18.1 million were diagnosed with the disease. The current rate of rise is expected to result in more than 20 million additional cases by 2025 (Asiimwe et al., 2021; Kudamba et al., 2022). This high rate of new cancer cases has far-reaching repercussions, including higher health, economic, and social expenses, which will continue to place a strain on the scarce resources and inadequate healthcare systems in developing nations. Consequently, there is an increasing inclination among individuals in these regions to seek treatment for cancer through herbal (traditional) and complementary medicine. The utilization of these therapeutic modalities in conjunction with cancer, particularly within various oncology care settings, remains a widely accepted practice (Asiimwe et al., 2021; Jenča et al., 2024; Kudamba et al., 2022).

The terms "herbal medicine" and "complementary medicine" are often used interchangeably to refer to a wide range of practices that are not part of standard Western medicine but are nonetheless employed in the upkeep of health, prevention of illness, diagnosis of disease, and treatment of disease and ill health across the spectrum of physical, social, and mental disorders (Jenča et al., 2024; Kudamba et al., 2022).

A 2018 systematic review revealed that patients utilize traditional and complementary medicine in isolation or in conjunction with conventional medicine. The vast majority of these patients (ranging from 55.8 to 100 percent) do not disclose this use to their doctors, primarily due to fear of retaliation and the rarity of doctor-initiated inquiries (Jenča et al., 2024). A multitude of prior studies have demonstrated that herbal medicine has been identified as the most prevalent form of complementary and alternative medicine (CAM) utilized by cancer patients, with its utilization exhibiting a tendency to increase following a cancer diagnosis (Kudamba et al., 2022).

Methodology

A comprehensive search strategy was employed to identify relevant studies, encompassing major bibliographic databases such as PubMed, Scopus, Web of Science, Google Scholar, and Google search. The objective was to ascertain the various molecular-based mechanisms of phytochemical components in cancer prevention, apoptosis modulation, and autophagy. Research on autophagy has also been conducted in related domains, including haematological, cancer, solid tumors, chemotherapy, and apoptosis.

Results

Clinical use of Herbs Having Anticancer Properties

A multitude of clinical trials have demonstrated the potential of various herbal treatments to elicit antineoplastic effects. The clinical application of a multitude of herbs is classified on a global scale due to their suppressive impact on specific cancer types (names of herbs are omitted) (Asiimwe et al., 2021; Jenča et al., 2024).

Breast Cancer

While in-vitro studies have not substantiated vitamins' anti-cancer effects, they have demonstrated potential in the prevention of breast cancer. A total of 2,972 individuals diagnosed with breast cancer were methodically assigned to receive either a vitamin-A formulation (fenretinide) at a dosage of 200 milligrams per day or no treatment at all. Premenopausal women who have been diagnosed with breast cancer have a significantly reduced risk of developing the disease again in the treated area 8.1 years after the conclusion of treatment. However, a lack of discernible variation is observed in total life expectancy. A body of research has indicated the potential for adverse long-term consequences associated with the administration of vitamin E to breast cancer patients. The present objective of their act is to induce nausea and vomiting in cancer patients with a related condition who are also eating healthily (Asiimwe et al., 2021; Ayoade et al., 2026; Bel'skaya & Dyachenko, 2024; Garutti et al., 2026; Jang & Kim, 2024; Jenča et al., 2024; Konieczny et al., 2025; Kupfer et al., 2025; Kyrø et al., 2025).

Lung Cancer

The high toxicity of numerous anti-cancer medications, including but not limited to docetaxel, etoposide, gemcitabine, paclitaxel, and vinorelbine, indicates that current anti-cancer treatment regimens frequently yield inadequate survival benefits. According to extant research, the utilization of herbal treatments and their phytoconstituents, which appear to exhibit reduced adverse effects, could constitute a promising strategy for the treatment of lung cancer. The therapeutic utilization of herbal plants in the treatment of lung cancer has a long history, with *Morus alba*, *Perilla frutescens*, and *Tussilago farfara* being notable examples. According to the medical community, up to 77% of lung cancer patients also use herbal treatments as adjuvant therapies in conjunction with conventional treatments, such as chemotherapy. In the treatment of lung cancer, herbal supplements are frequently used to augment the anticancer impact and mitigate adverse effects. While the primary rationale for employing natural treatments remains to be demonstrated, it is imperative to acknowledge that certain herbal remedies

may exert deleterious effects or diminish the effectiveness of conventional therapeutic interventions (Ayoade et al., 2026; Gerber et al., 2006; Jenča et al., 2024; Jeon et al., 2025; Jimoh et al., 2025; Kudamba et al., 2022; Xi et al., 2025).

Pancreatic Cancer

A recent study has revealed a significant reliance of cancer stem cells on the sonic hedgehog homolog (SHH) signaling pathway. This finding has elucidated the role of Smoothed (SMO) in this system. The hypothesis that decreased SHH control is a driving factor in the persistence of pancreatic cancer's progression is one that merits further investigation. The SMO antagonists GDC-0449, PF-04449913, and others are currently being assessed for their potential in treating pancreatic cancer. Cyclopamine, a steroidal alkaloid derived from the plant *Veratrum californicum*, has been shown to block SHH signaling by binding directly to the SMO protein's 7-helix bundle. The recruitment of bone marrow precursor cells (BMPCs) into cancer cells and the formation of tumor blood vessels are both negatively affected by cyclopamine, and further research is necessary to determine the extent of this effect. The conclusions of this study suggest that a thorough description of this TCM-derived phytochemical is necessary for the development of SMO-selective anti-cancer medicines in the future (Feldmann et al., 2007; Jenča et al., 2024; Kudamba et al., 2022; Mahadiuzzaman et al., 2024; Nair et al., 2024; Sigafos et al., 2021; Swain et al., 2024).

Integrating Herbal Supplements into Standard Cancer Care as Adjuvants (I.E., in Chemotherapy and/or Radiotherapy)

A considerable number of physicians are implementing adjuvant therapies, including herbal supplements, to enhance the efficacy of chemotherapy and mitigate its severe adverse effects in cancer treatment (Jenča et al., 2024). Furthermore, the combination of conventional cancer treatment with herbal medicine has been demonstrated to enhance treatment efficacy and quality of life while reducing adverse effects. A substantial body of research has demonstrated the efficacy of herbal treatments in curing cancer, with reported success rates ranging from 29% to 99% among Asian patients and 26% to 47% among American patients. A substantial body of research has been conducted on the use of herbal supplements in conjunction with chemotherapy and radiotherapy, with a focus on clinical trials. These studies have been primarily conducted in China and other regions. However, the extant literature on this subject is seldom cited in PubMed. A substantial body of research has been dedicated to the evaluation of herbal medications through a series of systematic reviews in clinical trials.

These reviews typically examine the use of herbal medications as adjunct therapies, aiming to mitigate the occurrence of diseases and mitigate the adverse effects associated with chemotherapy and/or radiotherapy. A plethora of herbal remedies have been utilized for millennia with documented success, including curcumin, ginseng, TJ-41, PHY906, Huachansu, and Kanglaite (Ameer et al., 2024; Ashadul Sk et al., 2025; Asimwe et al., 2021; Bray et al., 2024; Ehrlich et al., 1982; Ferro et al., 2007; Fesik & Shi, 2001; Franek et al., 2005; Guo et al., 2024; Gutsche et al., 2025; Ha, 2011; Hargreaves & Crabtree, 2011; Hofseth & Wargovich, 2007; Hurley & Young, 2). As indicated in the works of Jenča et al. (2024), Jimoh et al. (2025), Li et al. (2024), Mustafa et al. (2024), Saxena et al. (2024), and Zhong et al. (2024), the subject has been examined in the context of several studies. While numerous herbal treatments have demonstrated efficacy in preliminary studies or small-scale clinical trials, the absence of large-scale, multicenter randomized clinical trials remains a conspicuous limitation. Furthermore, the variability in dosage, preparation methods, and potential interactions with standard chemotherapy limit the immediate clinical translation of these findings.

Lung Cancer

In a randomized controlled trial (RCT) involving 63 patients with non-small-cell lung cancer (NSCLC), the use of Sheng-mai Injection and Gu-jin Granule increased median survival time ($P = 0.014$) and response rate up to 48.5% (16/33), compared to the control group ($P = 0.037$). In a subsequent clinical trial, the utilization of Shenqifuzheng injection was found to yield substantial enhancements in quality of life (QoL) and response rate among 232 patients diagnosed with non-small cell lung cancer (NSCLC). Furthermore, an increase in scores was observed in role, social, and economic status ($P 0.05$ or $P 0.01$), also based on the QLQ-C30 questionnaire. In a subsequent randomized controlled trial (RCT), Feiji Recipe therapy demonstrated a marked enhancement in therapeutic efficiency and a significant reduction in the deleterious effects of chemotherapy (Chen et al., 2009; Jenča et al., 2024; H.-S. As demonstrated in the works of Lin & Li (2007) and Tian et al. (2010), the efficacy of this approach has been extensively researched.

Colon Cancer

According to extant research, the bioavailability of CYP3A substrate anti-cancer medicines taken orally is contingent on the activity of cytochrome P-450 enzymes in the gastrointestinal tract wall.

Echinacea, kava, grape seed, and St. John's wort (*Hypericum perforatum*) represent a subset of herbal supplements believed to exert an influence on cytochrome P450 (CYP). Given the increasing trend of

cancer patients resorting to herbal therapies, it would be advantageous for researchers to prioritize the exploration of the potential synergies between these supplements and conventional therapeutic modalities. St. John's wort has been demonstrated to enhance the metabolic process of irinotecan, a camptothecin derivative that has the potential to induce DNA damage upon interaction with topoisomerase I. This enhancement is attributed to the induction of CYP3A expression in the intestines and liver. Consequently, St. John's wort is employed in the management of advanced colon cancer that has metastasized. Preliminary epidemiological studies have indicated positive trends, suggesting that the incorporation of herbal remedies as an adjuvant therapy may enhance the prognosis of patients diagnosed with advanced colon cancer. A hypothesized anti-proliferation and immune-activation model of tumor development and degeneration has been attributed to the therapy mechanisms of traditional Chinese medicine (TCM) in cancer patients with metastasis (Abiri et al., 2024; Asiimwe et al., 2021; Au-Yeung et al., 2008; Auyeung & Ko, 2010; Baak et al., 2011; Ernst & Cassileth, 1998; Labrie et al., 2022; Mathijssen et al., 2002; Zhang & Benet, 2001).

Hepatic Cancer

"Liver stasis" is the term used in Traditional Chinese Medicine (TCM) to describe cases of unresectable hepatocellular carcinoma (UHCC). A clinical trial has demonstrated the efficacy of Shentao Ruangan pills, hydroxycamptothecin, and chemotherapy in reducing symptoms, enhancing treatment tolerance, diminishing tumor size, and augmenting body defense. These findings suggest that TCM can effectively mitigate the prevalence of adverse effects and prolong survival in patients with UHCC. Despite the potential for individual studies to be rejected at the international level due to methodological shortcomings, these studies nevertheless provide support for the use of Traditional Chinese Medicine (TCM), which may facilitate further trials for individuals diagnosed with UHCC. It was indicated that future TCM clinical studies for UHCC should have adequate procedural quality and be conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement. Conducting well-designed, large-scale, multicenter, randomized, double-blind controlled trials is imperative (Jenča et al., 2024; Jiang, 2005; Ju et al., 2005; Lin et al., 2005; Liu et al., 2005; M.-B.). As indicated by Meng et al. (2008) and Mwaka et al. (2020), the effectiveness of these interventions merits further investigation.

Plant Compounds Trigger Apoptosis

It is well established that apoptotic pathways play a pivotal role in cancer therapy. A plethora of

phytochemicals have been utilized traditionally as analgesics and antivirals. Concurrent with the expansion of our knowledge of cancer mechanisms is the emergence of antitumor qualities, such as the targeting of apoptotic pathways in cancer. Multicellular organisms may undergo apoptosis, or programmed cell death. Unchecked cell growth is a hallmark of cancer, and this phenomenon is made possible by a lack of apoptosis. Apoptosis is a complex process involving numerous signal transduction pathways. The process of mitochondrial protuberance, initiated by the presence of apoptotic proteins, has been observed to increase the permeability of the mitochondrial membrane. This increase in permeability has been shown to facilitate the release of apoptotic effectors. Upon release, mitochondrial-derived small cysteine proteases (SMACs) migrate into the cytosol, where they bind to and inactivate inhibitor of apoptosis proteins (IAPs) to prevent apoptosis arrest. IAPs frequently impede the activity of caspases, a protein family that plays a pivotal role in the process of programmed cell death, thereby enabling its progression. Upon its release from the mitochondria, CYT-C associates with Apaf-1 and ATP, thereby forming the apoptosome. The subsequent binding of the apoptosome to pro-caspase-9 results in its cleavage, thus releasing active caspase-9. This, in turn, promotes the activation of effector caspase-3 (Jenča et al., 2024; Kudamba et al., 2022; Maskarinec et al., 2000; Mathijssen et al., 2002; M.-B.). Meng et al., 2008; Z. Meng et al., 2009; Mitra & Dash, 2018). Recent findings indicate that certain phytochemicals, including curcumin and resveratrol, can modulate autophagy and apoptosis in a context-dependent manner. For instance, curcumin has been demonstrated to induce autophagy-associated cell death in certain cancer types while promoting apoptosis through modulation of Bcl-2 and caspase signaling. Resveratrol, a natural polyphenol, has been shown to influence both pathways via AMPK activation and mTOR inhibition, underscoring the intricate interplay between survival and death signals in cancer cells. In summary, apoptosis is a highly regulated form of programmed cell death that plays a pivotal role in the elimination of damaged or cancerous cells. The regulation of this process involves the permeabilization of the mitochondrial membrane, the release of cytochrome c, and the activation of caspases. A considerable number of phytochemicals have been observed to exert anticancer effects by targeting these pathways, either by promoting pro-apoptotic signals (e.g., upregulation of Bax, caspase-3) or by inhibiting anti-apoptotic proteins (e.g., Bcl-2, IAPs). It is imperative to comprehend the mechanisms underlying this process, as this knowledge is essential for the identification of compounds capable of selectively inducing apoptosis in cancerous cells while sparing normal tissues.

Conclusion

The global incidence of cancer is increasing, prompting researchers to continually evaluate novel diagnostic and therapeutic interventions to combat the disease. The intricacy of cancer pathobiology poses a significant challenge in the development of novel, targeted anticancer drugs.

The development and control of cancer are influenced by unique critical cellular mechanisms, including autophagy and apoptosis. It has been observed that a multitude of cancerous neoplasms are demonstrating a propensity to exhibit chemoresistance, a phenomenon that has been attributed to the presence of genetic aberrations within the apoptotic signaling pathways that are implicated in the process of cell death. In order to enhance the efficacy of cancer research, scientists may consider the potential of autophagy as a distinct cell fate mechanism. In order to achieve a comprehensive understanding of the inherent capabilities of autophagy and apoptosis, it is imperative to undertake a more extensive array of in vitro and in vivo studies that delve into the intricacies of cancer pathobiology. It is imperative that future research prioritize the implementation of standardized clinical trials. Such an approach is essential for the assessment of efficacy and safety across diverse populations. Integrating systems biology approaches may also provide deeper insight into how phytochemicals orchestrate complex cellular responses. In addition, pharmacokinetic profiling and herb-drug interaction studies are imperative to ensure safe integration with standard therapies.

Declarations

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Material

No new data was generated or analyzed in this study.

Conflicts of Interest / Competing Interests

The authors declare that there are no conflicts of interest.

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Authors' Contributions

C.D: Validation, Writing of the original draft, Supervision.

I.F: Resources, Writing of the original draft, Visualization.

L.A: Investigation, Data curation.

Y.T: Validation, Formal analysis.

M.F: Validation, Data curation.

D.C: Conceptualization, Visualization, Supervision.

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Use of Generative AI and AI-Assisted Technologies

The authors declare that no generative AI or AI-assisted technologies were used in the preparation of this work.

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