Plant Products and Their Use in Cancer Therapy

Dr. K. Narendra Kumar reddy[1], Dr. P. Swetha[2], Dr. Harika Patnala[3], Dr. P. Devi Guna Sireesha[4]*, Dr. A. Ravi Kumar[4]

[1]Professor and Dean, Vikas Group of Institutions, Nunna, Vijayawada, Andhra Pradesh, India.

[2]Assistant professor, KVSR sidhartha college of pharmaceutical sciences, Vijayawada, Andhra Pradesh, India.

[3]MLR Institute of Technology, Dundigal, Laxman Reddy Avenue, Hyderabad, Telangana- 500043, India.

[4]Professor and HoD, Dept. of Pharmacognosy, Nimra College of Pharmacy, Ibrahimpatnam, Vijayawada, Andhra Pradesh, India.

[4]*Associate Professor and HoD, Dept. of Pharmacology, Nimra College of Pharmacy, Ibrahimpatnam, Vijayawada, Andhra Pradesh, India.

Coresponding author:

Dr. P. Devi Guna Sireesha,

Associate Professor and HoD,

Dept. of Pharmacology,

Nimra College of Pharmacy,

Ibrahimpatnam,

Vijayawada-521456,

Andhra Pradesh, India.

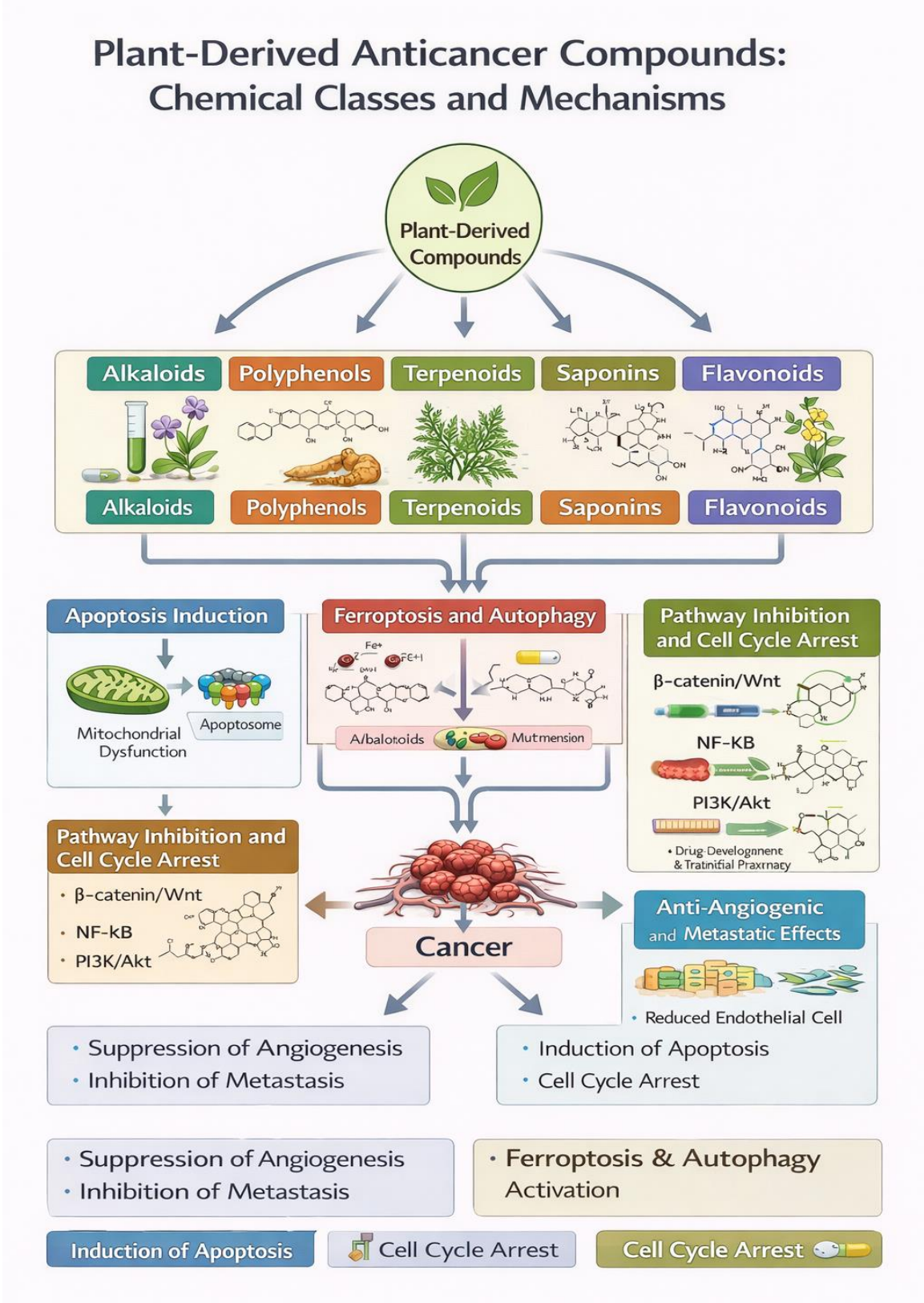
Abstract

Cancer, a leading global health challenge with over 2 million projected U.S. cases in 2025 primarily affecting breast, lung, prostate, and colorectal tissues, drives uncontrolled cell proliferation through dysregulated pathways. Plant-derived compounds including FDA-approved taxanes, vinca alkaloids, camptothecins, and emerging polyphenols (curcumin, resveratrol, EGCG), alkaloids, and terpenes exhibit multifaceted anticancer activity via apoptosis induction, ferroptosis, autophagy, cell cycle arrest, anti-angiogenesis, and metastasis inhibition targeting Wnt/β-catenin, PI3K/Akt, and NF-κB signaling. Polyherbal formulations from Traditional Chinese Medicine (Jianpi Bushen) and Ayurveda (Kanchnar guggulu, Habb-e-Ustukhuddus) demonstrate clinical superiority in phase III trials, enhancing chemotherapy completion, reducing toxicity and improving quality of life through synergistic multi-target effects validated by reverse pharmacology. 2025 trends integrate herbal therapies with precision oncology, AI-driven personalization, CAR-T immunotherapy, bispecific antibodies, radiopharmaceuticals and multi-omics profiling, fostering evidence-based integrative frameworks that mitigate resistance and optimize outcomes. This comprehensive synthesis bridges traditional wisdom with modern science, highlighting herbal oncology's transformative potential.

Keywords

Herbal anticancer agents, Polyherbal formulations, Phytochemical mechanisms, Precision medicine trends, Apoptosis ferroptosis

Graphical Abstract



Introduction

Cancer represents a diverse group of diseases characterized by the uncontrolled growth and proliferation of abnormal cells that can invade other tissues and spread throughout the body.[1] It occurs when normal cellular mechanisms for controlling growth and division become dysregulated, allowing cells to divide indefinitely and evade programmed cell death. The disease stands as a leading cause of mortality globally, accounting for nearly 10 million deaths annually.[2]

In 2025, the United States is projected to diagnose approximately 2,041,910 new cancer cases with an estimated 618,120 deaths. The most prevalent malignancies in descending order include breast cancer, prostate cancer, lung and bronchus cancer, colorectal cancer, melanoma, bladder cancer, and kidney cancer. Among men, prostate, lung, and colorectal cancers represent approximately 48% of new diagnoses, while in women, breast, lung, and colorectal cancers account for roughly 51% of all new cancer cases.[3] Globally, breast, lung, colorectal, prostate, stomach, and cervical cancers constitute the predominant forms of malignancy.

Cancer remains a leading cause of global morbidity and mortality, despite significant advances in diagnosis and therapeutic interventions. Conventional anticancer therapies such as chemotherapy, radiotherapy, and targeted agents are frequently associated with dose-limiting toxicities, drug resistance, and limited selectivity toward malignant cells. These limitations have intensified the search for safer, multi-targeted, and biologically compatible alternatives. In this context, plant-derived anticancer compounds have gained substantial attention due to their structural diversity, pleiotropic mechanisms of action, and long-standing use in traditional medicine systems.[3]

Plants represent an valuable reservoir of bioactive secondary metabolites, including alkaloids, polyphenols, flavonoids, terpenoids, saponins, and quinones, many of which exhibit potent anticancer properties. Several clinically established anticancer drugs— such as paclitaxel, vincristine, vinblastine, camptothecin derivatives and etoposide— originate from plant sources, underscoring the translational relevance of phytochemicals in oncology. Unlike single-target synthetic agents, plant-derived compounds often modulate multiple signaling pathways

simultaneously, thereby interfering with cancer initiation, progression, angiogenesis, metastasis, and therapy resistance.[4]

Mechanistically, phytochemicals exert anticancer effects through diverse molecular pathways, including induction of programmed cell death (apoptosis, ferroptosis, and autophagy), inhibition of oncogenic signaling cascades (PI3K/Akt, Wnt/β-catenin, NF-κB, and MAPK), regulation of cell cycle checkpoints, suppression of angiogenesis, and reversal of epithelial–mesenchymal transition. Their ability to selectively target cancer cells while sparing normal tissues makes them attractive candidates for chemoprevention, monotherapy, or combination therapy alongside conventional anticancer agents.[5]

Furthermore, advances in molecular biology, systems pharmacology, and nanotechnology have enhanced the understanding of phytochemical mechanisms and improved their bioavailability, stability, and therapeutic index. Polyherbal formulations and plant-derived nanoformulations are emerging as promising strategies to overcome pharmacokinetic limitations and enhance anticancer efficacy. Consequently, systematic classification of plant-derived anticancer compounds based on their chemical classes and mechanisms of action is essential for rational drug discovery and development.[6]

Plant-Derived Anticancer Compounds: Chemical Classes and Mechanisms

Plant-derived products demonstrate remarkable potential as anticancer agents due to their structural diversity and bioactive properties.[4] The therapeutic efficacy of these botanical compounds stems from multiple chemical classes and their sophisticated molecular mechanisms of action.

Alkaloids and Monoterpenes

Several FDA-approved anticancer agents originate from plant sources, including vinca alkaloids (vincristine, vinblastine), taxanes (paclitaxel from Pacific yew, docetaxel), and camptothecin derivatives.[5] These alkaloid-based compounds function through distinct mechanisms such as topoisomerase inhibition and microtubule destabilization. Paclitaxel, derived from Taxus brevifolia, exhibits efficacy against breast, ovarian, lung cancers and Kaposi's sarcoma.[7]

Camptothecin, extracted from the Chinese tree Camptotheca acuminata, led to the development of topotecan and irinotecan for treating ovarian, lung, and colorectal malignancies.[6]

Polyphenols and Flavonoids

Polyphenolic compounds represent the most extensively researched plant metabolites in cancer therapy. Curcumin from turmeric, resveratrol from grapes, ellagic acid from pomegranate, and epigallocatechin gallate (EGCG) from green tea have demonstrated promising anticancer potential through multiple signaling pathways.[8][9][10]

Ellagic acid, a polyphenol from pomegranate, functions by inhibiting tumor cell migration and invasion through the extracellular matrix while preventing angiogenesis, demonstrating activity against colorectal, breast, prostate, lung, bladder, and ovarian cancer cell lines. Flavonoids, representing the most abundant polyphenols in aromatic and medicinal plants, display therapeutic effects through nutraceutical applications for cancer prevention. Hesperetin, naringenin, and apigenin exemplify flavonoids with documented anticancer potential.

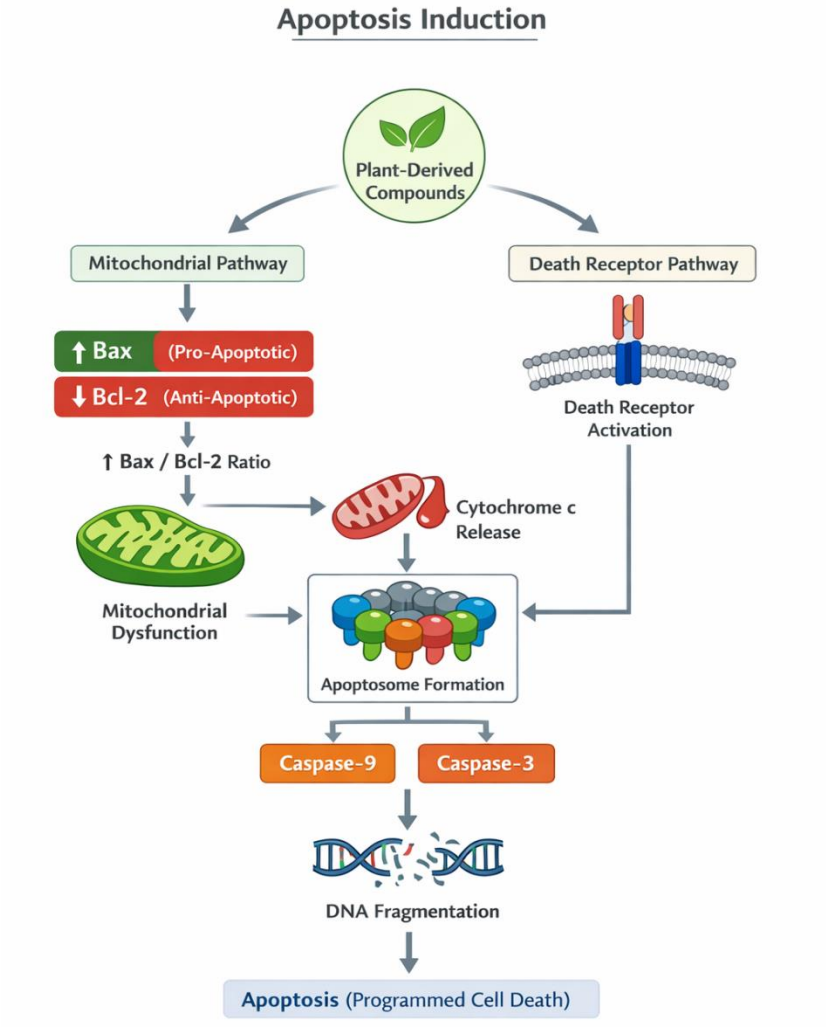
Terpenes and Other Bioactive Compounds

Hinokitiol (β-thujaplicin), a diterpene from Chamaecyparis obtusa, and mahanine, an alkaloid compound, demonstrate efficacy against multiple carcinoma cell types. Rosemary (Rosmarinus officinalis) extract serves as a potent antioxidant and anti-inflammatory agent with anticancer properties attributed to diterpenes including carnosic acid, carnosol, and rosmanol that modulate key signaling pathways.

Mechanisms of Action in Cancer Cell Death

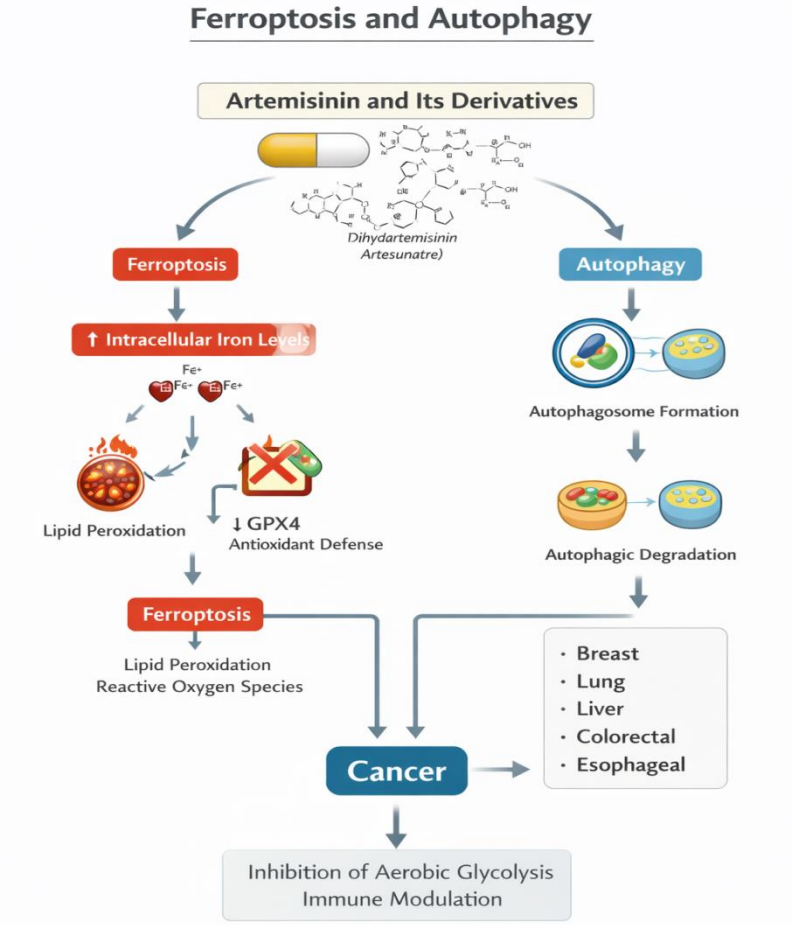
Apoptosis Induction

Plant-derived compounds predominantly trigger apoptosis through mitochondrial and death receptor pathways. Polyherbal formulations induce pro-apoptotic markers including upregulation of Bax (pro-apoptotic protein) and downregulation of Bcl-2 (anti-apoptotic protein), resulting in elevated Bax/Bcl-2 ratios that lead to mitochondrial membrane depolarization and cytochrome c release.[11] This cascade activates caspase-3 and caspase-9, culminating in DNA fragmentation and programmed cell death.[12]



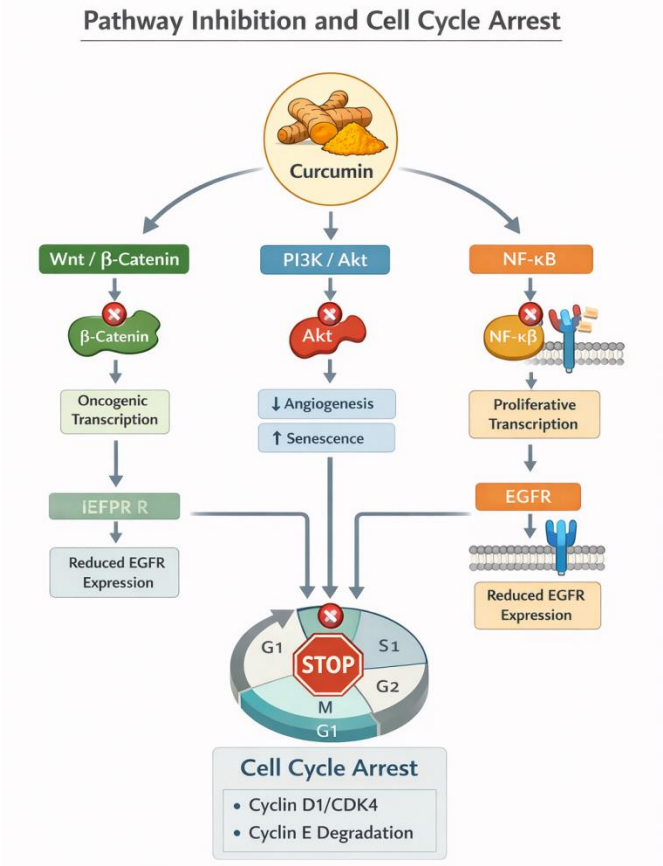
Ferroptosis and Autophagy

Artemisinin and its derivatives (dihydroartemisinin, artesunate, artemether) represent emerging therapeutic agents that operate through multiple cell death mechanisms. These compounds induce ferroptosis by increasing intracellular iron levels and inhibiting the GPX4-dependent antioxidant defense system.[13] Ferroptosis represents an iron-dependent, non-apoptotic cell death pathway characterized by lipid peroxidation and reactive oxygen species accumulation. Additionally, artemisinin derivatives activate autophagy pathways, suppressing aerobic glycolysis and modulating immune responses across various cancer types including breast, lung, liver, colorectal, and esophageal malignancies.[14]



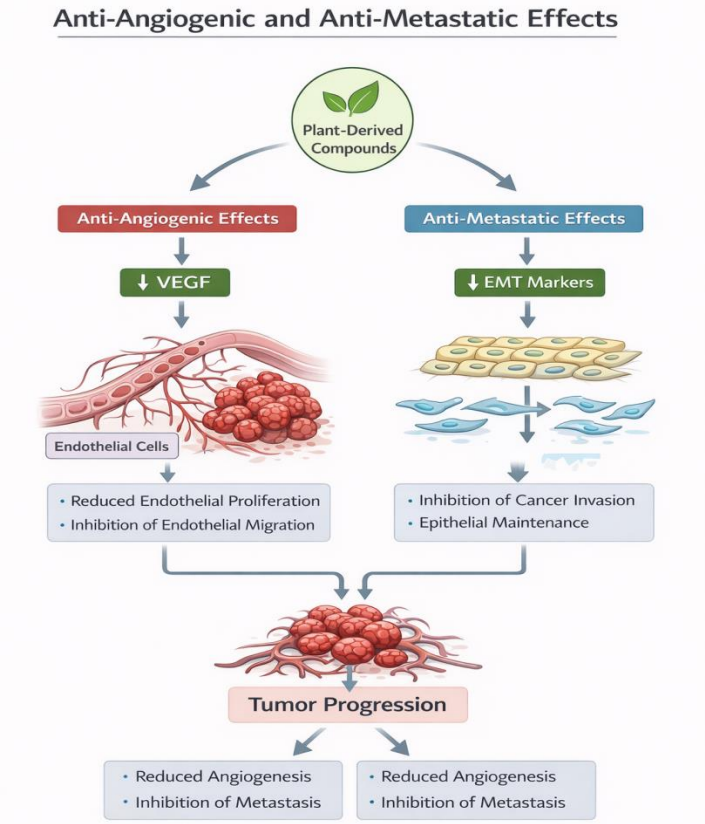
Pathway Inhibition and Cell Cycle Arrest

Curcumin blocks multiple oncogenic signaling cascades. The compound inhibits β-catenin activity in the Wnt/β-catenin pathway, suppresses the PI3K/Akt pathway (preventing angiogenesis and promoting senescence), and inhibits NF-κB phosphorylation, thereby blocking proliferative transcription processes. Curcumin simultaneously reduces epidermal growth factor receptor (EGFR) protein expression on cell membranes, diminishing sensitivity to growth factor ligands. These mechanisms collectively result in G1 phase cell cycle arrest through cyclin D1/CDK4 complex blockade and cyclin E degradation.[15]



Anti-angiogenic and Anti-metastatic Effects

Plant compounds suppress tumor progression through inhibition of neovascular formation and metastatic dissemination. Multiple phytochemicals reduce vascular endothelial growth factor (VEGF) expression, inhibit endothelial cell proliferation and migration, and suppress cancer cell invasion through downregulation of epithelial-mesenchymal transition markers while promoting epithelial phenotypes.[12]



Clinical Translation and Reverse Pharmacology

Modern oncological research validates traditional remedies through reverse pharmacology—systematically investigating mechanisms by which established traditional formulations exert their effects.[16] This translational approach bridges traditional knowledge with contemporary biomedical science, generating evidence-based integrative strategies through:

- Preclinical studies elucidating molecular mechanisms
- Rigorous randomized controlled clinical trials
- Pharmacokinetic and pharmacodynamic profiling
- Integration with genomic and imaging biomarkers

Drug-Herb Interactions and Safety

Cancer patients increasingly utilize herbal products for symptom control and immune enhancement, creating potential for herb-drug interactions with conventional chemotherapy agents. While herbal supplements like Echinacea show no documented interaction with

chemotherapy agents in major databases, many herbal products lack comprehensive interaction data, necessitating careful oncologist and pharmacist assessment of frequency and dosage. Approximately 65.5% of cancer patients express concerns about herbal product safety during chemotherapy.[17]

Conclusion

Plant-based anticancer agents represent a rich, evidence-supported therapeutic reservoir demonstrating remarkable potential in modern cancer management. From FDA-approved plant-derived chemotherapy agents to emerging nanoformulations enhancing traditional herbal bioavailability, botanical compounds function through sophisticated mechanisms including apoptosis induction, ferroptosis, autophagy activation and multi-target signaling pathway modulation. Recent trends emphasizing integrative oncology, precision medicine integration, AI-driven patient stratification and advanced immunotherapy approaches create unprecedented opportunities for synergistic combination strategies maximizing therapeutic efficacy while minimizing adverse effects. Continued bioprospecting, rigorous clinical trials and translational research bridging traditional medical wisdom with modern molecular science will unlock the full therapeutic potential of plant-derived anticancer compounds in personalized cancer care.

References:

1. Cragg, G. M., & Newman, D. J. (2021). Plant-derived anticancer compounds as new perspectives in drug discovery. Frontiers in Pharmacology, 12, 7922180.

2. da Silva, F. M., et al. (2025). Natural anticancer agents: Prospection of medicinal and aromatic plants. PMC. https://pmc.ncbi.nlm.nih.gov/articles/PMC12011705/ [12]Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 1981 to 2019. *J Nat Prod.* 2020;83(3):770–803.

3. Cragg, G. M., & Pezzuto, J. M. (2016). Natural products as a vital source for the discovery of cancer chemotherapeutic and chemopreventive agents. *Medical Principles and Practice, 25*(Suppl. 2), 41–59.

4. Greenwell, M., & Rahman, P. K. S. M. (2015). Medicinal plants: Their use in anticancer treatment. *International Journal of Pharmaceutical Sciences and Research, 6*(10), 4103–4112.

5. Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly four decades from 1981 to 2019. *Journal of Natural Products, 83*(3), 770–803.

6. Pan, S. Y., Zhou, S. F., Gao, S. H., Yu, Z. L., Zhang, S. F., Tang, M. K., Sun, J. N., Ma, D. L., Han, Y. F., Fong, W. F., & Ko, K. M. (2013). New perspectives on how to discover drugs from herbal medicines. *Evidence-Based Complementary and Alternative Medicine, 2013*, Article 627375.

7. Khan, M. A., Khan, S., Ahmad, A., Rasheed, S., Zahra, S. S., Khan, M. S., & Khan, M. I. (2023). A polyherbal formulation Habb-e-Ustukhuddus induces apoptosis in lung and breast cancer cell lines. *Journal of Ethnopharmacology, 321*, 116844.

8. Li, J., Wang, Y., Zhang, H., Liu, X., & Chen, Z. (2025). Nanoparticle-based delivery systems for phytochemicals in cancer therapy. *Drug Development and Industrial Pharmacy*.

9. Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2021). Improving curcumin bioavailability: Current strategies and future perspectives. *Molecular Pharmaceutics, 18*(6), 2180–2195.

10. Binaytara Foundation. (2025). *Top oncology innovations that shaped the first half of 2025*. https://binaytara.org/cancernews/article/top-oncology-innovations-that-shaped-the-first-half-of-2025

11. Patel, R., Sharma, P., Mehta, R., & Joshi, M. (2025). A review on integrative approaches in oncology: Bridging ayurvedic and modern medicine. *Frontiers in Natural Products, 2*, Article 1635197.

12. Efferth, T. (2024). Artemisinin and its derivatives as potential anticancer agents: A mechanistic review. *International Journal of Molecular Sciences, 25*(4), 1987.

13. Gupta, S. C., Prasad, S., Tyagi, A. K., Kunnumakkara, A. B., & Aggarwal, B. B. (2024). Curcumin administration routes in breast cancer treatment. *Cancers, 16*(2), 415.

14. Singh, R., Meena, J., Kaur, R., & Sharma, A. (2025). Incredible use of plant-derived bioactives as anticancer agents. *RSC Advances, 15*, 11234–11258.

15. Aggarwal, B. B., & Shishodia, S. (2006). Molecular targets of dietary agents for prevention and therapy of cancer. *Biochemical Pharmacology, 71*(10), 1397–1421.

16. Fang, J., Seki, T., & Maeda, H. (2009). Therapeutic strategies by modulating oxygen stress in cancer and inflammation. *Advanced Drug Delivery Reviews, 61*(4), 290–302.

17. Wang, H., Khor, T. O., Shu, L., Su, Z. Y., Fuentes, F., Lee, J. H., & Kong, A. N. (2012). Plants versus cancer: A review on natural phytochemicals in preventing and treating cancers and their druggability. *Anti-Cancer Agents in Medicinal Chemistry, 12*(10), 1281–1305.