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Antioxidants Impact on Cancer Therapy

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Abstract:

With about 13% of all deaths globally being caused by cancer, it is the most common cause of death. The most common treatment for malignant cancer is chemotherapy. Anticancer medications come with a wide range of negative effects. Every drug, in every class, has a unique mix of side effects that can lead to patient noncompliance and a decline in quality of life. Reactive oxygen species (ROS) production that is excessive and the subsequent accumulation of oxidative stress are two of the main factors that contribute to unfavourable reactions, particularly for medications that target DNA. Several dietary supplements have been studied to reduce these undesirable side effects, and antioxidants have become increasingly popular as adjuvants in chemotherapy. Many dietary supplements have been tried to reduce these unwanted side effects, but antioxidants have become increasingly popular as chemotherapy adjuvants. But many doctors advise against taking antioxidant-rich dietary supplements because they could interact with treatments that work by producing free radicals to destroy cancer.

Keywords: Antioxident, Free radicals, Chemotherapy, Reactive oxygen species (ROS), Cancer.

Introduction:

According to evidence, the plant kingdom is a strong contender for cancer treatment and chemoprevention because of the abundance and variety of antioxidants like polyphenols, (-)-Epigallocatechin 3-gallate, flavonoids, gallic acid, glycosides, verbascoside, calceorioside, epicatechin, quercetin, curcumin, lovastatin, genestein, beicalein, vitamin A, vitamin C, polyphenols, and numerous additional substances that have the ability to stop the growth of various cancer cells in vitro and in vitro, including colon cancer, fibroblasts, skin, liver, cervix, breast, and several additional cancerous cells.

Reactive oxygen species (ROS) are byproducts of metabolic reactions taking place in organelles such the endoplasmic reticulum, mitochondrial respiratory complex, and peroxisomes, as well as procedures like the oxidation of fatty acids and the detoxification of xenobiotics (2). Picomolar amounts of ROS are formed under typical circumstances, and the body's antioxidant mechanism eliminates any excess ROS. However, occasionally, this process will be impaired or unbalanced, causing an accumulation of free radicals and aggravating diseases like cancer, cardiovascular conditions, diabetes, etc. Higher levels of free radicals are produced by metabolically active cells, and these free radicals can affect cellular homeostasis, which can result in the growth of cancer and metastasis.

Cancer cells are extremely metabolically active and hypoxic cells that also tend to produce more ROS as a result of their rapid growth and inadequate vascular irrigation. ROS damage DNA by diffusing through the mitochondrial membrane and also serve as signal-transducing messengers in numerous redox-sensitive molecular pathways involved in cell survival, therapeutic resistance, and progression (1). Strong antioxidants have been utilised as an important technique for cancer prevention because oxidative stress has a significant role in characteristics of cancer such as angiogenesis, invasiveness, and potential to metastasize.

Free radicals: What are they, and do they contribute to the growth of cancer?

Free radicals are extremely reactive substances that may cause cell damage. When an atom or molecule (a substance made up of two or more atoms) receives or loses an electron, they are produced (a small negatively charged particle found in atoms). Free radicals are created by the body normally and are essential to many regular cellular functions. Free radicals can harm the body in excessive concentrations and harm all significant cellular components, including DNA, proteins, and cell membranes. Free radical damage to cells, particularly DNA damage, may contribute to the development of cancer and other diseases(3,4)

When we breathe or exercise, our bodies manufacture free radicals, and we are also exposed to more free radicals from environmental contaminants like cigarette smoke, air pollution, and UV rays from the sun (5)

The majority of free radicals produced in living tissue are oxygen-containing free radicals. The term "reactive oxygen species," or "ROS," is another term for them (3-4).

Reactive oxygen species (ROS):

Reactive oxygen species (ROS) are a class of oxygen-containing free radicals. Among the most prevalent reactive oxygen species are hydrogen peroxide, the hydroxyl radical, and superoxide anion (H_2O_2). As a result of oxidative phosphorylation, mitochondria are the main sources of hydrogen peroxide and superoxide anion. Greater ROS production occurs in cells with high metabolic rates. A type of free radical that is not a ROS is reactive nitrogen species (RNS). The RNS most frequently formed during L-arginine metabolism is nitric oxide (NO).

Antioxidant:

Antioxidants are substances that interact with and destroy free radicals, stopping them from doing harm. The term "free radical scavengers" also applies to antioxidants.

Some of the antioxidants the body uses to resist free radicals are produced by the body. These antioxidants are also known as endogenous antioxidant. However, the body must get the remaining antioxidants it need from external (exogenous) sources, primarily the diet. These exogenous antioxidants are also known as dietary antioxidants. eg. lycopene, vitamins A, C, and E (alpha-tocopherol), beta-carotene. (3),(6)

Antioxidants have a place in adjuvant chemotherapy because they react with and get removal of oxidising free radicals, preventing cellular damage. However, several antineoplastic drugs used in cancer chemotherapy work by producing free radicals, which further damages cells and causes the death of cancerous cells.

Antioxidants are molecules that may shield cells from the harm imposed by free radicals and may be involved in heart disease, cancer, and other disorders. Antioxidants stop the electron "stealing" reaction and destroy free radicals by donating one of their own electrons. Antioxidants are frequently referred to as "mopping up" free radicals, which refer to the fact that they balance the radical's electrical charge and stop it from stealing electrons from other molecules.(7)

Increased exogenous antioxidant levels have been demonstrated in lab and animal studies to inhibit the forms of free radical damage linked to the growth of cancer.

Antioxidant in Cancer Therapy:

Chemotherapy, radiation therapy, and immunotherapy are frequently used either alone or in combination for a range of tumours despite recent advancements in local and systemic treatment techniques. Radiation therapy uses high-energy particles/waves, including x-rays and gamma rays, to kill tumour cells. Immunotherapy treatments are intended to activate the host's own immune system to attack cancer cells. Chemotherapy targets cancer cells with chemically modified agents/natural compounds with cytotoxic properties. One of the effects of chemotherapy and radiation therapy is the production of ROS, which, through its direct and indirect effects on tumour cells, induces DNA damage and/or affects the DNA replication machinery, leading to aberrations in a number of cellular signalling pathways that ultimately lead to chemotherapy- or radiation therapy-induced cell death(8-9)

Antioxidant	Effect of antioxidant
Lycopene	Lycopene is a red carotenoid with anti-oxidant, anti-inflammatory, and cancer-preventive qualities that can be found in ripe tomatoes, grapefruits, and red melons (10). Singlet oxygen is quenched by lycopene, which also neutralises free radicals and protects DNA from oxidative damage. As a result, it stops possible conversion of healthy cells into cancerous ones. (11)
Vitamin E	Vitamin E is an anti-oxidant that enters the body through the skin quickly and is absorbed into cellular membranes where it prevents lipid peroxidation. Specifically, the vitamin E isoform -tocotrienol offers the best defence. Vitamin E also has ant proliferative qualities that disrupt signal transmission and cause cell cycle arrest.
Polyphenols	It has been proposed that polyphenols antioxidant properties can protect against a variety of disorders like cancer that are brought on by reactive oxygen species (ROS). There is strong evidence that the polyphenols found in tea, red wine, chocolate, fruit juices, and olive oil have the potential to promote tumor growth and carcinogenesis at the cellular level (Theoharides). For example, Possibly interacting with reactive intermediates (12). Activated mutagens and carcinogens (13)

Beta-carotene (BC)/ vitamin A (retinol)	Beta-carotene is an antioxidant. It defends the body from dangerous molecules known as free radicals. In dark green and orange fruits and vegetables, beta-carotene (BC), a provitamin A carotenoid, is a source of retinoids. According to observational research, increasing dietary BC intake along with higher BC plasma concentrations is linked to a lower risk of developing a number of malignancies. ⁽¹⁴⁻¹⁵⁾
Lutein	A variety of biological features, such as anti-inflammatory, antioxidant, and anti-cancer effects, are present in lutein ⁽¹⁶⁾ and exerts cytotoxic and growth-inhibitory effects on a number of cancer cell lines and animal models ⁽¹⁶⁻¹⁷⁾ . Human prostate cancer cells are unable to proliferate when lutein is present. ⁽¹⁸⁾
Rosmanic acid	By enhancing lipid peroxidation, antioxidant state, and detoxification enzyme activity, rosmanic acid reduces the development of oral cancer. In mouse skin cancer models, rosmanic acid has been shown to have powerful anticancer and apoptotic effects. ⁽¹⁹⁾

Antioxidants in chemotherapy:

Because of two crucial aspects, antioxidants' role in cancer treatment is debatable. "First, the data on the use of antioxidants in cancer therapy may be divided into two categories based on the two different types of antioxidant doses: a preventative dose, which is a low dose, and a therapeutic dose, which is a high dose. The research has demonstrated protection of both tumour cells and normal cells for the preventative dose. The results indicate that at the therapeutic dose, it inhibits the proliferation of cancer cells but not of healthy cells. As a result, it's confusing that researchers are looking at data for preventive dosing.

The question of whether additional antioxidants given during chemotherapy can protect normal tissue without negatively affecting tumour control has been the subject of numerous original research publications. Variations in study design, intervention regimen, cancer type, time of observation, inclusion criteria, and statistical analysis make it difficult to draw firm conclusions about the possibility of decreased tumour control as a result of supplementing chemotherapy with antioxidants. Contrarily, a recent analysis has conclusively shown that antioxidants, when taken concurrently with chemotherapy, (a) do not interact with it, (b) augment its cytotoxic effects, (c) protect normal tissue, and (d) improve patient survival and therapeutic response (20), (21)

Chemotherapy raises oxidative stress, which is essential for the death of cancer cells, but a higher degree of oxidative stress may frequently make some anti-cancer medications ineffective. Cancer cells replicate slowly under situations of increased oxidative stress, which may reduce the effectiveness of chemotherapy (22)

There is growing evidence that antioxidants may be advantageous when used in conjunction with specific forms of chemotherapy. The University of Kansas Medical Center is conducting a randomised controlled experiment to determine the safety and effectiveness of adding antioxidants to chemotherapy in patients with newly diagnosed ovarian cancer due to the possibility of positive outcomes. (23) Greenlee and colleagues observed that 663 (86.2%) of the 764 patients in the Long Island breast cancer patient research project were getting adjuvant therapy for their breast cancer. 401 (60.5%) of the 663 women reported utilising antioxidants during adjuvant therapy. Antioxidants were utilised by 286 of 462 women (61.9%) when receiving tamoxifen

therapy, 210 of 310 women (38.7%) while receiving chemotherapy, and 196 of 464 women (42.2%) while receiving radiation. (24) The same group reported data in 2012 examining the relationships between antioxidant consumption after breast cancer diagnosis and outcomes in 2264 women with breast cancer. 81% of women claimed to have used antioxidant supplements following diagnosis. Vitamin E use was associated with a decreased risk of all-cause mortality and frequent use of vitamin C and vitamin E was associated with a decreased risk of BC recurrence among antioxidant users, but frequent use of combination carotenoids was associated with an increased risk of both breast cancer and all-cause mortality (25-26)

Due to inadequate nutrition and therapy, cancer patients frequently lack vitamins, including folic acid, vitamin C, pyridoxine, and other nutrients. Due to lipid peroxidation caused by chemotherapy, serum levels of antioxidant vitamins and minerals are decreased, increasing the level of oxidative stress. Therefore, supplementing with specific antioxidants and nutrients can improve the health of individuals receiving a continuous chemotherapy regimen (23)

Antioxidants in radiation therapy:

The use of antioxidant supplements during radiation therapy presents a dilemma for radiation oncologists since antioxidants that shield healthy cells from reactive oxygen species may also benefit cancer cells, decreasing the effectiveness of treatment. Damage to healthy cells over time, including tissue damage and a higher chance of neoplastic transformation. (27) Antioxidants can prevent it, as evidenced by experiments. Recent research has shown that antioxidants cause cancer cells to undergo apoptosis and shield patients from the unpleasant side effects of radiation therapy, which may make these substances effective in adjuvant therapy in the future.

Conclusion:

These articles demonstrate the role of antioxidants in the treatment of cancer patients or those who are cancer carriers. Also describe how antioxidants reduce the toxicity caused along by chemotherapy agents. These articles describe the effectiveness of cancer treatment, particularly chemotherapy, rises with antioxidant. Additionally, it demonstrates antioxidants lengthen survival duration and lower Ros levels.

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