

## HERBAL MEDICINES USED IN CANCER TREATMENT

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### ABSTRACT

Cancer is a disease characterized by the uncontrolled growth of abnormal cells in the body that can form malignant tumors. Current treatments for cancer typically include chemotherapy, radiation therapy, and surgery. There is growing evidence suggesting that cancer patients often use herbal medicines alongside chemotherapy. Medicinal plants and their bioactive compounds have gained increasing recognition as valuable complementary therapies in cancer treatment. Additionally, recent research has explored the biochemical and cellular mechanisms through which herbal medicines may interact within the tumor microenvironment. These studies also highlight the potential role of specific phytochemicals in cell-based cancer vaccines. Numerous clinical studies have demonstrated the beneficial effects of herbal therapies in cancer care. Natural products, including plant extracts, herbal formulations, and isolated bioactive compounds, hold significant promise for both the prevention and treatment of cancer. Based on this evidence, we conclude that herbal medicines can serve as effective adjuvants to help manage chemotherapy-induced side effects and potentially enhance the efficacy of conventional treatments.

[11]However, there is an urgent need for more in-depth pharmacodynamics (PD) evaluations and safety assessments of herbal drug combinations, particularly in the context of chemotherapy. Additionally, multicenter clinical trials are necessary to validate the therapeutic benefits of combining chemotherapy with herbal drugs in cancer treatment. This review aims to explore the various herbal plants and their medicinal properties that are being investigated for use in cancer therapy.[3]

### I. INTRODUCTION

Herbal medicines have been utilized for centuries across different cultures to treat a variety of ailments, and their use in managing diseases with fewer side effects has significantly increased in recent years. Cancer remains a significant public health issue, particularly in developed nations. However, advancements in early detection and medical treatment over the past few decades have led to notable improvements in patient survival rates. A large number of cancer patients undergo chemotherapy or chemoradiotherapy, which have proven effective in treating cancer.[17] Despite their effectiveness, these treatments often come with harmful side effects due to their toxic impact on normal, healthy cells and tissues. Common side effects include nausea, vomiting, loss of appetite, diarrhea, oral mucositis, and peripheral neuropathy. As a result, there has been increasing interest in finding alternatives, such as herbal medicines, which are believed to have fewer or less severe side effects. These herbal treatments can come in the form of whole plant extracts or isolated bioactive compounds derived from plants. One of the main challenges with chemotherapy is the severe side effects it often causes. Chemotherapeutic agents primarily target rapidly dividing cells, including cancer cells, but also affect healthy cells in the bone marrow, hair follicles, and the gastrointestinal mucosa. This damage to normal tissues contributes to the undesirable side effects commonly experienced by patients undergoing cancer treatment.[2]

#### 1. Clinical use of herbal medicines exhibiting anticancer activities.

Herbal medicines with anticancer properties have been explored and utilized in clinical settings for their potential to treat or manage cancer, either alone or as complementary therapies alongside conventional treatments like chemotherapy. While more rigorous clinical evidence is needed to confirm their efficacy and safety, numerous medicinal plants and their bioactive compounds have demonstrated anticancer activities in both preclinical and clinical studies. Below are some examples of herbal medicines that have been used in clinical practice, showcasing their anticancer activities:

### 1.2. Turmeric (*Curcuma longa*) – Curcumin

Curcumin, the active compound found in turmeric, has been widely studied for its anticancer properties. It has shown potential to inhibit tumor growth, metastasis, and angiogenesis (the formation of new blood vessels that feed tumors). Clinical trials have examined curcumin's ability to enhance the effects of chemotherapy and reduce side effects such as nausea and fatigue. While clinical evidence is still in development, curcumin has been tested in combination with chemotherapy drugs like paclitaxel and cisplatin in various cancer types, including breast, colon, and pancreatic cancers.[8]

### 1.3. Green Tea (*Camellia sinensis*) – Epigallocatechin Gallate (EGCG)

Green tea, particularly its polyphenolic component EGCG, has gained attention for its potential to prevent cancer and inhibit the progression of established tumors. EGCG has been shown to exert antioxidant, anti-inflammatory, and anti-cancer effects by targeting multiple molecular pathways involved in cancer cell survival, proliferation, and apoptosis (programmed cell death). Clinical trials have investigated the effects of green tea extract in cancers such as prostate, breast, and colorectal cancer. Some studies suggest that EGCG may enhance the effectiveness of chemotherapy and radiotherapy while reducing side effects.[5]

### 1.4. Ginseng (*Panax ginseng*)

*Panax ginseng* is a well-known adaptogen that has been used traditionally to improve overall vitality and immune function. Several studies have indicated that ginseng possesses anticancer properties, including the ability to inhibit tumor growth, enhance immune response, and reduce the side effects of chemotherapy. Clinical trials have investigated ginseng's role in managing chemotherapy-induced fatigue and improving quality of life for cancer patients. There is also evidence suggesting that ginseng may help improve the response to certain chemotherapy drugs, such as doxorubicin and cisplatin.[13]

### 1.5. Garlic (*Allium sativum*)

Garlic contains sulfur compounds, such as allicin, which have demonstrated anticancer properties in both laboratory and clinical studies. Research suggests that garlic may help prevent cancer by promoting detoxification, inhibiting the growth of cancer cells, and inducing apoptosis in tumor cells. Clinical trials have investigated garlic's role in reducing the risk of colorectal, stomach, and prostate cancers. Some studies have suggested that garlic supplements may also have synergistic effects when used in combination with chemotherapy drugs.[9]

### 1.6. Ashwagandha (*Withania somnifera*)

Ashwagandha, an adaptogenic herb commonly used in Ayurvedic medicine, has been shown to have anticancer properties through its ability to regulate oxidative stress, inflammation, and immune response. Preclinical studies suggest that withanolides, the active compounds in ashwagandha, can inhibit the growth of cancer cells in various cancers, including breast and lung cancer. Clinical studies have explored ashwagandha's role in improving the quality of life of cancer patients, reducing stress, and managing chemotherapy-related side effects like fatigue and anxiety.[11]

### 1.7. Milk Thistle (*Silybum marianum*) – Silymarin

Milk thistle, with its active ingredient silymarin, has been studied for its liver-protective and anticancer effects. Silymarin is known to possess antioxidant, anti-inflammatory, and anti-proliferative properties, and clinical trials have explored its use in cancer prevention and in managing liver toxicity caused by chemotherapy drugs like cisplatin and doxorubicin. Milk thistle has also been researched for its potential to inhibit the growth of various tumor types, including breast, prostate, and liver cancers.[4]

### 1.8. Mistletoe (*Viscum album*)

Mistletoe extract has been widely used in Europe as a complementary treatment for cancer. It has been shown to enhance immune function, improve the quality of life, and reduce side effects of chemotherapy, such as fatigue, nausea, and pain. Clinical studies have demonstrated that mistletoe can stimulate the immune system, induce apoptosis in tumor cells, and improve overall survival in certain types of cancer, particularly in breast, colon, and lung cancers. It is often used alongside conventional therapies to reduce adverse effects and enhance recovery.[7]

### 1.9. Bitter Melon (*Momordica charantia*)

Bitter melon has been traditionally used in many cultures for its potential health benefits, including its anticancer properties. Studies suggest that bitter melon may inhibit the growth of cancer cells, particularly in cancers of the pancreas, liver, and breast, through mechanisms such as the inhibition of cancer cell proliferation and induction of apoptosis. While clinical trials are limited, some studies have examined its use as a complementary therapy in pancreatic cancer, often in combination with other conventional treatments.[19]

## II. FOR BREAST CANCER

Although a definitive role for vitamins and selenium in preventing breast cancer has not been established, some anticancer effects have been observed in laboratory studies. In a randomized controlled trial, 2,972 women with either invasive or noninvasive breast carcinoma were given either 200 mg of a vitamin A derivative (Fenretinide) daily or no treatment. [5]After 97 months of follow-up, a significant reduction in the recurrence of local breast cancer was observed in premenopausal women receiving Fenretinide (HR: 0.65; 95% CI: 0.46–0.92). Phytoestrogens are classified into two main categories: water-soluble isoflavones and fat-soluble lignans. Isoflavones are found in high amounts in soybeans, while lignans are present in foods such as flaxseeds, wheat, fruit, and vegetables. Of the six clinical trials conducted on this topic, only one found a reduced risk of breast cancer associated with isoflavones. [13]However, none of the studies demonstrated significant differences in metastasis or overall survival. Interestingly, some studies suggest that long-term use of vitamin E may have adverse effects on breast cancer patients. These effects may be due to the malabsorption or maldigestion of nutrients in cancer patients, especially those suffering from additional health issues. Therefore, it is generally recommended that cancer patients focus on maintaining a balanced and healthy diet. Soy-derived phytoestrogens are often suggested for alleviating menopausal symptoms in women undergoing tamoxifen therapy for breast cancer. Isoflavones such as genistein and daidzein, which are found in soy, share structural similarities with  $17\beta$ -estradiol and can exhibit weak estrogenic effects. However, there is currently no conclusive evidence to support the use of phytoestrogens for either breast cancer treatment or the management of menopausal symptoms.[16]

### 2.2 For prostate cancer

Prostate cancer is known for its long latency, significant dietary influences, and limited treatment options in advanced stages. As a result, many patients turn to complementary and alternative medicine (CAM) in the hope that these therapies may offer viable treatments with fewer side effects. Despite the lack of robust evidence supporting their efficacy, many prostate cancer patients use vitamin and mineral supplements with the belief that these can help prevent or treat inflammation-related conditions without causing harm. This belief is particularly prevalent in several Asian cultures, but it requires further scientific validation through systematic, evidence-based research.[7]

Vitamins, such as A, C, D, and retinoids, are essential organic compounds that humans cannot synthesize and must obtain through diet to maintain health and prevent metabolic disorders. Although the use of vitamins and supplements is common among prostate cancer patients, the effectiveness of these supplements in cancer prevention or treatment remains unproven.[6] For example, a study among smokers suggested that daily consumption of more than 100 IU of vitamin E reduced the risk of advanced prostate cancer by 56%, compared to non-users. However, results from the SELECT trial—a large chemoprevention study—showed that vitamin E supplementation actually increased the risk of prostate cancer among healthy men, suggesting that vitamin E may be more beneficial for addressing inflammation-related aspects of the disease rather than exerting a direct anticancer effect.[11]

Further research is necessary to resolve these discrepancies in how vitamin E affects healthy versus cancerous populations. In addition to vitamins, medicinal herbs and their polyphenolic compounds, commonly found in plants, may contribute to the lower incidence of prostate cancer. Polyphenols, such as isoflavones, are phytoestrogens that can bind to estrogen receptors, potentially influencing cancer cell behavior.[8]

Several specific plant compounds have been studied for their effects on prostate cancer, including those in green tea and soy. Green tea, for example, contains active polyphenols like epicatechin, epigallocatechin, and epigallocatechin-3-gallate (EGCG), which have been shown to halt the progression of prostate cancer cells in

laboratory settings. However, the concentrations required to see these effects are much higher than what is typically achieved through moderate tea consumption. In a Phase II clinical trial, green tea extract demonstrated limited efficacy in reducing prostate-specific antigen (PSA) levels in patients with androgen-independent metastatic prostate cancer, though the treatment also caused significant side effects, including nausea, diarrhea, and fatigue.[1]

Soy isoflavones have been shown to inhibit 5 $\alpha$ -reductase, an enzyme responsible for converting testosterone to the more potent dihydrotestosterone, and are being studied for their potential as chemopreventive agents.[15] Scutellaria baicalensis, a traditional Chinese herb, contains high levels of baicalin, a flavonoid that suppresses inflammation and prostate cancer cell growth. Studies suggest that baicalein, another flavonoid found in the plant, can impair prostate cancer cell proliferation and induce cell cycle arrest, at concentrations that can be achieved in humans.[16]

Lycopene, a compound found in tomatoes, has been investigated for its potential to reduce prostate cancer risk. Clinical studies have shown that lycopene intake may decrease oxidative damage in prostate cancer patients, although whether lycopene itself or other components in tomato products are responsible remains unclear[12]. More randomized controlled trials are necessary to determine lycopene's precise role in chemoprevention.

PC-SPES, a herbal supplement marketed for prostate health, was once widely used as a complementary treatment for prostate cancer. This botanical blend, containing extracts from eight herbs, was designed based on traditional Chinese medicine. Clinical studies indicated potential antitumor effects, but the product was recalled in the early 2000s due to contamination with prescription drugs, and it has never been approved by the FDA for cancer treatment. Research into its efficacy is still ongoing, and more evidence is needed before any firm conclusions can be drawn regarding its clinical use.[9]

Additionally, recent studies have explored the use of phytochemicals from plants such as *W. chinensis*, which demonstrated potent anti-inflammatory effects in both lab and animal models. These findings suggest potential applications for such compounds in prostate cancer prevention, but further human trials are needed to assess their effectiveness as complementary therapies.[17]

### 2.3 For lung cancer

Lung cancer remains one of the most lethal forms of cancer, and the lungs are also a common site for metastasis from tumors originating in other organs. Conventional chemotherapy regimens, which often include drugs like gemcitabine, paclitaxel, docetaxel, etoposide, and vinorelbine, tend to offer limited survival benefits and are associated with significant toxicity. In recent years, there has been growing interest in the potential use of herbal medicines and their bioactive compounds as adjuncts to traditional cancer treatments. These natural remedies may present a promising alternative due to their potentially lower toxicity profiles.[8]

Research suggests that a substantial proportion of lung cancer patients—up to 77%—use herbal remedies alongside standard chemotherapy, highlighting their appeal as complementary treatments. Some studies have indicated that certain herbal medicines may help mitigate chemotherapy side effects or support overall well-being. However, it is crucial to recognize that some complementary and alternative medicine (CAM) therapies could have unintended negative effects, such as diminishing the effectiveness of conventional treatments.[2] Furthermore, the rationale for using these herbal remedies is often based on anecdotal evidence, case reports, and hypothetical mechanisms, as opposed to robust clinical data. As such, more rigorous research is needed to fully understand the safety and efficacy of these alternative therapies in the context of lung cancer treatment.[4]

### 2.4. For Liver Fibrosis and Cancer

Liver fibrogenesis is a gradual process marked by an imbalance between the production and breakdown of extracellular matrix components, often triggered by the activation of hepatic stellate cells (HSCs).[13] Over the past decade, the incidence of deaths from hepatocellular carcinoma (HCC) has risen steadily. In traditional Chinese medicine (TCM), a compound known as Compound 861, which combines 10 herbs including *Salvia miltiorrhiza* (known as sage), *Astragalus membranaceus*, and *Spatholobus suberectus*, has been explored for its antifibrotic effects. These herbs work synergistically, with certain ones acting as "king herbs" due to their

potent pharmacological activity, and others acting as modifiers that enhance immune function and reduce toxicity.[15]

Experimental studies have shown that Compound 861 may offer promising results in treating liver fibrosis. Two open-label trials involving patients with chronic hepatitis B demonstrated beneficial effects on liver fibrosis, with most patients showing clinical and histological improvements. However, since these studies lacked rigorous controls, further well-designed clinical trials are needed to confirm the effectiveness and safety of Compound 861 for managing hepatitis B-related liver fibrosis.[9]

Similarly, clinical research has highlighted the potential of Sho saiko-to (TJ-9), a Japanese traditional herbal formula made up of seven herbs, in treating liver diseases, including liver fibrosis. These studies indicate that it may have therapeutic benefits for liver conditions, although more controlled trials are necessary to establish its role in clinical practice.[8]

In the context of cancer treatment, small-molecule inhibitors of Smoothed (SMO) signaling, such as GDC-0449, IPI-926, XL-139, and PF-04449913, are being investigated for their potential in treating pancreatic cancer. Cyclopamine, a steroidal alkaloid derived from *Veratrum californicum*, is known to effectively inhibit SMO signaling by binding directly to the SMO protein. This interaction can disrupt the function of the PTCH-1 receptor, which is involved in the SHH signaling pathway, and may have downstream effects on tumor progression. Additionally, cyclopamine has shown potential in reducing the recruitment of bone marrow precursor cells (BMPCs) to tumors and in limiting the formation of tumor vasculature. Given its promising effects, this compound, derived from a TCM herb, warrants further investigation as a potential SMO-targeting anticancer drug. [5]

### III. USE OF HERBAL SUPPLEMENTS AS ADJUVANTS IN CONVENTIONAL ANTICANCER THERAPIES

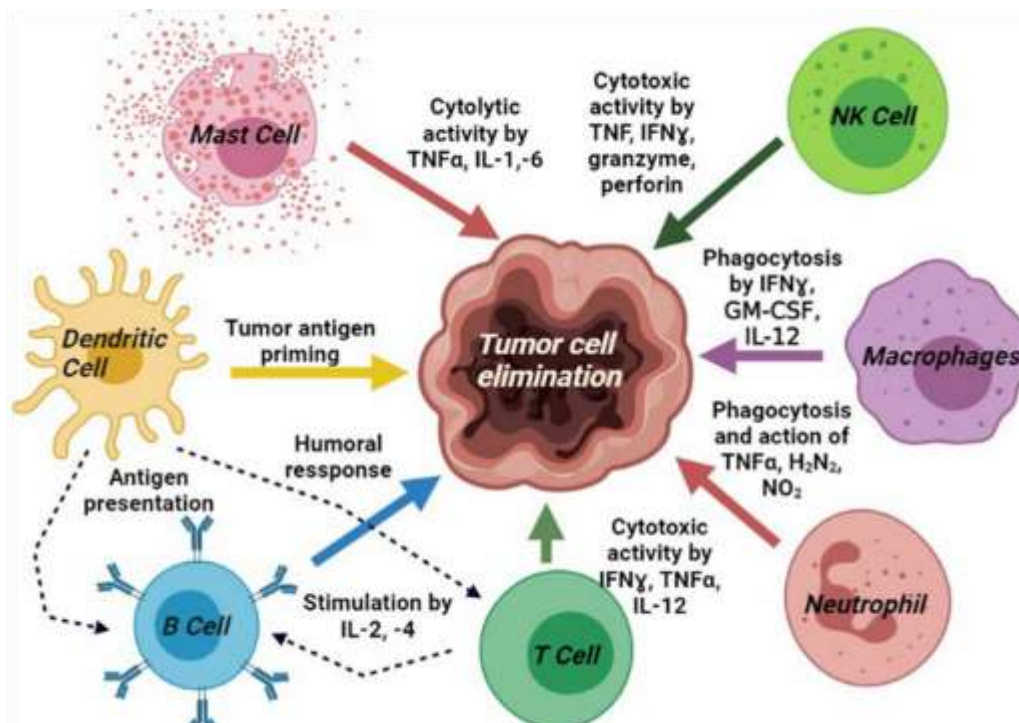


Fig 1: Herbal supplements

### IV. HERBAL MEDICINES AS ADJUVANT FOR DENDRITIC CELL-(DC-)BASED VACCINES

An adjuvant is a substance used in vaccine formulations to enhance or promote antigen delivery and presentation, thereby boosting the immune response. In addition to facilitating antigen presentation, adjuvants can also stimulate cytokine production and activate antigen-presenting cells (APCs) within the tumor or tissue microenvironment. Certain herbal medicines have demonstrated immunomodulatory properties that may support these processes.[4]

For example, bioactive polysaccharides from *Ganoderma lucidum* (Reishi) have been studied for their potential immunostimulatory and anticancer effects. One particular polysaccharide fraction from Reishi has been shown to activate immune cells, including dendritic cell maturation, and increase cytokine production, displaying potent adjuvant-like effects in animal models. Similarly, polysaccharides from *Dioscorea batatas* have been found to promote TNF- $\alpha$  secretion through Toll-like receptor 4 (TLR4)-mediated signaling pathways, which are critical for immune responses.[3]

In addition to these examples, several phytochemicals have been shown to enhance the efficacy of gene-based cancer vaccines. For instance, the compound shikonin has been reported to improve the anti-tumor effects of cancer vaccines by stimulating the expression of RANTES at the site of skin immunization. Furthermore, a phytochemical mixture extracted from the butanol fraction of *Echinacea purpurea* stems and leaves exhibited immunomodulatory effects, particularly in terms of modulating dendritic cell mobility and cellular function in vivo in mice.[7]

These findings suggest that certain herbal medicines may be effectively utilized in cell-based vaccine systems, providing additional support for enhancing the immune response and improving cancer vaccine efficacy.[3]

## V. INDUCTION OF IMMUNOGENIC CELL DEATH BY HERBAL MEDICINES

Immunogenic cell death (ICD) refers to a form of regulated cell death that triggers an immune response, making it a promising strategy in cancer immunotherapy. Unlike other forms of cell death, ICD releases specific signals that alert the immune system to recognize and attack tumor cells. These signals include the release of damage-associated molecular patterns (DAMPs), such as calreticulin (CRT) exposure on the cell surface, the release of high mobility group box 1 (HMGB1), and the secretion of ATP, all of which activate dendritic cells and promote an effective anti-tumor immune response.[5]

Recent studies have highlighted the potential of herbal medicines in inducing ICD, thereby enhancing anti-cancer immunity. Several bioactive compounds derived from plants have shown the ability to trigger ICD, either alone or in combination with conventional therapies, amplifying the overall anti-tumor effects. Below are key examples of herbal medicines and their mechanisms of inducing ICD.[2]

## VI. CONCLUSION

Herbal medicine is experiencing a resurgence as more patients seek alternatives to synthetic drugs due to the growing concerns over the side effects of conventional pharmaceuticals. Given these circumstances, further research into polyherbal formulations is essential. It is important not to dismiss these treatments simply because they may not yet align with modern scientific standards. Traditional systems like Ayurveda and other herbal practices have long been based on the therapeutic use of medicinal plants, and their value should be acknowledged.[12] There is a clear need to develop evaluation techniques that combine both traditional and contemporary methods. This would enhance the quality and consistency of herbal products, while also encouraging practitioners to engage more deeply in the standardization process. Encouraging patients to disclose their use of herbal remedies offers an opportunity for healthcare providers to guide them toward more effective conventional treatments. By taking a thorough history of both pharmaceuticals and supplements, physicians can open a discussion about the relative merits of herbal treatments versus regulated medications, particularly in relation to the severity of the patient's condition. For patients with chronic illnesses such as HIV/AIDS or cancer, it is crucial to note that some side effects of herbal remedies may resemble the symptoms of the disease or its treatments. This overlap can make it challenging to determine whether the issue is related to the illness or the herbal remedy. For patients who are hesitant about conventional medicine, a physician can foster a more open and trusting relationship by demonstrating a balanced understanding of both alternative and mainstream approaches to health.[18]

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