

Significance of Dietary Antioxidants in Averting Cancer

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Abstract

Reactive oxygen species are constantly produced in our body due to various factors like environmental pollution, unhealthy diet habits, cellular metabolism etc. Epidemiological studies suggest that the intakes of antioxidants are inversely related to the cancer risk. While the cell culture studies confirm the effect of antioxidants against cancer, the clinical trials remains inconclusive. The human population is heterogeneous regarding Reactive oxygen species (ROS), so screening the human population for developing the risk of cancer will provide a scientific ground for the application of antioxidants. Research is increasingly showing that those who eat antioxidant-rich foods reap health benefits. Foods, rather than supplements, may boost antioxidant levels because foods contain an unmatched array of antioxidant substances.

Keywords: Reactive oxygen species; Free radical; tumor; Dietary antioxidants

Introduction

An uncontrolled rapid cell growth/division or proliferation can be called as cancer. A cancerous cell to be called as malignant tumor where as normal cell called as benign tumor [1]. Although there are many kinds of cancer, they all start because abnormal cells grow out of control. Untreated cancers can cause serious illness and it also may leads to death. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells. Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases [2]. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer [3]. Causes of cancer, including genetic factors; lifestyle factors such as tobacco use, diet, and physical activity; certain types of infections; and environmental exposures to different types of chemicals and radiation [4]

Dietary antioxidants are substance that protects cells, tissues and DNA against the oxidative damage by free radicals. Dietary antioxidants include the micronutrients like vitamin A, vitamin C (ascorbic acid), vitamin E, beta-carotene, bioflavonoid and polyphenols etc [5]. Dietary antioxidants will help to reduce the free radicals circulating inside the body. Various dietary antioxidants have shown considerable promise as effective agents for cancer prevention by reducing oxidative stress which has been implicated in the development of many diseases, including cancer. Therefore, for reducing the incidence of cancer, modifications in dietary habits, especially by increasing consumption of fruits and vegetables rich in antioxidants are increasingly advocated. Numerous epidemiological studies have conducted to test the role of dietary antioxidants on prevention of cancer and vitamin C is found to have most significant effect [6]. Reactive oxygen species are produced inside the body as a result of cellular metabolism or the effect of environmental factors such as pollution and certain dietary factors. Dietary antioxidants act as a biological defense against cancer prevention. Vitamin C is an important antioxidant in extracellular fluid and inhibits the peroxidation of unsaturated lipids by scavenging or quenching free radical [7]. Vitamin C may prevent certain type of oxidative damage produced by infiltrating macrophages and neutrophils within the inflamed colon. The chemo preventive effects elicited by these natural dietary compounds are believed to include

anti-oxidative, anti-inflammatory activity, induction of phase II enzymes, apoptosis, and cell cycle arrest [8].

Types of Cancer

Carcinoma

Carcinoma is a malignant neoplasm of epithelial origin. It is a tumor that arises in the tissues that line the body's organs like the nose, the colon, the penis, breasts, prostate, urinary bladder, and the ureter. About 80% of cancer cases [9] are carcinomas [10]. The diagnosis of breast cancer falls into two broad categories, either estrogen receptor (ER)-positive or ER-negative, based on the level of ER in the cancer cells [11].

Sarcoma

Sarcomas are tumors that originate in bone, muscle, cartilage, fibrous tissue or fat. Ewing sarcoma (Family of tumors) and Kaposi's sarcoma are the common types of sarcomas [12].

Leukemia

Leukemia's are cancers of the blood or blood-forming organs. When leukemia develops, the body produces a large number of abnormal blood cells. In most types of leukemia, the abnormal cells are white blood cells.

Lymphoma

Lymphomas affect the lymphatic system, a network of vessels and nodes that acts as the body's filter. The lymphatic system distributes

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nutrients to blood and tissue, and prevents bacteria and other foreign “invaders” from entering the bloodstream.

Adenomas

Adenomas are cancers that arise in the thyroid, the pituitary gland, the adrenal gland, and other glandular tissues [13].

What Causes Cancer?

Radiation

High levels of radiation like those from radiation [14] therapies and x-rays (repeated exposure) can damage normal cells and increase the risk of developing leukemia, as well as cancers of the breast, thyroid, lung, stomach and other organs [15,16].

Ultraviolet (UV) radiation

UV radiations from the sun are directly linked to melanoma and other forms of skin cancer. These harmful rays of the sun cause premature aging and damage the skin. Artificial sources of UV radiation, such as sun lamps and tanning booths, also increase the risk of skin cancer. By wearing protective clothing and sunscreens and by avoiding prolonged exposure to the sun, one may reduce the risk of skin cancer [17].

Viruses

Some viruses, including hepatitis B and C, human papillomaviruses (HPV) [18], and the Epstein Barr virus, which causes infectious mononucleosis, have been associated with increased cancer risk. Immune system [19] diseases, such as AIDS, can make one more susceptible to some cancers.

Toxins

Bacterial protein toxins are among the most potent cell-killing molecules known [20].

Chemicals

Long term exposure to chemicals such as pesticides, uranium [21], nickel, asbestos, radon and benzene can increase the risk of cancer. Such carcinogens may act alone or in combination with another carcinogen, such as cigarette smoke, to increase the risk of cancer and other lung diseases [22].

Tobacco

Cigarette smoking and regular exposure to tobacco smoke greatly increase lung cancer [23]. Cigarette smokers are more likely to develop several other types of cancer like those of the mouth, larynx, esophagus, pancreas, bladder, kidney and cervix [24]. Smoking may also increase the likelihood of developing cancers of the stomach, liver, prostate, colon and rectum [25]. The uses of other tobacco products, such as chewing tobacco, are linked to cancers of the mouth, tongue and throat. The risk of cancer decreases soon after a smoker quits, while precancerous conditions often diminish after a person stops using smokeless tobacco.

Alcohol

Heavy drinkers face an increased risk of cancers of the mouth, throat, esophagus, larynx and liver. Some studies suggest that even moderate drinking may slightly increase the risk of breast cancer [26]. All cancers caused by cigarette smoking and heavy use of alcohol could be prevented completely.

Diet

High-fat, high cholesterol diets are proven risk factors for several types of cancer such as those of the colon, uterus and prostate. Obesity may be linked to breast cancer among older women as well as to cancers of the prostate, pancreas, uterus, colon and ovary. Many cancers that are related to dietary factors could be prevented. Healthy food choices and a well balanced diet including fiber, vitamins, minerals and low fat items may help to reduce cancer risk [27].

Others

Regular screening examinations by a health care professional can result in the detection of cancers of the breast, colon, rectum, cervix, prostate, testis, oral cavity, and skin at an earlier stage, when treatment is more likely to be successful. Self-examinations for cancers of the breast and skin may also result in detection of tumors at early stages. The screening-accessible cancers listed above account for about half of all new cancer cases. Primary ovarian carcinoid tumors are very rare; they represent less than 0.1% of all ovarian cancers [28].

Hereditary risk factors

Twenty percent of cancers are hereditary. This means that the abnormal gene responsible for causing cancer is passed from parent to child, posing a greater risk for that type of cancer in all descendants of the family. However, just because someone has a cancer-causing gene doesn't mean they will automatically get cancer. If hereditary cancer is suspected, family members should consider genetic counseling and testing to determine their risk. If diagnosed in the early stages, such cancers are most responsive to treatment [29]. Multiple Or Bilateral Cancers In Families In some families, cancers of one or more types develop in several family members significantly more often than the average cancer occurrence. Families with above average occurrence of breast cancer, for example, have been observed to have more cancers of the ovary, colon, or endometrium (body of the uterus) than expected. Osteosarcoma (OS) is the most frequent primary malignant tumor of the skeletal system in children and young adolescents [30].

Infection

Some viruses are linked to certain cancers. For example, people with persistent infection with the hepatitis B virus or the hepatitis C virus [31] have an increased risk of developing cancer of the liver. Another example is the link between the human papillomavirus (HPV) and cervical cancer. Most (possibly all) women who develop cervical cancer have been infected with a strain (subtype) of HPV at some point in their life. But, most viruses and viral infections are not linked to cancer [32].

Immune system

People with a poor immune system have an increased risk of developing certain cancers. For example, people with AIDS [33], or people on immunosuppressive therapy.

Rare or Unusual Types of Cancers

Soft tissue sarcomas of the head and neck are rare mesenchymal malignant neoplasms [34].

Antioxidants

Antioxidants are the agents which are having the capacity of delaying or to stop the oxidation processes [35], which is occurring under the influence of atmospheric oxygen or reactive oxygen species

[36]. By involving in the defense mechanism of the organism against the pathologies which are associated to the attack of free radicals, antioxidants can prevent the formation of free radicals. Anti oxidants works as enzymes, like superoxide dismutase, catalase, glutathione peroxidase or non enzymatic compounds, such as uric acid, bilirubin [37], albumin, metallothioneins. Endogenous Antioxidants can works as nutritional supplements [38] or pharmaceutical products, containing as active medicaments.

Epidemiological studies suggest that cancer incidence increased in last few years in Asian population [39]. Cancer is the second leading cause of death in the world after cardiovascular diseases [40]. So, there should be prevention method using the dietary supplements. Antioxidants are substances that may protect your cells against the effects of free radicals. Free radicals are molecules produced when your body breaks down food, or by environmental exposures like tobacco smoke and radiation. Free radicals can damage cells, and may play a role in heart disease, cancer and other diseases [41].

Sources of Antioxidants

Antioxidants are abundant in fruits and vegetables, as well as in other foods including nuts, grains, and some meats, poultry, and fish. The list below describes food sources of common antioxidants.

Natural compounds

Vitamin E, vitamin C (Ascorbic Acid) [42], β -carotene, vitamin E, flavonoids, minerals [43], vitamin D and vitamin K3 [44], Lutein, Lycopene, Selenium.

Synthetic compounds

Butylhydroxyanisole, Butylhydroxytoluene, Gallates, etc are also called as Neutraceuticals

In fact antioxidants are not only preventing the deleterious of free radicals [45] in the human body but also capable in the deterioration of fats [46] and other constituents of food stuffs [47].

Ideal features of antioxidants:

- Capable to work at minute concentrations
- Should not cause harmful effects
- Should be in a pleasant flavor, odor
- Should be easily soluble in fat
- Easily available & inexpensive

Benefits of Antioxidants

Antioxidants play a major role in the prevention of formation of free radicals and oxidative stress, cancer prophylaxis and therapy. By having the active component of tyrosine [48] or other phenol oxidases these phenols and poly phenols target analytes can be detected in many cancers [49-60]. Antioxidants are plays an important role in the aging [61] factor so can there might be a less chance of oxidation in the human body [62].

The epidemiological studies suggests that fruits and vegetables are the best protection against the development of diseases caused by oxidative stress, such as cancer, type 2 diabetes [63] obesity, coronary heart disease, [64] hypertension and [65] cataract [66].

In addition to antioxidants fruits and vegetables also contains the dietary plants such as aryteneoids, benzoic acid derivatives, phenolic compounds [67], flavonoids, ligans, ligins, proanthocyanides, stilbenes, coumarins [68] spices, berries, chocolate, cereals, nuts or seeds blackberries, walnuts, strawberries, artichokes, cranberries, brewed coffee, raspberries, pecans, blueberries, ground cloves, grape juice and unsweetened baking chocolate were also contains good amount of antioxidants [69].

Fruit juices, beverages and hot drinks contains good amounts of antioxidants, like polyphenols, vitamin C, vitamin E, [70]. Maillard reaction products, β -carotene, and lycopene [71]. Epidemiologic studies suggest that the usage of fruit juices, beverages and hot drinks was found to decrease the morbidity and mortality caused by degenerative diseases [72-77]. The total antioxidant potential is one of the key factors in investigating the relationship between dietary antioxidants [78] in cardiac [79] and distal gastric cancer [80] caused by the oxidative stress [81]. Usage of fruits and vegetables, as well as of grains and nuts involved in the decreasing the risk/occurrence of the chronic diseases [82-83]. Phytochemicals, plant derived molecules containing the antioxidant power can play against the chronic diseases [85].

Fiber rich foods contains good amount of phenolics are plays a major role in the prevention of chronic diseases such as neurologic disorders [86] these are also one of the sources of antioxidants [87]. By consuming high amount of flavonoids, human body can enhance the anti-proliferative and anti-inflammatory activity, [88] so can there might be a chance in the prevention of cancer and inflammatory diseases [89].

Role of Dietary Antioxidants in Cancer

The antioxidant activity of dietary nutrients is also susceptible to its environment, the presence of proteins and other antioxidants.

Formation of Free Radicals

Free radicals and other reactive oxygen species are derived either from normal essential metabolic processes in the human body or from external sources such as exposure to X-rays, ozone, cigarette smoking, air pollutants and industrial chemicals [90]. Some internally generated sources of free radicals are [91-93].

- mitochondria
- phagocytes
- xanthine oxidase
- reactions involving iron and other transition metals
- arachidonate pathways
- peroxisomes
- exercise
- inflammation
- Ischaemia /reperfusion.

Some externally generated sources of free radicals are

- cigarette smoke
- environmental pollutants
- radiation

- ultraviolet light
- certain drugs, pesticides, anaesthetics and industrial solvents
- ozone

Rancidity is also one of the factors which form the free radicals in cells. Rancidification is the decomposition of fats, oils and other lipids by hydrolysis or oxidation, or both. Hydrolysis will split fatty acid chains away from the glycerol backbone in glycerides. Antioxidants are often added to fat-containing foods in order to retard the development of rancidity due to oxidation [94].

Initiation

In the above reaction LH is the substrate molecule, for example, a lipid, with R· as the initiating oxidizing radical, [95] A highly reactive allyl radical (L·) is generated from the lipid in the above oxidation reaction, this allyl radical can able to react with the oxygen and forms a lipid peroxy radical (LOO·).

Propagation

By means of oxidation with the lipid the peroxy radicals further produces a lipid hydroperoxides (LOOH), these hydroperoxides break down to a broad range of compounds, like radicals, ketones, alcohols,

alkyl formats, aldehydes, [96] and hydrocarbons, including the alkoxy radical (LO·).

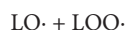
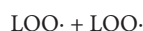
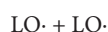
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These lipid hydroperoxides [97] often involved in transition metal ion catalysis, in reactions parallel to those involved in hydrogen peroxide, and yields lipid peroxy [98] and lipid alkoxy radicals.

Termination

Termination reactions have the combination of radicals to form non-radical products:



These Primary antioxidants may either delay or inhibit the initiation step by reacting with a lipid radical or inhibit the propagation step by reacting with peroxy or alkoxy radicals [99].

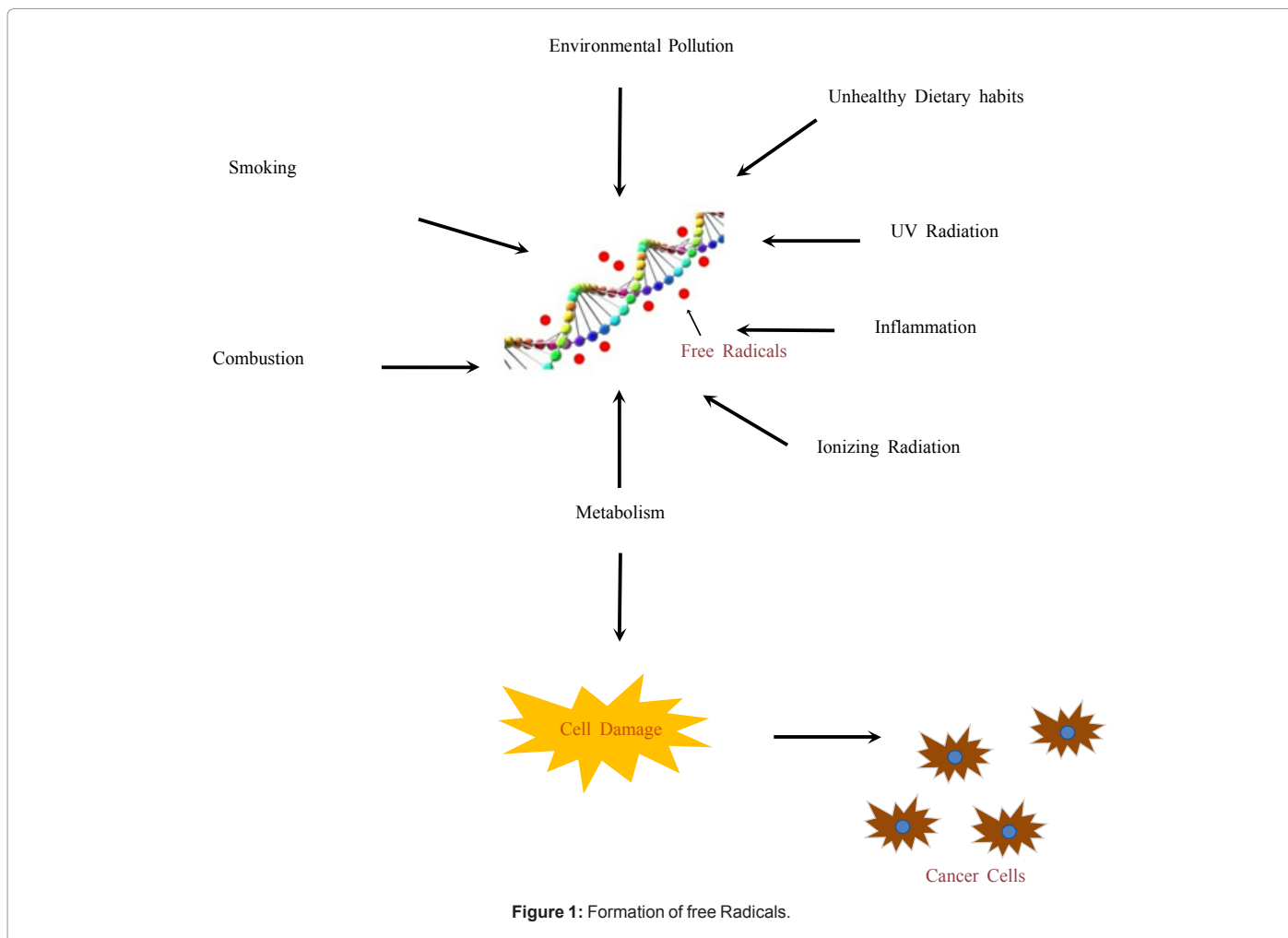


Figure 1: Formation of free Radicals.

Mechanism of Action of Antioxidants on Free Radicals

The antioxidants decrease the adverse effect of reactive oxygen [100]. These Reactive Oxygen Species (ROS) include hydroxyl radicals ($\cdot\text{OH}$), superoxide anions (O_2^-), singlet oxygen ($^1\text{O}_2$), hydrogen peroxides (H_2O_2), organic peroxides (R-OOH), and nitric oxide, peroxyxynitrite which are formed due to various environmental and dietary factors. Antioxidants heal these free radicals by providing them with the missing electron, so that they don't attack other cells and deprive them of electrons, so the damage to these cells is minimized. Additionally, antioxidants can restore a cell to its original condition, repairing the damage done to it by free radicals. Antioxidants also help to convert the free radicals into waste that is then ultimately removed from the body (Figure 1).

Conclusion

By this we can conclude that dietary antioxidants can provide a wide sort of health benefits, caused by the in the presence of free radicals on key biomolecules like lipids or nucleic acids. We can also prevent the various diseases which are occurring in the presence of Reactive Oxygen Species (ROS) like cancer and oxidative stress related diseases.

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