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Nutraceuticals as Adjunctive Treatment in Cancer Exploring Efficacy and Mechanism of Action

Wasiullah[1], Piyush Yadav[2], Mohit Vishwakarma[3,*], Nitesh Maurya[4]

Abstract

Dietary habits are a critical factor in cancer prevention, with plant-based diets rich in vegetables and fruits associated with reduced cancer risk. Nutraceuticals – bioactive compounds derived from food and supplements – have gained attention for their potential in cancer prevention and therapy. Phytochemicals, such as flavonoids, polyphenols, and alkaloids exhibit anti-cancer properties through mechanisms including antioxidant activity, anti-inflammatory effects, inhibition of tumor growth, and induction of apoptosis. Key nutraceuticals include alkaloids (e.g., caffeine, taxol), polyphenols (e.g., curcumin, quercetin), and omega-3 fatty acids (e.g., DHA, EPA), all of which influence cancer cell signaling, DNA repair, and immune response. Additionally, traditional herbal remedies, such as those in Traditional Chinese Medicine (e.g., Yangzheng Xiaoji), and marine-derived compounds (e.g., Trabectedin, Kahalalide F) show promise in inhibiting cancer cell adhesion, inducing apoptosis, and blocking angiogenesis. These natural compounds, with their diverse mechanisms, present potential alternatives or adjuncts to conventional cancer treatments, offering a pathway to less toxic, more effective therapies.

Keywords: Cancer treatment, phenols, lignans, lipids, alkaloids, flavonoids

INTRODUCTION

Numerous studies have shown that dietary habits are key factors in the development of chronic diseases, including cardiovascular disease, diabetes, gallstones, neurodegenerative diseases, cataracts, and various types of cancer. This strong connection between diet and disease highlights the considerable influence that food choices can have on overall health. Cancer has become a major global health issue, especially with increasing life expectancy, urbanization, and the resulting shifts in environmental conditions and lifestyle choices. The development of cancer involves a multi-stage process that includes initiation, progression, and promotion, often driven by changes in specific genes. Cancer risk cannot be solely attributed to one factor; rather, it is influenced by a combination of genetic, environmental, and lifestyle factors. Although, many high-risk cases may have a genetic predisposition, dietary choices can significantly influence the outcome [1, 2].

***Author for Correspondence**
Mohit Vishwakarma
E-mail: mohitjnp2018@gmail.com

[1]Principal, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India
[2]Professor & Head, Department of Pharmaceutical Chemistry, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India
[3]Assistant Professor, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India
[4]Scholar, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India

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The most common types of cancer, as identified by population studies, include those of the lung, breast, colon, and prostate. These cancers are particularly prevalent in Western countries, whereas their incidence is lower in Asian nations. In many Asian cultures, a typical diet is plant-based, featuring more vegetables and fruits and lower levels of fat and meat consumption [3]. This dietary pattern has led to hypotheses suggesting that diet and environmental factors have a profound impact on cellular functions and overall health [4].

In addition to essential nutrients, plant-based diets often contain a vast array of non-nutrient compounds that are not typically classified as essential nutrients but still play a significant role in promoting health. Traditional medicinal systems worldwide have long utilized these plant-derived substances for health management, although many of these claims remain scientifically unproven [5, 6].

NUTRACEUTICALS

Phytochemicals are bioactive compounds present in plants that promote health benefits by either directly affecting specific molecular targets or indirectly interacting with metabolic pathways as stable conjugates [7, 8]. Through the course of evolution, plants have developed a diverse array of phytochemicals to protect themselves from oxidative stress caused by reactive oxygen species and to serve as part of their defense mechanisms. In recent years, the demand for food products rich in bioactive compounds has surged, extending beyond just food to include dietary supplements and pharmaceuticals. Products that include phytochemical-enriched extracts for their health benefits, yet are not classified as "food," prompted the creation of the term "nutraceuticals." This term bridges the gap between food and pharmaceuticals. Coined by Dr. Stephen DeFelice in 1989, nutraceuticals are defined as "foods, food ingredients, or dietary supplements that provide specific health or medical benefits, including disease prevention and treatment, beyond basic nutritional functions."

Initially, the concept of nutraceuticals was associated with natural foods providing basic nutritional value necessary for health. For example, in the early 19th century, food industries began fortifying salt with iodine to prevent goiter, marking an early attempt at functional foods. Over time, the understanding of nutraceuticals expanded, and they began to be recognized as beneficial in treating various nutritional disorders, with increasing self-prescription use. In the 21st century, awareness of nutraceuticals has grown significantly, positioning them as potent therapeutic supplements and contributing to the broader field of complementary and alternative medicine (CAM) [9, 10].

The concept of using food as medicine dates to ancient times, with Hippocrates, commonly known as the father of modern medicine, famously declaring, "let food be your medicine and medicine be your food." This emphasizes the deep connection between proper nutrition and human health, especially in the therapeutic potential of foods [11].

Plant-based products can be classified as food, food supplements, functional foods, or nutraceuticals, depending on the extent of their processing. A pure extracted phytomolecule is considered a nutraceutical, whereas a semi-purified plant product that is not consumed as a regular food falls under the category of functional food. Food supplements, in contrast, are products designed for regular consumption to support overall health. Plant-based foods offer a wide range of beneficial compounds, including micronutrients, polyunsaturated fatty acids, and secondary metabolites like glucosinolates, flavonoids, polyphenols, phytoestrogens, phytosterols, lignans, terpenes, and phytates, among others [12].

CLASSIFICATION OF NUTRACEUTICALS BASED ON PHYTOCHEMICAL CONTENT

This study does not specifically focus on vitamins and minerals. However, it is important to note that whole fruits and vegetables, as well as the phytochemicals derived from them, may be rich in vitamins and minerals. Phytochemicals from fruits and vegetables can be studied according to their mechanisms of action, the diseases they target, or their biochemical classification [13–18]. For example, based on their mechanism of action, compounds like aqueous cinnamon extract, green tea extract, curcumin, steroidal saponins derived from fenugreek, and chitooligosaccharides sourced from marine life, which function as Matrix Metalloproteinase (MMP) inhibitors, can be categorized together. However, each of these nutraceuticals demonstrates a range of mechanisms through which they act (Figure 1).

Therefore, the study of nutraceuticals and their potential in cancer treatment is initially approached from a chemical classification perspective. There are several biochemical categories of nutraceuticals,

including alkaloids, lipids, organic acids, polysaccharides, organosulphurs, phenols, phytic acids, phytosterols, and terpenes.

Functional foods and other nutraceuticals are composed of compounds from various biochemical groups. The main categories of alkaloids, organic acids, and polysaccharides will be covered briefly. Nutraceuticals from secondary and tertiary groups will also be briefly mentioned. The focus will then shift to those nutraceuticals relevant to the treatment of breast, cervical, and ovarian cancers.

Alkaloids

Alkaloids are bioactive, nitrogen-containing organic compounds found in plants, typically with a ring structure. These substances may belong to various biochemical groups based on their chemical makeup and physiological effects. Alkaloids are often found alongside other phytonutrients in functional foods. For instance, tea leaves from *Camellia sinensis* contain not only alkaloids but also flavonoids, steroids, gallic tannins, and catecholic tannins (flavanols). Alkaloids can be divided into various subclasses depending on their chemical structure and biological activity.

For example, coffee's aroma comes from trigonelline, a bitter alkaloid, while its bitter taste is primarily due to caffeine, a purine-like alkaloid. Other significant alkaloids include colchicine from *Colchicum autumnale* (autumn crocus or meadow saffron), scopolamine (or hyoscine) from *Hyoscyamus niger* (henbane or stinking nightshade), physostigmine from *Physostigma venenosum* (Calabar bean), reserpine from *Rauwolfia serpentina* (Indian snakeroot or devil pepper), and taxol from *Taxus brevifolia* (pacific yew).

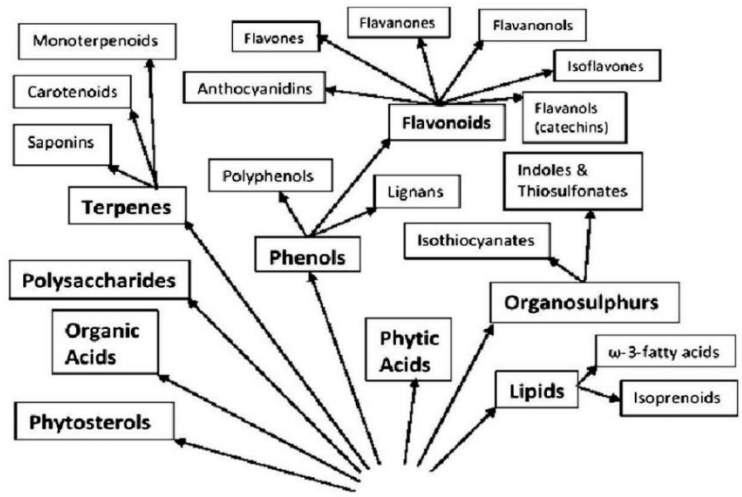

Figure 1. Nutraceuticals biochemical classification.

Organic Acids and Polysaccharides

Organic acids and polysaccharides are broad categories of chemical compounds that encompass various biochemical groups, with each constituent falling into more specific phytonutrient classes based on its structure and biological activity [19].

Organic Acids

Organic acids are carbon-containing acids that play significant roles in inflammation regulation, antioxidant activity, cancer prevention, and liver protection. Examples include cinnamic acid from *Aloe vera*, ellagic acid (a polyphenolic organic acid) present in berries, green tea, guava, pecans, and walnuts, ferulic acid found in oats and rice, gallic acid in tea, oxalic acid in coffee, spinach, and tea, and salicylic acid in peppermint. Ellagic acid acts as a reactive epoxide scavenger, inhibiting DNA methylation and DNA topoisomerase activity [20, 21].

Polysaccharides

Polysaccharides, especially those from mushrooms, are known for their immune-boosting and cancer-preventive properties. Fibrous polysaccharides help bind carcinogens, reduce bile acid levels, and influence estrogen metabolism. Polysaccharides from the traditional Chinese, a serine protease, to enter and trigger apoptosis (programmed cell death). medicine adaptogen ginseng can enhance the expression of granzyme and perforin, which in turn increases the concentration of natural killer cells in the bloodstream, boosting NKC cytotoxicity and reducing the adverse effects of radiation therapy. Perforin creates pores in target cells, allowing granzyme.

Organosulphur Compounds

The characteristic pungent odor of sulfur is a defining feature of organosulfur compounds, which include indoles, thiosulfonates, and isothiocyanates. These compounds, like indole-3-carbinol (I3C) and diindolylmethane (DIM), are commonly found in cruciferous vegetables [22]. In addition, cephalosporins, derived from *Acremonium* fungi, and penicillin, obtained from *Penicillium* fungi, are also categorized as organosulfur compounds [23].

Fats and Oil

Facts and oils include various subgroups, such as fats, waxes, glycolipids, phospholipids, and polyprenyl compounds. Within these, steroids, fat-soluble vitamins, and isoprenoids (or terpenoids) fall under the category of polyprenyl compounds. Essential fatty acids, like omega-3 and omega-6 polyunsaturated fatty acids (PUFAs), are crucial for maintaining health [24–29].

Isoprenoids

Isoprenoids are known to boost antioxidant activity by enhancing receptor function. Compounds like farnesol (found in floral essential oils) and geraniol (extracted from citronella, geranium, lemon, palmarosa, and rose oils) exhibit in vivo cytotoxic effects against liver cancer, leukemia, and melanoma in mice. Isoprenoids also play a role in safeguarding cell membrane phospholipid bilayers from oxidative harm caused by free radicals. The production of isoprenoids by microorganisms, such as Escherichia coli and Saccharomyces cerevisiae can help reduce the risk of supply shortages. Given these properties, studying isoprenoid-phospholipid conjugates for their potential medicinal benefits is both biologically plausible and ecologically sensible [30–32].

Omega-3 Polyunsaturated Fatty Acid

Primary forms of omega-3 PUFAs are docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). These compounds are linked to a reduced risk of coronary heart disease and offer a range of cardiovascular benefits, including Omega-3 polyunsaturated fatty acids (PUFAs) which are known for their boosting, platelet-aggregating, and anti-inflammatory properties. The immune- lowering triglyceride levels, reducing blood pressure, decreasing inflammatory markers, improving endothelial function, preventing certain arrhythmias, reducing vasoconstriction, enhancing fibrinolysis, and decreasing fibrin formation. Omega-3 polyunsaturated fatty acids also reduce the risk of microalbuminuria and sudden cardiac arrest [33–40].

Furthermore, omega-3 PUFAs contribute to the formation of resolvins and protectins, suppress pro-inflammatory molecules, such as COX-2, IL-1β, and TNF-α, and activate peroxisome proliferator-activated receptor (PPAR) gamma. This activation helps inhibit cell proliferation and induces apoptosis in cancer cells. DHA exhibits a stronger, dose-dependent pro-apoptotic effect on DU145 prostate carcinoma cells compared to EPA. DHA's pro-apoptotic action is mediated through several signaling pathways, including MAPK, NF-κB, p53, and PI3K-Akt.

Phenols

Phenols, often recognized for their presence in the vibrant colors of fruits and vegetables, are based on a phenylalanine structure. The phenol group encompasses various compounds, including coumarins, flavonoids, lignans, polyphenols, quinones, stilbenes, tannins, and xanthones. Flavonoids are made up

of several subclasses, such as anthocyanidins, flavones, flavanones, flavanonols, isoflavones, and flavanols. For instance, each gram of *Camellia sinensis* leaf extract contains 700 mg of phenols, with 14 mg being flavonoids [41–46].

Coumarins

Coumarins are aromatic benzopyrones known for their distinct fragrance. These compounds are found in plants, such as *Artemisia scoparia* (yin-chen wormwood), citrus species (like oranges), and *Glycyrrhiza uralensis* (licorice). In the case of moldymelilotus species (sweet clover), fungi convert coumarin into 4-hydroxycoumarin, which then dimerizes to form a dicoumarol precursor to warfarin. One key difference between cassia cinnamon (*Cinnamomum cassia*) and true *Ceylon cinnamon* (*Cinnamomum verum*) is the significantly higher coumarin content in cassia, while *Ceylon cinnamon* contains only trace amounts. However, while coumarin has been investigated for its potential to reduce melanoma recurrence and inhibit renal cell carcinoma, these effects did not hold up in subsequent trials. Coumarin exhibits dose-dependent cytotoxicity against the Hep2 cell line, and carbon-4 substituted coumarins show antiproliferative activity against breast and liver cancers. These compounds also play a role in inhibiting several enzymes and processes, such as aromatase, protein kinase, quinone reductase, sulfatase, 17β-HSD3, Cdc25, DNA intercalation, HDACs, Hsp90, microtubulin, NF-κB, and TNF-α. Moreover, carbon-4 substituted coumarins can reduce the activity of selective estrogen receptor modulators.

Flavonoids

Flavonoids demonstrate a broad spectrum of biological activities and mechanisms of action. These compounds act as antioxidants, anti-angiogenic agents, anti-proliferatives, reactive oxygen species (ROS) scavengers, electrophiles, metal chelators, hydrogen peroxide producers, nitrosation inhibitors, and modulators of phase I detoxification enzymes. The flavonoid family consists of several subclasses, including flavones, flavanones, flavonols, flavanonols, isoflavones, flavanols, anthocyanidins, and anthocyanins. Flavonoids, such as apigenin, kaempferol, nobiletin, quercetin, and rutin are typically found in foods like cocoa, fruits, leafy vegetables, herbs, spices, legumes, tea, and red wine. Rutin, a flavonoid-disaccharide compound present in citrus fruits, is the main active ingredient in the homeopathic remedy Ruta. In cancer research, rice bran oil-derived tricin has been shown to arrest MDA MB 468 breast cancer cells in the G2/M phase of the cell cycle, suggesting potential therapeutic applications.

Lignans

Lignans are also classified as phytoestrogens. These compounds can be found in foods like berries, flaxseeds, sesame seeds, and whole grains. Matairesinol and secoisolariciresinol, two key lignans, act as weak estrogen agonists, increase sex hormone-binding globulin (SHBG) levels, and inhibit the enzyme aromatase. Like the isoflavone phytoestrogen genistein, the lignan metabolite enterolactone functions as a dose-dependent agonist-antagonist, selectively modulating cancer cells.

Polyphenols

Polyphenols are known for their antioxidant properties. They influence cancer development by inhibiting key enzymes, such as cyclooxygenase, DNA topoisomerase, and DNA methylation, while also promoting phase II detoxification processes and modulating cell signaling pathways. Examples of polyphenol include compounds present in cocoa, curcumin (derived from turmeric), phenolics in rice bran oil, caffeic acid, ferulic acid, and esters of ferulic acid.

Tannins

The astringency of fruits is often attributed to the presence of tannins. Tannins from plant sources are classified into two main types: hydrolyzable tannins, which are esters of ellagic acid or gallic acid, and condensed, non-hydrolyzable tannins, which consist of oligo- or polymeric proanthocyanidins. Another distinct class of tannins, known as phlorotannins, is derived from brown algae. Tannins typically contain 12 or more hydroxyl groups and five or more phenyl groups. Gallic acid and flavan-3-ols are sometimes

categorized as pseudo-tannins. Condensed, non-hydrolyzable tannins, such as flavan-3-ols, are also referred to as flavonols, a category that includes compounds like catechins, which were mentioned earlier.

Hydrolysable or Pyrogallol-Type Tannins

Punicalagin, ellagic acid, and punicalin are examples of ellagitannins, while gallagic acid is categorized as a gallotannin. Carob pods contain 0.95 mg/g of hydrolyzable tannins, while carob fruit has a gallic acid content ranging from 0.237 mg/g to 1.647 mg/g, making it the third highest source of gallic acid after chestnuts and cloves. Carob fruit fiber is known to contain at least three varieties of gallic acid-based tannins: epigallocatechin with four gallic acid units, hexose-bound tannins containing two to five gallic acid units, and pentose-bound tannins with two gallic acid units. Moreover, carob fruit fiber also contains prodelphinidin dimers and trimers.

An Herbal Mixture

Yangzheng Xiaoji, a traditional Chinese medicine (TCM) formula made from 16 herbs, reduces the adhesion of cancer cells in a dose-dependent way. This includes A549 lung cancer cells, MCF- 7 breast cancer cells, HRT18 colorectal cancer cells, HGC27 gastric cancer cells, and MG-63 osteosarcoma cells. This action occurs through the PI3K pathway and anti-angiogenesis mechanisms. Additionally, the extract of Yangzheng Xiaoji, DME25, suppresses cancer growth by inhibiting the phosphorylation of the focal adhesion kinase (FAK) pathway.

ENTIRE PLANT-BASED NUTRACEUTICALS

Cardamon

In female Swiss albino mice, cardamom, garlic, and saffron offer chemoprotective benefits against skin cancer induced by DMBA. Cardamom particularly enhances phase detoxification and antioxidant activity in the skin and liver of DMBA-treated mice. It contains a variety of phytochemicals, some of which are highlighted below. Phase I clinical trials on limonene, a primary compound in cardamom, indicate that it may aid in inhibiting breast, colorectal, and prostate cancers with low toxicity at doses up to 100 mg/kg. Limonene is converted into perillyl alcohol, which prevents G-protein isoprenylation. It has been shown to inhibit gastric and lung cancers, as well as leukemia.

1, 8-Cineole has been shown to both promote and suppress apoptosis in SK-MEL-28 human melanoma cells, B16-F1 murine melanoma cells, and Molt 4B and HL-60 human leukemia cells. Linalool acts through p53 upregulation to target leukemia and inhibits renal adenocarcinoma and amelanotic melanoma. α-Pinene and α-Terpineol demonstrate anti-inflammatory effects on oral buccal cells. Myrcene possesses chemoprotective effects against DMBA in rats and promotes apoptosis in human hepatoma cell lines. Trans-nerolidol exhibits cytotoxicity against A-549 human lung carcinoma cells and DLD-1 colorectal cancer cells. *Artemisia capillaris* (wormwood), is known for its ability to inhibit various cancers, including CNE-2 nasopharyngeal carcinoma, DMBA-induced breast cancer, SMMC-7721 human hepatoma, HL-60 leukemia, HepG2, Huh-7 human liver cells, HeLa cervical cancer, and mouse liver cells, contains borneol, a compound also found in cardamom. Borneol demonstrates antioxidative, cytotoxic, DNA-damaging, and DNA-protective effects in Caco-2 and VH10 cells.

Marine-Derived Compounds

Ecteinascdia turbinata is the source of the active compound trabectedin, which is approved for treating platinum-sensitive ovarian cancer and soft tissue sarcoma, has shown both in vitro and in vivo inhibition of transcription factors. Kahalalide F, derived from *Elysia rufescens*, serves as the basis for the synthetic compound PM02734, which is currently in Phase II clinical trials to assess its ability to induce apoptosis in H322 and A549 cell lines. In Phase I trials, Kahalalide F demonstrated inhibitory effects on breast, liver, and pancreatic cancers, as well as melanoma. *Spisula polynyma*-derived ES-285-HC1 has exhibited inhibitory effects against solid tumors, including hepatocellular carcinoma, prostate, and renal cancer in vivo.

Dicathais orbita, which contains indole derivatives, such as tyrindoleninone, tyrindolinone, 6-bromoisatin, and 6, 6′-dibromoindirubin, exhibited apoptotic activity in vivo against rat distal colon cells exposed to azoxymethane. Tyrindoleninone and 6-bromoisatin derived from Dicathais orbita demonstrated double the apoptotic effect on the KGN tumor-derived granulosa cell line compared to normal human granulosa cells (66% vs. 31%, respectively). The potential biological activity of compounds containing 6-bromoisatin will be explored in a forthcoming article on oncologic homeopathic remedies.

Mechanism of Action for Treatment of Cancer

The mechanism of action for cancer treatment refers to the specific molecular, cellular, or biochemical pathways through which therapeutic agents exert their anti-cancer effects. Cancer treatments can work in various ways, including inducing cell death, inhibiting tumor growth, blocking angiogenesis (blood vessel formation), or enhancing the immune system's ability to target cancer cells.

Induction of Apoptosis (Programmed Cell Death)

Apoptosis is a controlled form of cell death crucial for eliminating cancer cells. Cancer therapies often aim to induce apoptosis through different mechanisms. DNA Damage: Drugs like cisplatin induce DNA damage by forming platinum-DNA adducts, which prevent DNA replication and transcription. The damaged DNA triggers apoptosis pathways through p53 activation and caspase activation. Mitochondrial Dysfunction: Mitochondria are crucial in the process of apoptosis. Chemotherapeutic drugs, such as doxorubicin damage mitochondrial membranes, leading to the release of pro-apoptotic factors like cytochrome c, which in turn activates caspases.

Modulation of Apoptotic Regulators: Some therapies, such as venetoclax, target anti-apoptotic proteins like BCL-2, making cancer cells more susceptible to apoptosis.

Inhibition of Cell Proliferation Cancer Cells

Inhibition of cell proliferation cancer cells often proliferate uncontrollably, and many therapies work by inhibiting these proliferative signals.

- *Cyclin-Dependent Kinase (CDK) Inhibition:* Drugs like palbociclib inhibit CDK4/6, which are necessary for the transition from the G1 to S phase of the cell cycle, halting cancer cell proliferation.
- *Growth Factor Receptor Blockade:* Erlotinib, a tyrosine kinase inhibitor, blocks the epidermal growth factor receptor (EGFR), preventing downstream signaling that leads to uncontrolled cell growth in non-small cell lung cancer (NSCLC).

Inhibition of Angiogenesis (Blood Vessel Formation)

Angiogenesis is crucial for tumor growth, as tumors need a blood supply for nutrients and oxygen.

- *VEGF Inhibition:* Bevacizumab, a monoclonal antibody against VEGF, inhibits the vascular endothelial growth factor, preventing angiogenesis and starving the tumor of oxygen and nutrients.
- *Tyrosine Kinase Inhibitors (TKIs):* Drugs like sunitinib and sorafenib target VEGFR (vascular endothelial growth factor receptor), inhibiting angiogenesis and tumor growth.

Precise Inhibition of Oncogenes and Tumor Suppressor Genes

Certain cancers are caused by mutations in specific genes. Targeted therapies are designed to block these mutated genes or their subsequent effects.

- *BCR-ABL Inhibition:* Imatinib, used for chronic myelogenous leukemia (CML), inhibits the BCR-ABL fusion protein, which results from the Philadelphia chromosome.
- *HER2 Inhibition:* Trastuzumab, a monoclonal antibody, targets the HER2 receptor, which is overexpressed in some breast cancers, interfering with signaling that stimulates cell growth.

Immune System Modulation (Immunotherapy)

Immunotherapies enhance the body's immune system to recognize and destroy cancer cells:

- *Checkpoint Inhibition:* Nivolumab and pembrolizumab are immune checkpoint inhibitors that block PD-1, a receptor that downregulates immune responses, thus enhancing T-cell activity against tumors.
- *Cytokine Therapy:* Interleukin-2 (IL-2) and interferon-alpha stimulate immune cells, such as T cells and natural killer (NK) cells, to combat cancer.
- *CAR-T Cell Therapy:* In CAR-T cell therapy, T cells are genetically engineered to produce chimeric receptors that are specific to tumor antigens, enabling them to identify and destroy cancer cells.

DNA Repair Inhibition

Cancer cells often have defective DNA repair pathways, and therapies targeting these defects can enhance the effects of DNA-damaging agents.

- *PARP Inhibition:* Olaparib blocks the enzyme PARP, which plays a role in repairing single-strand DNA breaks. In cells with mutations in the BRCA1/2 genes, the inhibition of PARP leads to DNA double-strand breaks and cell death.

Chemotherapy and Radiation

Traditional therapies like chemotherapy and radiation aim to kill rapidly dividing cells.

- *Chemotherapy:* Drugs like paclitaxel and doxorubicin inhibit cell division or cause DNA damage, leading to cancer cell death.
- *Radiation Therapy:* High-energy radiation induces DNA damage, especially in rapidly dividing cells, which leads to apoptosis or necrosis in tumor cells.

Marine-Derived Compounds

Natural products from marine organisms are being explored for their anticancer properties.

- *Trabectedin:* Derived from Ecteinascidia turbinata, Trabectedin inhibits transcription factor activity and DNA repair mechanisms in cancer cells, showing effectiveness in ovarian cancer and soft tissue sarcoma.
- *Kahalalide F:* Derived from Elysia rufescens, Kahalalide F induces apoptosis and inhibits cancer growth, with effects seen in breast, liver, and pancreatic cancers.

CONCLUSIONS

Nutraceuticals, especially those derived from plants, offer promising adjunctive treatments in cancer therapy by leveraging bioactive compounds, such as phytochemicals. These compounds, including alkaloids, lipids, phenols, and organosulphur, exhibit diverse mechanisms of action that can inhibit cancer cell growth, reduce inflammation, and promote apoptosis. Given the strong connection between diet and disease, integrating nutraceuticals into cancer management – alongside conventional therapies – could enhance treatment efficacy and improve patient outcomes. While further research is needed to fully understand their mechanisms, nutraceuticals represent an important avenue for the future of cancer treatment, bridging the gap between nutrition, health promotion, and pharmacology.

Cancer therapies involve a range of strategies designed to target and destroy cancer cells. These approaches include:

1. *Induction of Apoptosis:* By triggering programmed cell death through DNA damage or mitochondrial dysfunction, therapies like cisplatin, doxorubicin, and venetoclax increase cancer cell death.
2. *Inhibition of Cell Proliferation:* Agents like palbociclib and erlotinib prevent cancer cells from proliferating uncontrollably, halting tumor growth.
3. *Angiogenesis Inhibition:* Drugs, such as bevacizumab and tyrosine kinase inhibitors starve tumors by blocking the formation of blood vessels.

4. *Targeted Therapy:* Targeting specific mutated genes or proteins, such as BCR-ABL in leukemia or HER2 in breast cancer, disrupts cancer cell growth and survival.
5. *Immunotherapy:* Enhances the immune system's ability to recognize and destroy cancer cells through checkpoint inhibitors (nivolumab, pembrolizumab), cytokine therapy, and CAR-T cell therapy.
6. *DNA Repair Inhibition:* Targeting defective DNA repair pathways, such as through PARP inhibitors (Olaparib) promotes cancer cell death.
7. *Traditional Therapies:* Chemotherapy and radiation damage rapidly dividing cancer cells, promoting their death.
8. *Marine-Derived Compounds:* Natural compounds like Trabectedin and Kahalalide F, sourced from marine organisms, show promise in inhibiting cancer cell growth and inducing apoptosis.

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