SJIF Impact Factor (2025): 8.688| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 10 | Issue: 10 | October 2025 - Peer Reviewed Journal

ANTI-CANCER PHYTOCHEMICALS: PLANT-DERIVED COMPOUNDS IN CANCER THERAPY

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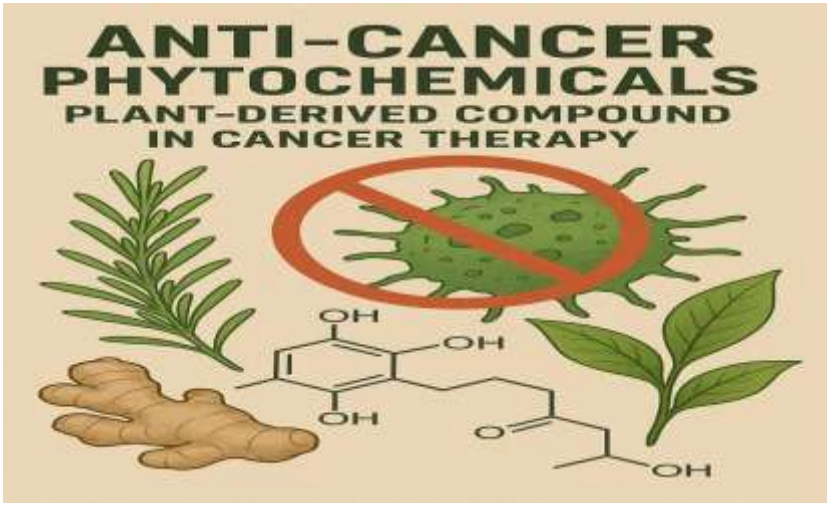
ABSTRACT
Cancer remains a leading cause of mortality worldwide, necessitating the exploration of novel therapeutic avenues. Phytochemicals, naturally occurring compounds in plants, have garnered significant attention for their potential anticancer properties. These bioactive molecules, including flavonoids, alkaloids, terpenoids, and phenolic acids, exhibit a range of mechanisms such as antioxidant activity, modulation of cell signaling pathways, induction of apoptosis, inhibition of angiogenesis, and regulation of epigenetic modifications. This review delves into the molecular mechanisms underlying the anticancer effects of various plant-derived compounds, highlighting their roles in targeting specific cancer-related pathways and their potential integration into existing cancer therapies. Furthermore, challenges related to the bioavailability, toxicity, and clinical application of these phytochemicals are discussed, alongside strategies to enhance their efficacy and safety in cancer treatment. Emerging trends in nanotechnology, combinatorial therapy, and molecular modeling are also highlighted to guide future research and therapeutic development.

1. INTRODUCTION

Cancer is characterized by uncontrolled cell proliferation, invasion of surrounding tissues, and potential metastasis. Traditional cancer treatments, including chemotherapy, radiotherapy, and surgery, have limitations such as toxicity, drug resistance, and relapse. Natural products, particularly plant-derived compounds or phytochemicals, have emerged as promising candidates for cancer therapy due to their diverse chemical structures and mechanisms of action. Historically, plant-derived drugs such as vincristine, vinblastine, paclitaxel, and etoposide have revolutionized cancer treatment, highlighting the potential of phytochemicals as anticancer agents.



2. MECHANISMS OF ACTION OF PHYTOCHEMICALS

Phytochemicals exert anticancer activity via multiple pathways:

2.1 Antioxidant Activity

Reactive oxygen species (ROS) contribute to DNA damage, tumor initiation, and progression. Phytochemicals such as resveratrol, quercetin, and epigallocatechin gallate (EGCG) can scavenge free radicals, enhancing cellular defense mechanisms and preventing oxidative damage.

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2.2 Apoptosis Induction
Apoptosis, or programmed cell death, is frequently disrupted in cancer cells. Phytochemicals like curcumin, genistein, and berberine induce apoptosis by activating intrinsic (mitochondrial) and extrinsic (death receptor) pathways, upregulating pro-apoptotic proteins (Bax, caspases) and downregulating anti-apoptotic proteins (Bcl-2, survivin).

2.3 Cell Cycle Arrest
Phytochemicals interfere with cell cycle regulators such as cyclins and cyclin-dependent kinases (CDKs). Flavonoids, for instance, can arrest the G2/M or G1/S transition, reducing cancer cell proliferation.

2.4 Inhibition of Angiogenesis
Tumor progression requires blood vessel formation. Compounds like curcumin, resveratrol, and silibinin inhibit angiogenic factors such as VEGF and HIF-1α, reducing nutrient supply to tumors.

2.5 Epigenetic Modulation
Phytochemicals also regulate epigenetic modifications, including DNA methylation and histone acetylation, which influence gene expression related to tumor growth. For example, EGCG inhibits DNA methyltransferases, restoring tumor suppressor gene activity.

3. MAJOR CLASSES OF ANTI-CANCER PHYTOCHEMICALS
3.1 Flavonoids
Flavonoids are polyphenolic compounds widely present in fruits, vegetables, and beverages. Examples include quercetin, kaempferol, luteolin, and apigenin. They modulate ROS, inflammatory pathways (NF-κB), and apoptosis, showing anticancer activity in breast, colon, and prostate cancers.

3.2 Alkaloids
Alkaloids, nitrogen-containing compounds such as vincristine, vinblastine, colchicine, and camptothecin, target microtubules, DNA topoisomerases, and signal transduction pathways, inhibiting cancer cell proliferation and metastasis.

3.3 Terpenoids
Terpenoids like taxol (paclitaxel), artemisinin, and curcumin demonstrate cytotoxicity against various cancers. They regulate multiple pathways including PI3K/Akt, MAPK, and NF-κB, affecting apoptosis, autophagy, and angiogenesis.

3.4 Phenolic Acids
Phenolic acids, such as caffeic acid, ferulic acid, gallic acid, are potent antioxidants and anti-inflammatory agents. They inhibit cell proliferation, metastasis, and invasion in colorectal, liver, and breast cancers.

4. PHYTOCHEMICALS IN CLINICAL TRIALS
Several phytochemicals have reached clinical trials for cancer therapy:
Curcumin: Enhances chemosensitivity, inhibits NF-κB signaling, and shows safety in phase I and II trials for colorectal, breast, and pancreatic cancer.

Resveratrol: Studied for chemopreventive effects in colon, breast, and prostate cancers; modulates p53 and apoptosis pathways.

EGCG: Evaluated for prostate and breast cancer prevention; regulates cell cycle arrest and apoptosis.
Genistein: Isoflavone from soy, tested for hormone-related cancers, modulating estrogen receptors and PI3K/Akt signaling.

5. CHALLENGES IN CLINICAL APPLICATION
Despite their potential, phytochemicals face several challenges:
Low Bioavailability: Poor solubility and rapid metabolism reduce therapeutic levels in vivo.
Standardization Issues: Variation in plant source, extraction methods, and dosage complicates reproducibility.
Potential Toxicity: High doses may produce off-target effects.
Regulatory Hurdles: Lack of standardized clinical protocols for herbal compounds limits approval.

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6. STRATEGIES TO ENHANCE EFFICACY

Nanotechnology: Liposomes, polymeric nanoparticles, and micelles improve solubility, stability, and targeted delivery.
Combination Therapy: Co-administration with chemotherapeutic drugs enhances anticancer efficacy and reduces resistance.
Structural Derivatives: Chemical modifications of phytochemicals can improve potency and reduce toxicity.
Bioenhancers: Piperine and other adjuvants increase absorption and bioavailability.

7. FUTURE PERSPECTIVES

Advancements in omics technologies, computational drug design, and molecular modeling will accelerate the identification of new anticancer phytochemicals. Integrating plant-derived compounds with immunotherapy and targeted therapy may revolutionize cancer management. Moreover, understanding synergistic effects among phytochemicals and standard drugs can optimize combinatorial therapy approaches.

8. CONCLUSION

Phytochemicals represent a promising class of anticancer agents due to their multi-targeted mechanisms, low toxicity, and potential for combination with conventional therapies. Addressing challenges related to bioavailability, standardization, and clinical validation is essential for translating these compounds into effective anticancer drugs. Ongoing research in molecular mechanisms, formulation strategies, and clinical trials will pave the way for plant-derived therapeutics in cancer therapy.

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