GENERAL HEALTH

Phytochemicals in Cancer: Molecular Insights and Anticancer Potential

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Received: 22 September 2025 **Published:** 06 October 2025 **Volume 12, Issue 4** (Oct–Dec 2025)
Article no.: e171 **Open access** · free to read

INTRODUCTION

Cancer is one of the leading causes of death worldwide. According to WHO (World Health Organization) projections, by 2050 there will be more than 35 million new cancer cases representing a 77% increase from 2022. High HDI (Human Development Index) countries are projected to experience a substantial absolute increase in cancer incidence (WHO & IARC, 2024). Due to this increasing cancer burden, new and effective treatment approaches, particularly those derived from plant sources, are widely explored.

Phytochemicals are naturally occurring, plant derived bioactive compounds that offer numerous health benefits to humans (Suresh & Abraham, 2020). The most commonly studied phytochemicals include flavonoids, saponins, ginsenosides, carotenoids, lignans, isoflavones, procyanidins, stilbenoids, indoles, catechins, phenolic acids, anthraquinones, polyphenols, phenylpropanoids, organosulfur compounds, coumarins, isothiocyanates, and others (Xiao & Bai, 2019). Phytochemicals have been used for centuries for various health benefits. With advances in research, these bioactive components from medicinal plants have been isolated, purified, and characterised. These developments have significantly improved the drug discovery process (Choudhari et al., 2020). Depending on their function in plant metabolism, phytochemicals are categorized into primary and secondary metabolites. Molecules such as sugars, amino acids, nucleic acids, proteins, and lipids are primary metabolites, as they are primarily involved in the growth and development of the plant. Secondary metabolites are not essential for growth and development; however, they are vital for the plant?s survival and acts as a defence system. These compounds have antimicrobial properties which protects plants from pathogens (Rabizadeh et al., 2022).

Phytochemicals can target multiple pathways and can be combined with conventional treatments; hence, they have great potential in cancer treatment. They can also be used as anticancer drugs because they have lower toxicity compared to other drugs.

KEY PHYTOCHEMICALS AND THEIR ANTICANCER ROLES

Curcumin: Curcumin, a diarylheptanoid, belongs to the group of natural compounds known as curcuminoids and is derived from the rhizome of Curcuma longa, a plant native to India. It is the main bioactive component of turmeric, a widely used extract (NCI PDQ, 2024). It has the ability to influence the signalling pathways involved in cell proliferation, apoptosis, and inflammation, which is why it is a widely studied phytochemical for cancer treatment. Curcumin can inhibit NF-?B and is therefore categorized as a potent tumor growth and metastasis inhibitor. By facilitating cytochrome c release, enhancing the expression of the pro-apoptotic protein Bax and the tumor suppressor p53, and suppressing the expression of anti-apoptotic proteins such as Bcl-2 and survivin, curcumin can induce apoptosis. (Aljabali et al., 2025).

Andrographolide: It is a bicyclic diterpenoid lactone derived from the leaves and roots of *Andrographis paniculata* (PubChem, n.d.). Research indicates that by blocking tumor adaptation to hypoxic conditions, andrographolide suppresses tumor growth. The action of andrographolide is linked to the suppression of hypoxia-inducible factor (HIF)-1? activity and its upstream PI3K/AKT/mTOR signalling pathway (Choudhari et

al., 2020). Uncontrolled cell proliferation is a key characteristic of tumor cells. By modulating proliferation-related processes, andrographolide can inhibit tumor cell proliferation (Hu et al., 2024).

Resveratrol: It is a polyphenolic compound naturally present in many fruits and vegetables, including peanut sprouts, grapes, and peanuts. It was first isolated from *Veratrum grandiflorum* or white hellebore plants (Zhang et al., 2021). In human leukemia HL-60 cells, resveratrol treatment inhibited the formation of free radicals induced by 12-O-tetradecanoylphorbol-13-acetate (TPA). Its antioxidant properties safeguard cells from oxidative stress. It also avoids lipid peroxidation within cell membranes and prevents DNA damage caused due to reactive oxygen species (ROS) (Ko et al., 2017).

Quercetin: It is a polyphenolic flavonoid compound commonly found in diverse range of plant-based sources. It is commonly present in berries, tea, stems, onions, wine, bark, roots, cilantro, apples, dill, lovage, vegetables, capers, and flowers (Aghababaei & Hadidi, 2023). It downregulates mutant p53 in breast cancer cells, leading to G1 phase arrest of the cell cycle. Quercetin notably reduced cell survival, proliferation and triggered apoptosis in melanoma cells via activation of the JNK/P38 MAPK signalling pathway. Quercetin also reduced cell viability and colony formation, and promoted G2/M cell cycle arrest, DNA damage, and apoptosis in cervical cancer (Rizeq et al., 2020).

Genistein: It is naturally found in a wide variety of plants like kudzu, soybeans, lupine, fava beans, coffee, *Flemingia vestita*, and *Psoralea*. It possesses the ability to suppress abnormal cell proliferation related to cancer. Its principal mode of action is through blocking the activity of enzymes involved in cell division and survival, especially targeting growth factors. It acts as a tyrosine kinase inhibitor and blocks DNA topoisomerase II activity. Importantly, genistein has shown promise in the management of leukemia in both *in vitro* and *in vivo* studies (Rathee et al., 2024).

Gingerol: It is a phenolic compound found in *Zingiber officinale*, commonly known as ginger. It can influence many essential cellular pathways associated with cancer development and tumor progression, including those regulating cell proliferation, apoptosis, and metastasis. It stimulates pro-apoptotic pathways and suppresses pro-survival signalling, resulting in apoptosis through elevated Bax expression and decreased Bcl-2 levels. Furthermore, it suppresses the NF-?B signalling pathway, which is active in various cancers and is linked to inflammation, cell survival, and metastasis (Noor et al., 2024).

Lycopene: It is found mainly in red carrots, tomatoes, pink guavas, watermelons, pink grapefruits, and apricots. It exhibits anticancer activity through modulating signal pathways, apoptosis, and optimizing enzymatic activity to suppress metastasis and invasion of tumor cells. Research has demonstrated the anti-tumor potential of lycopene, showing that lycopene juice increases serum lycopene and antioxidant levels while also reducing oxidative stress?induced DNA damage. Furthermore, animal studies with supplementation of whole-dried tomato powder rich in lycopene led to reduced tumor progression in rats with xenografted prostate tumors. This finding indicates the antitumor activity of lycopene and its potential as a promising agent in the management of prostate cancer (Moran et al., 2022).

Procyanidin: It is found at elevated levels in berries, grapes, cocoa, and apples. It has been reported to increase the gene expression of tumor suppressor genes such as IGF-2R and PTEN. It also acts as an inhibitor of P-gp (a multidrug-resistant gene), indicating its potential as an additive to conventional therapy. Recent findings highlight its anticancer potential in lung and breast cancers (Rizeq et al., 2020).

Cyanidin: It is a major anthocyanin present in large amounts in the skin of fruits such as plums, hawthorn, apples, grapes, cranberries, red cabbage, blackberries, cherries, and raspberries. Cyanidin and cyanidin-3-O-?-D-glucoside have demonstrated a protective effect against DNA cleavage and a dose-dependent activity in neutralizing free radicals. A tumor-suppressive effect was demonstrated in lung large-cell carcinoma models using nude mice. Research has suggested that cyanidin can block the proliferation of colon cancer cells and reduce the expression of genes associated with the production of iNOS and COX-2 enzymes. Another study

confirmed that cyanidin-3-glucoside (C3G) inhibited the activation of the Fyn kinase signalling pathway. C3G was found to suppress the activation of the ErbB2/cSrc/FAK pathway in breast cancer cells subjected to ethanol, potentially lowering the likelihood of metastasis (Kowalczyk et al., 2024; Rathee et al., 2024).

CONCLUSION:

Phytochemicals, naturally present bioactive compounds obtained from plants, possess remarkable capability in cancer prevention and control due to their potential to influence several cellular pathways linked to tumor initiation, progression, and metastasis. Compounds such as curcumin, resveratrol, quercetin, procyanidin, genistein, gingerol, lycopene, and cyanidin, among others, have exhibited anticancer properties through apoptosis induction, cell cycle arrest, antioxidant activity, and inhibition of pro-survival signalling pathways. Their minimal side effects and reduced cytotoxicity compared to existing chemotherapeutics emphasize their efficacy as supplementary compounds or alternatives in cancer intervention. Ongoing investigations into the cellular mechanisms, biochemical pathways, and signalling processes will be crucial to optimize their utility in fighting tumor growth and promoting well-being.

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Competing interests

The authors declare that they have no competing interests.

How to cite this article (Vancouver)
CB R. Phytochemicals in Cancer: Molecular Insights and Anticancer Potential. CHEARS Chronical. 2025;12(4):e171. Available from: https://chears.in/journal/volume-12/issue-4/phytochemicals-in-cancer-molecular-insights-and-anticancer-potential-171
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https://chears.in/journal/volume-12/issue-4/phytochemicals-in-cancer-molecular-insights-and-anticancer-potential-171