



Antioxidant supplements and cancer

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Abstract

Reactive oxygen species (ROS) can cause cancers. Owing to the causal role of ROS in raising cancers and the fact that different antioxidant promoters are considered tumor inhibitors, so far, epidemiological surveys show that an appropriate consumption of antioxidant-rich foods and supplements is inversely associated to cancer risk. However, some clinical trials with antioxidants do not support this idea. This paper will review the research conducted on the associations between antioxidant supplements consumption and cancers risk, especially on breast, prostate, lung and skin cancers.

Introduction

Cancer is a general term for a large group of disorders that can influence any part of the body. One describing feature of cancer is the rapid creation of abnormal cells that grow elsewhere their usual boundaries, and which can then attack adjacent parts of the body and spread to other organs, the end process is referred to as metastases. As a matter of fact, metastases are the main reason of death from cancer (1). Hence, information about the causes of cancer, and interferences to inhibit and manage the disease are extensive. Cancer can be decreased and controlled by applying evidence-based strategies for cancer prevention, primary detection of cancer and managing of patients with cancer (1).

Free radicals are highly reactive chemicals which have the potential to damage cells. In fact, free radicals associated mutagenesis that can result in cancer beginning and development is a regular event in normal human cells (2).

An antioxidant is a molecule, which prevents the oxidation of other molecules. Oxidation is a chemical reaction containing the loss of electrons which can give free radicals. In sequence, these radicals can commence chain reactions. At what time the chain reaction occurs in a cell, it can make destruction or death to the cell. In brief, antioxidants are biochemical compounds, inhibiting oxidation, a procedure which could be destructive to the human body (3).

In the pages that follow, it will be explained influence antioxidant supplements on can-

Key point

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cers, especially on breast, prostate, lung and skin cancer which were the most common cancers in 2015.

Materials and Methods

For this mini-review, we used a variety of sources by searching through PubMed/Medline, Scopus, EMBASE, EBSCO and directory of open access journals (DOAJ). The search was conducted, using combination of the following key words and or their equivalents; cancer, free radicals, breast cancer, antioxidants, reactive oxygen species, superoxide dismutase, immunotoxicity and antioxidant supplements.

Reactive oxygen species and antioxidant

Reactive oxygen species (ROS) are gotten from the metabolism of molecular oxygen (4). ROS involve superoxide anion radical, singlet oxygen, hydrogen peroxide, and the very irritable hydroxyl radical. The toxic effects of oxygen are said to result from its metabolic decrease to these very reactive and toxic species (5). ROS are considered

as secondary messengers in cell signaling and they are required for numerous biological processes in normal cells. Under physiological conditions, ROS are continuously produced by ROS producers and removed through ROS scavenging systems in order to continue redox homeostasis (6). If changes occur in redox equilibrium, which can have endogenous or exogenous causes, they can either lead to a rise in ROS levels or rate of creation, resulting in cell harmful oxidative stress and irregular cell signaling, or a reduction in ROS, leading to a distraction of cell signaling and thus distraction of cellular homeostasis. Thus, this procedure can damage to cells, especially the harm to DNA, may play a role in the growth of cancer and other health conditions (7,8). Antioxidants may act for the cancer cell's "Achilles Heel", as non-transformed have lower speed of ROS creation, and thus they are fewer dependent on their detoxification by antioxidants. Actually, studies have shown that inactivating antioxidant processes trigger ROS-mediated cell death in a type of cancer cell (9). Many researchers have argued that the destruction of redox scavenging, or antioxidant systems commences a new therapeutic window and has potential to selectively persuade cancer cell death via oxidative stress, whereas sparing normal cells. Indeed, investigations have indicated that deactivating antioxidant mechanisms trigger ROS-mediated cell death in cancer cell types in vitro and vivo (9,10). Thus, the design of twin pro-oxidant therapies has the capacity to be efficient in selectively extermination cancer cells. If ROS-generating agents combine with ROS inhibitors (e.g. glutathione [GSH], thioredoxin [TRX] or superoxide dismutase [SOD]), can reduce the power of cancer cells to adapt to either agent. Even while various antioxidant proteins and regulators are upregulated in cancers they can be usefully targeted to cause antitumor influences, and it will be essential which discover the processes and redox regulation properties which are enriched in tumor cells and subsequently use them as clinically relevant therapeutic targets (6).

Antioxidant and breast cancer

In recent years, breast cancer is a common cancer worldwide; specially in developed countries (11).

Also, in 2015, around 231 840 women were detected with breast cancer (12).

Due to the fact that dietary factors might also influence breast cancer inhibition, researcher advise that high antioxidant intake may decrease the risk of developing cancer (13). Although, the effects of antioxidant supplements during radiation treatment, chemotherapy and hormonal cure on therapy toxicities, tumor reaction, recurrence, and existence are unknown (14) and guidelines regarding the use of antioxidant supplements during cancer treatment are variable (15). In fact, the purpose of these therapies is to cause the apoptotic cascade, via processes such as changing DNA repetition and interrupting mitochondrial membranes. But, these therapies may also destruct healthy tissues.

Some researchers have assumed that antioxidant supple-

ments can provide protection against these cure toxicities (16). In fact, investigations have shown that a complex mixture of antioxidants exhibit in whole foods may be more efficient than isolated antioxidants in cancer progress (17). As well, investigations have shown that fruits and vegetable consumption are associated with a decreased breast cancer risk which may be owing to high intake of antioxidants (18). For example, a declined risk of breast cancer has been reported in smokers with high consumption of α -carotene and β -carotene. However, previous research has shown that there is no generally association between dietary carotenoids consumption and breast cancer risk among smokers (19).

Antioxidant and prostate cancer

Prostate cancer is the most shared cancer in males and occurs mainly in older men (the average is about 66 years old). In 2015, around 220 800 new cases of prostate cancer were detected. Prostate cancer can be a life-threatening disease, however most men detected with prostate cancer will survive. In general, role of diet food in prostate cancer is not clear, but numerous factors have been examined (20). Recent evidence suggests that intake antioxidants act by suppressing metabolic paths, preventing cellular destruction and inhibiting prostate special antigen in prostate cancer cell series (21).

For instance, tomato and products of tomato such as lycopene are associated with decreased risk of prostate cancer (22). Chiefly, various fruits like mango, olives, grapes, strawberry, figs, and various vegetables have lycopene which have been shown to have antioxidant, anti-mutagenic, and anti-inflammatory properties in vitro and in vivo. Also, researchers have found positive effects in the treatment of prostate cancer cells and prevention of cancer cells growth (23).

Likewise, vitamin E has been achieved to be an antioxidant agent, detoxifying free radicals, intervening with the cellular processes, in cell growth and differentiation involving the processes engaged in prostate cancer, and is the most popular supplement used by men. Besides, selenium is known to act as an antioxidant, anti-proliferative factor and research has shown that selenium in induction of apoptosis and modulation of androgen levels is a trace element. It can be found in seafood, meat, and grains (23). In the United States, National Cancer Institute (NCI) assessed effect of selenium and vitamin E on the risk of prostate cancer. After 2 years, the experiment determined that selenium or vitamin E, alone or in mixture at the doses and formulations consumed, did not inhibit prostate cancer in this population of relatively healthy men (24). However, in 2011, Klein et al published a paper in which they showed after 7 years, 17% more patients of prostate cancer among men intake vitamin E alone than men intake a placebo (25). Considering that, no rise in prostate risk was observed for men specified to intake selenium alone or vitamin E combined with selenium compared with men specified to intake a placebo (26).

Antioxidant and lung cancer

In recent years, lung cancer is common and lethal for both women and men, and the quantity of deaths each year is growing (27). The estimated number is about 158040 lung cancer death occurred in 2015. It is accounted for nearly 27% of all cancer deaths. Also, the estimated number 221200 new patients of lung cancer were supposed in 2015, accounting for nearly 13% of all cancer detection (27).

Previous studies have reported that antioxidants and nutritional fibers might have a main role in the inhibition of lung cancer progress. The protecting effects of vegetables and fruits are considered to be intervened by numerous components, including β -carotene, fiber, vitamins, α -tocopherol, retinoids, phytoestrogens and folate (28). A number of studies have found that the consumption of vegetables and fruits are related with significant decreases in the chance of lung cancer. For the subgroup study of sex, the association was significant in women on vegetables consumption and lung cancer nonetheless not in men. Likewise, the association was greater in women than men on fruits consumption and lung cancer risk (29).

As mentioned above, vitamin E is an antioxidant and belongs to a category of vital lipid-soluble antioxidants containing of tocopherols and tocotrienols (30).

Recently investigators have examined effects of tocopherols on lung cancer risk and they did not find significant association between dietary consumption of tocopherols and lung cancer risk (31). In addition, previous research has shown that nutritional inflammatory indicator has related with asthma and lung function experiments. In the same way, entire antioxidant function has an effect inverse to that of the nutritional inflammatory indicator and perhaps protects the lungs from oxidative stress owing to the upper concentrations of bioactive combinations with antioxidant properties (32). A possible process of nutrition's performance may be via its effect on the creation of inflammatory cytokines, involving bronchoconstrictive leukotrienes in lung tissue. Worth mentioning, omega-III and omega-VI fatty acids expenditure have been shown to decrease the creation of these cytokines (33).

Antioxidant and skin cancer

Skin cancers are of the most common cancers with around 80100 detected new patients of skin cancers in 2015. In point of fact, skin DNA molecules are continually "bombed" by ROS creating from endogenous procedures, environmental reasons and radiation fonts.

Antioxidants might influence by reducing free radicals and by increasing the DNA enzyme restoration systems via a posttranscriptional gene management of transcription factors. Although the skin owns an elaborate antioxidant protection system to deal with oxidative stress, extreme and chronic display to UV light or other oxidizing factors can break down the cutaneous antioxidant and protected reaction capacity, due to oxidative damage and immunotoxicity, early skin aging, and skin cancer (34).

Recent evidence suggests that nutritional changes and specific nutrients may help to decrease oxidative stress and

free radical creation and thus slow down the skin damage procedure. In other words, vitamins C and E and many others, exogenous antioxidants, cannot be manufactured by the human body and must be taken up by the food. Indeed, only defense of our skin against ultraviolet radiation is its endogenous defense (melanin and enzymatic antioxidants) and antioxidants eaten with the food (vitamin A, C, E, etc.). Therefore, diet antioxidants play a key role in keeping the homeostasis of the oxidative equilibrium. Vitamin C, vitamin E (α -tocopherol), β -carotene, and other micronutrients (e.g. carotenoids, polyphenols) and selenium have been assessed as antioxidant components in the human diet (34).

Results and Discussion

Cancer death rates have been constantly decreasing for the past 2 decades (12).

In 2015, there assessed about 1 658 370 new cancer cases detected and 589 430 cancer deaths in the United States (27), which nearly 171 000 of the estimated 589 430 cancer deaths would be made by tobacco smoking. Moreover, the World Cancer Research fund has assessed that up to 25% of the cancer cases that appear in economically developed countries like the United States are associated to overweight or obesity, physical inactivity and/or poor nutrition, thus could also be inhibited (Table 1) (27).

This statistic have shown that we should try to decrease or control cancers risk. For example, we should take a suitable diet.

An antioxidant supplement can be generally expressed as any dietary supplement which exerts antioxidant actions.

Table 1. Estimated new cancer cases and deaths, United States, 2015^a

	Estimated new cases for both sexes	Estimated deaths for both sexes
All sites	1 658 370	589 430
Breast	234 190	40 730
Genital system	329 330	58 670
Prostate	220 800	27 540
Skin (excluding basal & squamous)	80 100	13 340
Melanoma of the skin	73 870	9 940
Digestive system	291 150	149 300
Respiratory system	240 390	162 460
Urinary system	138 710	30 970
Lymphoma	80 900	20 940
Endocrine system	64 860	2 890
Leukemia	54 270	24 450
Oral cavity & pharynx	45 780	8 650
Brain & other nervous system	22 850	15 320
Myeloma	26 850	11 240
Soft tissue (including heart)	11 930	4 870
Bones & joints	2 970	1 490
Eye & orbit	2 580	270
Other & unspecified primary sites	31 510	43 840

^a More deaths than cases may return lack of specificity in recording underlying cause of death on death certificates and/or an undercount in the case estimate.

These compounds can be bought over the counter individually or in mixture with other antioxidants, vitamins, or vitamins and minerals as constituents of multivitamins. Many cancer patients suppose which antioxidant supplements taken during therapy may reduce oxidative damage to wholesome tissues, have through anti-cancer activity, or give general health assistances. Some supplements consumed primarily for specific targets (e.g., soy isoflavones to counter hot flashes, melatonin to improve immune function, and glutamine to inhibit stomatitis) moreover have general antioxidant actions (35)

Altogether, many experimental studies, including case-control studies and group studies have search whether the consumption of dietetic antioxidant supplements is associated with decreased risks of cancer in people. In general, these investigations have yielded mixed results (36).

In fact, extra great randomized controlled experiments are needed to provide perfect scientific evidence about the potential advantages or harms of taking antioxidant supplements in the course of cancer therapy.

For instance, some randomized controlled experiments involved only little numbers of patients, have examined whether intake antioxidant supplements for the period of cancer cure modifies the efficiency or decreases the toxicity of specific treatments (14). Even though these experiments had mixed results, specific found which people who took antioxidant supplements for the period of cancer treatment had worse results, particularly if they were smokers (37).

In Table 2, association between some cancers with antioxidant supplements have been shown.

Conclusion

On the whole, we should consume antioxidant supplements with caution until exact scientific evidences are

provided and more is known about them. As well, cancer patients should advise their doctors about their custom of any nutritional supplement.

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Conflicts of interest

The authors declared no competing interests.

Ethical considerations

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Table 2. Relation between antioxidants and some cancers

Cancer	Antioxidant	Effect on cancer	References
NMSC	Vitamin A, C, E & β -carotene	No effect	(38,39)
	Selenium	Increased risk	(40)
Bladder	Vitamin C	Increased risk	(41)
Prostate	High-dose vitamin E	Increased risks	(41)
	Vitamin E & selenium	Decreased risks	(41)
Breast	β -Carotene, retinol, vitamin C & E	Decreased risks	(35)
Gastrointestinal	β -Carotene, vitamins A, E and selenium, alone & blended	High-dose vitamin E may increase death; selenium may be beneficial in the inhibition of cancer; other antioxidants no effect	(42)
	Vitamin C	Decreased risks	(43)
Lung	Combination of β -carotene & vitamin A	No benefit and may have an adverse effect on the incidence of lung cancer and on the risk of death from lung cancer	(44)
	Tocopherol (in vitamin E)	Intake may reduce the risk of lung cancer but requires further investigation	(31)
Esophageal	High-dose β -carotene	Increased risk	
	Vitamin C & β -carotene	Decreased risk	(45,46)
Colorectal	Carotene, riboflavin & vitamin C	Decreased risk	(47)
	Calcium & vitamin D	Increased risk	(47)
Oral cavity & pharyngeal	Vitamin E & polyphenols, flavonoids, proanthocyanidin	Decreased risk	(48,49)
Digestive system	Lycopene, polyphenols (in tomato and garlic & onion), phenolic constituents (in olive oil)	Decreased risk	(50)

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