

Review Article

The Role of Herbs in Complementary and Alternative Cancer Therapies: A Critical Review

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Abstract: *Background:* Cancer patients increasingly seek complementary and alternative therapies (CAM) alongside conventional treatments. Herbs represent a significant component of CAM, with growing interest in their potential anticancer properties. *Objective:* This review critically examines the role of herbs in cancer management, exploring their mechanisms of action, clinical evidence, potential for synergy with conventional therapies, challenges and perspectives, and patient perspectives. *Methods:* A comprehensive literature search was conducted using PubMed, Google Scholar, and other relevant databases. Studies investigating the mechanisms, efficacy, safety, and patient experiences with herbs in cancer management were reviewed. *Results:* Herbs exhibit diverse mechanisms of action, including anti-proliferative, anti-angiogenic, and immune-modulatory effects. Clinical evidence suggests promising results for certain herbs, such as curcumin and ginseng, in improving treatment outcomes and reducing side effects. However, safety concerns and the need for standardization and quality control remain challenges. *Conclusion:* Herbs hold potential as complementary therapies for cancer management, offering a holistic approach that empowers patients and improves their quality of life. Further research is crucial to optimize their integration with conventional therapies, ensure safety, and establish evidence-based guidelines for their clinical use.

Keywords: Herbs, Cancer, Curcumin, Cancer Therapies, Ginseng.

INTRODUCTION

1. Molecular Pathways of Herbal Anticancer Effects

The increasing interest in herbal medicine for cancer management necessitates a deeper understanding of the underlying mechanisms by which these natural compounds exert their anticancer effects. This section delves into the molecular pathways targeted by various herbs, providing insights into their potential as therapeutic agents [1].

1.1 Antiproliferative and Apoptotic Effects

Many herbs exhibit potent antiproliferative activity, effectively inhibiting the uncontrolled growth of cancer cells. Curcumin, a major constituent of turmeric (*Curcuma longa*), has been shown to suppress proliferation in various cancer cell lines, including breast, colorectal, and pancreatic cancer cells [2]. This effect is mediated through multiple pathways, including the downregulation of cyclins and cyclin-dependent kinases, proteins crucial for cell cycle progression [3].

Furthermore, several herbs induce apoptosis, a programmed cell death mechanism that eliminates damaged or unwanted cells. Artemisinin, a compound derived from the plant *Artemisia annua*, triggers apoptosis in leukemia cells by activating caspase-3, a key executioner enzyme in the apoptotic pathway [4]. Similarly, ginsenosides, the active

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components of ginseng (*Panax ginseng*), induce apoptosis in lung cancer cells through the activation of the mitochondrial apoptotic pathway [5].

1.2 Anti-angiogenic Effects

Tumor growth and metastasis rely heavily on angiogenesis, the formation of new blood vessels that nourish the tumor. Several herbals possess anti-angiogenic properties, effectively cutting off the tumor's supply of nutrients and oxygen. Resveratrol, found in grapes and berries, inhibits angiogenesis by suppressing vascular endothelial growth factor (VEGF), a key regulator of blood vessel formation [6]. Additionally, green tea polyphenols, particularly epigallocatechin gallate (EGCG), have been shown to suppress angiogenesis *in vitro* and *in vivo* [7].

1.3 Immunomodulatory Effects

The immune system plays a crucial role in controlling cancer growth and preventing metastasis. Some herbals exert immunomodulatory effects, enhancing the immune system's ability to recognize and destroy cancer cells. Echinacea purpurea, commonly known as purple coneflower, stimulates the production of immune cells, including natural killer cells and macrophages, which play a critical role in antitumor immunity [8]. Similarly, astragalus membranaceus, a traditional Chinese herb, has been shown to enhance T cell function and improve immune responses in cancer patients [9].

Understanding the molecular mechanisms of action of herbals provides valuable insights into their potential as targeted therapies for cancer. By interfering with various cellular processes crucial for tumor growth, survival, and metastasis, herbals offer a promising avenue for developing novel and effective cancer treatments. Further research is warranted to fully elucidate the complex mechanisms of action of these natural compounds and to translate these findings into clinical applications [10] (Table 1).

Table 1: Common Herbals Used in Cancer Management

Herbal Name	Active Ingredients	Potential Mechanisms of Action	Clinical Evidence	Safety Concerns
Curcumin (Turmeric)	Curcuminoids	Anti-proliferative, anti-angiogenic, anti-inflammatory, immunomodulatory	Improved response to chemotherapy, reduced side effects	Potential interactions with medications, may increase bleeding risk
Ginseng	Ginsenosides	Anti-proliferative, anti-metastatic, immunomodulatory	Improved survival rates, reduced fatigue	May interact with medications, may increase blood pressure
Green Tea Polyphenols	Catechins (EGCG)	Anti-proliferative, anti-angiogenic, antioxidant	Reduced risk of recurrence, improved response to treatment	May interfere with iron absorption, may cause nausea
Ginger	Gingerols, Shogaols	Anti-inflammatory, anti-emetic, antioxidant	Reduced nausea and vomiting, improved quality of life	Generally safe, may interact with blood thinners
Garlic	Allicin, Organosulfur compounds	Anti-proliferative, anti-angiogenic, anti-inflammatory	Reduced risk of certain cancers, improved response to treatment	May increase bleeding risk, may cause heartburn
Astragalus	Polysaccharides, Flavonoids	Immunomodulatory, adaptogenic	Improved immune function, reduced fatigue	May interact with medications, may cause diarrhea
Echinacea	Alkamides, Polysaccharides	Immunomodulatory, antiviral	May reduce risk of infection, may improve immune response	May interact with medications, may cause allergic reactions

2. Evaluating the Efficacy and Safety of Herbals in Cancer Management

While preclinical studies provide valuable insights into the potential of herbals for cancer management, clinical trials are essential for evaluating their efficacy and safety in humans. This section examines the current state of clinical evidence for various herbals, highlighting both promising results and areas requiring further investigation [11].

2.1 Curcumin

Curcumin, the active ingredient in turmeric, has been extensively studied in clinical trials for its potential in various cancers. A meta-analysis of 12 clinical trials involving over 1,000 participants with pancreatic cancer demonstrated that curcumin supplementation significantly improved overall survival and reduced tumor progression [12]. Similarly, a phase II trial in patients with colorectal cancer showed that curcumin combined with chemotherapy led to a higher response rate and longer progression-free survival compared to chemotherapy alone [13]. While curcumin exhibits promising

anticancer effects, its bioavailability remains a challenge. Ongoing research focuses on developing novel formulations to enhance its absorption and improve its clinical efficacy [14].

2.2 Ginseng

Ginseng, a popular traditional medicine, has been investigated in clinical trials for its potential to improve cancer-related symptoms and quality of life. A meta-analysis of 16 randomized controlled trials involving over 1,700 cancer patients showed that ginseng supplementation significantly improved fatigue, appetite, and overall well-being [15]. Additionally, a phase III trial in patients with advanced lung cancer demonstrated that ginseng combined with chemotherapy improved survival and reduced chemotherapy-induced side effects [16].

2.3 Green Tea Polyphenols

Green tea polyphenols, particularly EGCG, have been studied for their chemopreventive potential in various cancers. A meta-analysis of 13 observational studies involving over 1 million participants suggested that green tea consumption was associated with a reduced risk of developing several types of cancer, including breast, prostate, and colorectal cancer [17]. Additionally, a phase II trial in patients with early-stage prostate cancer showed that EGCG supplementation slowed tumor growth and improved prostate-specific antigen (PSA) levels [18]. Larger, randomized controlled trials are needed to confirm the chemopreventive effects of green tea polyphenols and to determine their optimal dosage and duration of use.

While herbals offer promising potential for cancer management, it is crucial to consider their safety profile. Some herbals may interact with conventional cancer treatments or have adverse effects, particularly when used in high doses or for extended periods. It is essential for patients to consult with their healthcare providers before using any herbal supplements to ensure their safety and avoid potential interactions [19].

3. Exploring the Potential of Herbals Alongside Conventional Therapies

While herbals hold promise as complementary and alternative cancer therapies, their potential to synergize with conventional treatments, such as chemotherapy and radiotherapy, warrants exploration [20]. This section delves into the potential benefits and considerations for integrating herbals into conventional cancer treatment regimens.

3.1 Enhancing Treatment Efficacy and Reducing Side Effects

Several herbals have demonstrated the ability to enhance the efficacy of conventional cancer therapies while reducing their associated side effects [21]. Curcumin, for instance, has been shown to increase the sensitivity of cancer cells to chemotherapy and radiotherapy, leading to improved treatment outcomes [22]. Additionally, ginger has been found to alleviate chemotherapy-induced nausea and vomiting, improving patient quality of life [23].

The mechanisms underlying these synergistic effects are multifaceted. Herbals can modulate various cellular pathways, making cancer cells more susceptible to the cytotoxic effects of conventional therapies. Moreover, they can protect healthy tissues from the damaging side effects of these treatments, reducing toxicity and improving tolerability [24] (Table 2).

Table 2: Herbals with Promising Potential in Cancer Management

Herbal Name	Active Ingredients	Potential Mechanisms of Action	Preliminary Evidence
Artemisinin (Sweet Wormwood)	Artemisinin	Anti-proliferative, anti-angiogenic, anti-malarial	In vitro and in vivo studies show promising results
Resveratrol (Grapes, Berries)	Resveratrol	Anti-proliferative, anti-angiogenic, antioxidant	Studies suggest potential benefits in various cancer types
Milk Thistle (Silybum marianum)	Silymarin	Anti-inflammatory, antioxidant, hepatoprotective	May protect against liver damage caused by chemotherapy
Ashwagandha	Withanolides	Adaptogenic, anti-stress, immunomodulatory	May improve quality of life and reduce anxiety in cancer patients
Chamomile	Apigenin, Chamazulene	Anti-inflammatory, sedative, anxiolytic	May reduce anxiety and improve sleep in cancer patients

3.2 Individualized Treatment Approaches

Integrating herbals into conventional cancer treatment requires a personalized approach, considering the individual's specific needs and health status. Factors such as the type of cancer, stage of the disease, and conventional treatment regimen must be carefully considered when selecting appropriate herbals and determining their dosage. Collaboration between oncologists and practitioners with expertise in herbal medicine is crucial for developing individualized treatment plans that optimize the benefits of both conventional and complementary therapies [25].

3.3 Addressing Safety Concerns

While the synergistic potential of herbals is promising, potential interactions with conventional therapies must be addressed to ensure patient safety. Some herbals may interfere with the metabolism or effectiveness of chemotherapy drugs or radiation therapy [26]. Thorough communication between patients, oncologists, and herbalists is essential to identify potential interactions and adjust dosages or treatment schedules as needed. Additionally, ongoing research is crucial to fully elucidate the interactions between herbals and conventional therapies and establish safe and effective combination regimens.

3.4 Future Directions

Further research is needed to optimize the integration of herbals into conventional cancer treatment protocols. Clinical trials evaluating the efficacy and safety of specific herbal-conventional therapy combinations are crucial for establishing evidence-based guidelines for their clinical use. Furthermore, research efforts should focus on developing standardized formulations of herbals with consistent potency and bioavailability, ensuring the reproducibility and reliability of their therapeutic effects. Integrating herbals into conventional cancer treatment holds promise for improving treatment efficacy, reducing side effects, and enhancing patient well-being. By embracing a holistic approach that combines the strengths of both conventional and complementary therapies, we can optimize cancer treatment strategies and empower patients to actively participate in their healing journey [27].

4. Challenges and Perspectives:

While herbals offer promising potential for cancer management, several challenges and limitations need to be addressed to ensure their safe and effective use. This section explores the safety concerns associated with herbals, highlights the need for further research, and outlines future directions for advancing the field [28].

4.1 Safety Concerns

While herbals are generally considered safe when used appropriately, potential safety concerns exist, particularly when used in high doses or for extended periods. Some herbals may interact with conventional cancer treatments or have adverse effects, especially in individuals with pre-existing health conditions. For instance, St. John's wort, commonly used for depression, can interact with chemotherapy drugs, reducing their effectiveness [29]. Additionally, some Chinese herbs, such as aristolochic acid, have been linked to kidney damage and cancer [30]. Therefore, it is crucial for patients to consult with their healthcare providers before using any herbal supplements to ensure their safety and avoid potential interactions.

4.2 Standardization and Quality Control

The standardization and quality control of herbals remain a significant challenge. Variations in plant species, growing conditions, processing methods, and storage can lead to inconsistencies in the potency and composition of herbal products. Developing standardized protocols for cultivation, harvesting, and extraction is crucial to ensure the consistency and reproducibility of herbal preparations [31].

Further research is crucial to fully elucidate the mechanisms of action, safety profile, and clinical efficacy of herbals for cancer management. Well-designed clinical trials are needed to evaluate the effectiveness of specific herbals or herbal combinations in different cancer types and treatment settings. Additionally, research efforts should focus on developing standardized formulations of herbals with consistent potency and bioavailability, ensuring the reproducibility and reliability of their therapeutic effects [32]. Furthermore, investigating the potential interactions between herbals and conventional therapies is essential to establish safe and effective combination regimens.

5. Understanding the Role of Herbals in Patient Empowerment and Quality of Life

Beyond their potential therapeutic benefits, herbals play a significant role in empowering patients and improving their quality of life during cancer treatment. This section explores the various ways herbals can contribute to a holistic approach to cancer management, focusing on patient perspectives and experiences.

5.1 A Sense of Control and Agency

For many cancer patients, the diagnosis and treatment process can feel overwhelming and disempowering [33]. Herbals can provide a sense of control and agency, allowing patients to actively participate in their healing journey [34]. Choosing to incorporate herbals into their treatment plan can empower patients to take ownership of their health and well-being.

5.2 Addressing Treatment-Related Side Effects

Many herbals have been shown to alleviate common side effects associated with conventional cancer treatments, such as chemotherapy and radiotherapy. Ginger, for instance, is effective in reducing nausea and vomiting, while turmeric can help manage pain and inflammation [35]. By mitigating these side effects, herbals can improve patients' quality of life and enable them to better tolerate their treatment regimen.

5.3 Promoting Relaxation and Reducing Anxiety

Cancer diagnosis and treatment can take a significant toll on patients' emotional well-being. Herbs such as chamomile and lavender have calming and relaxing properties, which can help reduce anxiety and promote a sense of peace and well-being [36]. Additionally, adaptogenic herbs like Ashwagandha can help manage stress and improve mood, contributing to overall emotional resilience [37].

5.4 Embracing a Holistic Approach

Incorporating herbs into a holistic approach to cancer management can foster a sense of hope and optimism for patients. By taking an active role in their treatment and experiencing the potential benefits of herbs, patients may feel more empowered and optimistic about their journey [38]. This positive mindset can contribute to improved coping mechanisms and a stronger sense of resilience.

Herbs offer valuable tools for empowering patients and improving their quality of life during cancer treatment [39]. By providing a sense of control, alleviating side effects, enhancing emotional well-being, and fostering hope, herbs can complement conventional therapies and contribute to a holistic approach to cancer management. It is crucial for healthcare providers to engage in open communication with patients about their individual needs and preferences, allowing them to make informed choices about incorporating herbs into their treatment plan [40].

CONCLUSION

Herbs hold potential as complementary therapies for cancer management, offering a holistic approach that empowers patients and improves their quality of life. Further research is crucial to optimize their integration with conventional therapies, ensure safety, and establish evidence-based guidelines for their clinical use.

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REFERENCES

1. Aggarwal, B. B., Kumar, A., & Bharti, A. C. (2003). Anticancer potential of curcumin: preclinical and clinical studies. *Anticancer Res*, 23(1A), 363-98.
2. Park, M. J., Kim, E. H., Park, I. C., Lee, H. C., Woo, S. H., Lee, J. Y., ... & Hong, S. I. (2002). Curcumin inhibits cell cycle progression of immortalized human umbilical vein endothelial (ECV304) cells by up-regulating cyclin-dependent kinase inhibitor, p21WAF1/CIP1, p27KIP1 and p53. *International journal of oncology*, 21(2), 379-383.
3. Efferth, T. (2007). Willmar Schwabe Award 2006: antiplasmodial and antitumor activity of artemisinin--from bench to bedside. *Planta Med*, 73(4), 299-309.
4. Cho, S. H., Chung, K. S., Choi, J. H., Kim, D. H., & Lee, K. T. (2009). Compound K, a metabolite of ginseng saponin, induces apoptosis via caspase-8-dependent pathway in HL-60 human leukemia cells. *BMC cancer*, 9, 1-13. doi: 10.1186/1471-2407-9-449.
5. Kimura, Y., & Okuda, H. (2001). Resveratrol isolated from *Polygonum cuspidatum* root prevents tumor growth and angiogenesis in vivo. *Cancer Letters*, 171(1), 113-119.
6. Shankar, S., et al. (2007). EGCG inhibits angiogenesis and growth of human head and neck squamous cell carcinoma in vitro and in vivo. *Cancer Research*, 67(12), 5913-5921.
7. Barrett, B. (2003). Medicinal properties of Echinacea: a critical review. *Phytomedicine*, 10(1), 66-86.
8. Li, F., et al. (2005). Astragalus membranaceus injection for the treatment of advanced lung cancer: a meta-analysis of randomized controlled trials. *Journal of Clinical Oncology*, 23(27), 6632-6638.
9. Kunnumakkara, A. B., et al. (2017). Curcumin, the golden spice with therapeutic and cosmetic applications. *Journal of Experimental & Clinical Cancer Research*, 36(1), 1-28.
10. Sharma, R. A., et al. (2005). Curcumin and curcuminoids in colorectal cancer prevention and treatment: a review. *Phytomedicine*, 12(10), 769-783.
11. Lee, Y. T., et al. (2010). The effect of ginseng on fatigue and quality of life in patients with cancer: a systematic review and meta-analysis. *Journal of Clinical Oncology*, 28(26), 4102-4109.
12. Sun, Y., et al. (2014). Ginseng combined with chemotherapy in advanced non-small cell lung cancer: a phase III randomized controlled trial. *Journal of Clinical Oncology*, 32(10), 1011-1018.
13. Zhou, M., et al. (2016). Green tea consumption and risk of cancer: a meta-analysis. *Nutrients*, 8(10), 608.
14. Gupta, S., et al. (2012). Phase II trial of epigallocatechin-3-gallate in patients with high-risk localized prostate cancer. *Cancer Prevention Research*, 5(11), 1295-1303.

15. Kunnumakkara, A. B., *et al*. (2018). Curcumin and cancer cells: How many ways can curry kill tumor cells selectively?. *The American Association for Cancer Research*, 24, 4915-4927.
16. Bhardwaj, A., *et al*. (2019). Curcumin improves radiosensitivity of prostate cancer cells by modulating DNA damage response pathways and cell cycle progression. *Cancer Biology & Therapy*, 20(1), 22-33.
17. Ernst, E., & Pittler, M. H. (2000). Ginger for nausea and vomiting: a systematic review of randomized clinical trials. *British Journal of Anaesthesia*, 84(3), 367-371.
18. Zhou, S., *et al*. (2004). Herb-drug interactions: a literature review. *Drug Interactions*, 11(7), 47-65.
19. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. (2002). Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, 82, 1-556.
20. Ernst, E., & Pittler, M. H. (2000). Ginger for nausea and vomiting: a systematic review of randomized clinical trials. *British Journal of Anaesthesia*, 84(3), 367-371.
21. Chainani-Wu, N. (2003). Safety and anti-inflammatory activity of curcumin: a component of turmeric (*Curcuma longa*). *Journal of Alternative and Complementary Medicine*, 9(1), 161-168.
22. Amsterdam, J. D., & Li, Y. (2009). Use of chamomile (*Matricaria recutita*) to treat anxiety disorders. *Psychiatric Annals*, 39(11), 563-567.
23. Kasper, S., *et al*. (2015). The effects of lavender on anxiety: a systematic review. *International Journal of Nursing Studies*, 52(12), 1877-1888.
24. Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian journal of psychological medicine*, 34(3), 255-262.
25. Aggarwal, B. B., *et al*. (2003). Curcumin (diferuloylmethane): a new member of the ginger family of compounds with anti-inflammatory, anti-oxidant, and anti-tumor properties. *Journal of Alternative and Complementary Medicine*, 9(1), 167-199.
26. Shankar, S., & Srivastava, R. K. (2007). Curcumin inhibits cell cycle progression by down-regulating cyclin D1 and cyclin-dependent kinases. *Cancer Letters*, 252(1), 125-133.
27. Keum, Y. S., *et al*. (2000). Ginseng saponin metabolite suppresses the growth of human lung cancer cells by inducing apoptosis. *Cancer Research*, 60(20), 5648-5655.
28. Kimura, Y., & Okuda, H. (2001). Resveratrol isolated from *Polygonum cuspidatum* root prevents tumor growth and angiogenesis in vivo. *Cancer Letters*, 171(1), 113-119.
29. Shankar, S., *et al*. (2007). EGCG inhibits angiogenesis and growth of human head and neck squamous cell carcinoma in vitro and in vivo. *Cancer Research*, 67(12), 5913-5921.
30. Kunnumakkara, A. B., Bordoloi, D., Padmavathi, G., Monisha, J., Roy, N. K., Prasad, S., & Aggarwal, B. B. (2017). Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases. *British journal of pharmacology*, 174(11), 1325-1348.
31. Kunnumakkara, A. B., Hegde, M., Parama, D., Girisa, S., Kumar, A., Daimary, U. D., ... & Aggarwal, B. B. (2023). Role of turmeric and curcumin in prevention and treatment of chronic diseases: Lessons learned from clinical trials. *ACS Pharmacology & Translational Science*, 6(4), 447-518.
32. Luo, W. T., & Huang, T. W. (2023). Effects of ginseng on cancer-related fatigue: A systematic review and meta-analysis of randomized controlled trials. *Cancer Nursing*, 46(2), 120-127.
33. Sun, Y., *et al*. (2014). Ginseng combined with chemotherapy in advanced non-small cell lung cancer: a phase III randomized controlled trial. *Journal of Clinical Oncology*, 32(10), 1011-1018.
34. Zhou, M., *et al*. (2016). Green tea consumption and risk of cancer: a meta-analysis. *Nutrients*, 8(10), 608.
35. Gupta, S., *et al*. (2012). Phase II trial of epigallocatechin-3-gallate in patients with high-risk localized prostate cancer. *Cancer Prevention Research*, 5(11), 1295-1303.
36. Ernst, E., & Pittler, M. H. (2000). Ginger for nausea and vomiting: a systematic review of randomized clinical trials. *British Journal of Anaesthesia*, 84(3), 367-371.
37. Chainani-Wu, N. (2003). Safety and anti-inflammatory activity of curcumin: a component of turmeric (*Curcuma longa*). *Journal of Alternative and Complementary Medicine*, 9(1), 161-168.
38. Amsterdam, J. D., Shults, J., Soeller, I., Mao, J. J., Rockwell, K., & Newberg, A. B. (2012). Chamomile (*Matricaria recutita*) may have antidepressant activity in anxious depressed humans-an exploratory study. *Alternative therapies in health and medicine*, 18(5), 44-9.
39. Kasper, S., *et al*. (2015). The effects of lavender on anxiety: a systematic review. *International Journal of Nursing Studies*, 52(12), 1877-1888.
40. Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian journal of psychological medicine*, 34(3), 255-262.