Beyond chemotherapy: The therapeutic promise of plant-derived compounds in cancer treatment



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Abstract

Cancer is the second leading cause of death worldwide. Despite significant advancements in treatment and control, there remain critical deficiencies and opportunities for improvement. Chemotherapy often comes with undesirable side effects, prompting interest in natural therapies, particularly plant-derived products, which may help mitigate these adverse effects. Currently, a limited number of plant products are utilized in cancer treatment, yet numerous others exhibit promising anticancer properties in vitro but have not yet been evaluated in humans. Further research is essential to assess the efficacy of these plant compounds for cancer treatment in clinical settings. This review will focus on various plant-derived chemical compounds that have recently shown potential as anticancer agents, detailing their mechanisms of action and the promise they hold for future therapeutic development.

Keywords: Phytoconstituents, Cancer, Natural Compounds

1. Introduction

Phytoconstituents, derived from plants, are increasingly being explored as adjuncts or alternatives in cancer treatment. Their potential benefits include enhancing the efficacy of conventional therapies, reducing side effects, and improving patients' quality of life.

Emerging cancer treatment strategies are shifting from solely cytotoxic approaches to more holistic methods that focus on managing cancer physiopathology. These integrative approaches aim not just to eradicate affected cells but to control the overall cancer phenotype. Numerous plant-derived products have demonstrated promise in anticancer therapies, with efforts made to characterize the effectiveness of individual constituents isolated from natural sources as chemopreventive agents.

In this context, Ayurveda, with its holistic treatment philosophy, offers a valuable alternative to isolated plant compounds. This ancient system of medicine incorporates a variety of herbs into treatment regimens for numerous diseases. The foundational texts of Ayurveda, such as the Charaka Samhita and Sushruta Samhita, dating back to approximately 1000 B.C., document the use of plant products in disease treatment. These texts describe cancer as either inflammatory or non-inflammatory swellings, referred to as Granthi (minor neoplasm) or Arbuda (major neoplasm) (1).

Phytoconstituents used in cancer treatment offer several advantages over conventional therapies, such as chemotherapy and radiation, due to their unique mechanisms, generally lower toxicity, and multi-targeted effects (Depicted in figure 1).

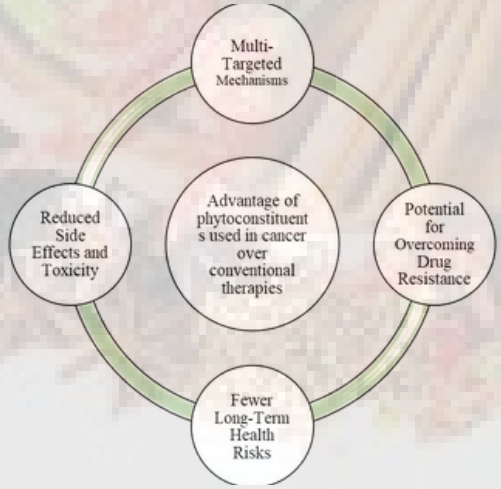

Figure 1. Advantage of phytoconstituents used in cancer

For example, *Tinospora cordifolia* is recognized for its anti-inflammatory and anticancer properties. In vitro studies have shown its potential against cancer cells. Similarly, *Andrographis paniculata* extracts exhibit anti-oncogenic effects, while oral administration of *Centella asiatica* extracts has been reported to slow tumor development and extend lifespan in tumor-bearing mice. Turmeric has also demonstrated the ability to inhibit tumor cell invasion and metastasis in vitro. Moreover, *Phyllanthus amarus* extracts significantly increased lifespan and reduced tumor size in models of Dalton's lymphoma ascites and Ehrlich ascites carcinoma (2).

Table 1. Anticancer activities of major chemical constituents of medicinal plants

Name of Plant	Major Chemical Constituents	*In Vivo* Effects	Ref
Tinospora cordifolia	20 β-hydroxyecdysterone, Cordioside, Columbin	*Tinospora cordifolia,* containing compounds like 20 β-hydroxyecdysterone, cordioside, and columbin, has demonstrated significant tumor regression and increased survival in mice with Ehrlich ascites carcinoma	(3)
Andrographis paniculata	Andrographolide	*Andrographis paniculata,* with its active compound andrographolide, has been shown to regress tumors in mice	(4)
Curcuma longa	Curcumin	*Curcuma longa*, containing curcumin, reduces VEGF and bFGF-mediated angiogenesis and prevents colon and gastric cancers in rodent models. These effects underscore curcumin's potential as a cancer-preventive agent	(5,6)
Phyllanthus amarus	Nirtetralin, niranthrin, phyllanthin, phyltetralin	*Phyllanthus amarus,* containing compounds like nirtetralin, niranthrin,phyllanthin, and phyltetralin, increases lifespan and reduces tumor size in mice with Dalton's lymphoma ascites (DLA) and Ehrlich ascites carcinoma (EAC). Additionally, it decreases N-nitrosodiethylamine (NDEA)-induced tumor incidence and exhibits anti-angiogenic effects in mice with Lewis lung carcinoma	(7-9)
Mappia foetida	Camptothecin	Induces partial or complete remission of breast carcinoma in the xenograft model system	(10,11)
Withania somnifera	Withaferin A	*Withania somnifera*, particularly withaferin A, is highly effective in producing over 50% tumor regression in Ehrlich ascites carcinoma (EAC) and Ehrlich ascitic tumor (EAT) models. Additionally, it enhances Th1 cytokine expression and increases T cell and CD40 expression in the EAT mouse tumor model, indicating its potential to boost immune response against tumors	(12)
Cedrus deodara	Lignans, Wikstromol, Matairesinol and dibenzyl butyrolactol	*Cedrus deodara,* containing lignans like wikstromol, matairesinol, and dibenzyl butyrolactol, demonstrates tumor regression in murine models	(13)
Boswellia serrata	Triterpenic acids	*Boswellia serrata,* rich in triterpenic acids, has shown effectiveness against brain tumors. This highlights its potential therapeutic application in treating neurological cancers	(14)

2. Current status of Phytoconstituents in cancer

2.1. Research and development

- **Active compounds:** Many plant-based compounds, such as curcumin (from turmeric), resveratrol (from grapes), and various alkaloids (like paclitaxel from the yew tree), are under investigation for their anticancer properties (15).
- **Mechanisms of action:** These compounds may work through various mechanisms, including apoptosis induction, anti-inflammatory effects, and inhibition of tumor angiogenesis.

2.2. Clinical trials

- **Combination therapies:** Clinical trials are increasingly testing combinations of Phytoconstituents with standard treatments (chemotherapy, radiotherapy) to assess synergistic effects (16).
- **Patient-centric studies:** Trials focus on quality of life improvements, symptom management, and survivorship outcomes (17).

2.3. Regulatory approval

- **Standardization challenges:** One of the significant hurdles is the lack of standardization and quality control in the production of phytoconstituents, making it difficult to ensure consistent therapeutic effects (18).
- **Regulatory framework:** Some phytoconstituents have gained approval in specific regions (e.g., Europe) for certain indications, but many remain classified as dietary supplements rather than drugs (19).
  1. The European Medicines Agency (EMA) has a specific pathway for herbal medicinal products under the Committee on Herbal Medicinal Products (HMPC).
  2. The FDA regulates many phytoconstituents as dietary supplements rather than drugs, which requires that they meet safety standards but do not need to demonstrate efficacy.
  3. The WHO has issued guidelines to support regulatory bodies in developing standards for traditional medicines, though specific regulations vary widely across countries.
  4. Traditional medicine systems like Ayurveda are recognized within national frameworks, with specific regulatory bodies overseeing herbal medicines.
  5. Kampo medicines, which are herbal formulations based on traditional Japanese medicine, are regulated as pharmaceuticals. Kampo products must meet strict quality and safety standards, and specific indications are approved based on clinical efficacy data.

2.4. Integrative oncology

- **Holistic approach:** There's a growing trend in integrative oncology that combines conventional cancer treatments with complementary therapies, including Phytoconstituents, focusing on the overall well-being of patients (20).

3. Future directions

- **Personalized medicine:** Research is moving towards understanding how individual genetic and metabolic profiles can affect the efficacy of phytoconstituents, aiming for more personalized cancer treatment strategies.
- **Ongoing studies:** New studies continue to emerge, examining the potential of various plants and their extracts in different cancer types.

4. Conclusion

This review revelled that phytoconstituents and its products possess antitumor activity with lesser side effect. It has to required isolation of plants constituents that may lead to discovery of novel anticancer agents.

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