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Review Article

Antioxidant Foods and Diseases: Natural Antioxidants for Healthy Life

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Abstract: In this review first, general information on oxidants, antioxidants and molecular mechanisms of some diseases are given in order to understand importance of natural antioxidants in our health and then, scientific background for the safe use of the natural antioxidants is explained.
Keywords: Free radicals, Antioxidants, Foods, Diseases, Healthy life

INTRODUCTION

Free Radicals

Free radicals are potentially damaging molecules released in the body through normal metabolic processes and are capable of attacking the healthy cells of the body, causing them to lose their structure and function. Free radicals are electrically charged molecules and so react with other substances in order to neutralize themselves, a process called oxidation [1]. In free radical-mediated oxidation reaction, a reaction is first initiated as another free radical is formed, leading to thousands of free radical reactions within seconds of the initial reaction. Antioxidants act to stabilize or deactivate free radicals before they attack cells and so are essential for maintaining optimal cellular and systemic health and well-being. Free radicals are also called reactive oxygen species (ROS), a term that encompasses all highly reactive, oxygen-containing molecules. They can react with membrane lipids, nucleic acids, proteins and enzymes, and other small molecules, resulting in cellular damage [2].

These free radicals are formed via normal and natural body processes [3]. Our ancestors' diet was natural and fresh enough to supply plentiful antioxidants to counter the formation of free radicals. Free radicals are formed via [4]:

- Normal aerobic metabolic processes.
- White blood cell (phagocytes) defensive mechanisms, by which bacteria and viruses are killed, and by which foreign proteins (antigens) are denatured.
- The natural detoxification of toxic substances (such as nicotine in cigarette smoke).

Antioxidants

Antioxidants are compounds that neutralize the damaging effects of oxidation reactions. Researches indicate that antioxidants help prevent the development of some diseases [5]. Oxidative stress is a situation with oxidant potency, which can compromise the body's immune response, heighten the inflammatory response, increase the incidence of apoptosis (programmed cell death), and has been implicated in some devastating reactions in the body [6].

Antioxidants are found naturally in the body and a variety of foods – especially fruits and vegetables. Oxidation is cellular damage caused by free radicals. Our bodies have a built-in "defense system" of antioxidants that serve to prevent damage from free radicals. The main source of these antioxidants is fruits and vegetables that we recognize as food, the heritage of our pre-agricultural lifestyles. These foods provide antioxidant nutrients such as vitamins A, C, E and selenium [7].

There is accumulating evidence implicating free radicals in the formation of several diseases including coronary heart disease, cancer etc [8]. Therefore, antioxidants draw special attention in the therapy of some diseases. In particular, antioxidant foods seem to have great potential in this regard.

As to the subject, many studies have been conducted throughout the world. Beneficial effects were observed in the patients with coronary heart disease and cancer when antioxidant foods (vegetables, fruits, legumes, herbs and spices) were ingested regularly [9].

ANTIOXIDANT FOODS AND CORONARY HEART DISEASE

Atherosclerosis is a complex process involving the deposition of plasma lipoproteins and the proliferation of cellular elements in the artery wall [10]. This chronic condition advances through a series of stages beginning with fatty streak lesions composed largely of lipid-engorged macrophage foam cells and ultimately progressing to complex plaques consisting of a core of lipid and necrotic cell debris covered by a fibrous cap. These plaques provide a barrier to arterial blood flow and may precipitate clinical events, particularly under conditions that favor plaque rupture and thrombus formation [11].

Dietary recommendations to reduce the risk of coronary heart disease have focused largely on the intake of nutrients that affect established risk factors, including plasma lipid and lipoprotein levels, blood pressure, and body weight [12]. Recent developments in our understanding of the atherosclerotic process and factors that trigger ischemic events have led to the consideration of dietary constituents that may alter risk through other mechanisms. Prominent among these are natural antioxidants, which are proposed to inhibit multiple proatherogenic and prothrombotic oxidative events in the artery wall.

Over the past 2 decades, considerable evidence has been gathered in support of the hypothesis that free-radical-mediated oxidative processes and specific products arising as a result of these processes play a key role in atherogenesis [13]. Oxidation of low-density lipoproteins (LDLs), which undergo multiple changes on oxidation are thought to be proatherogenic since oxidation of LDL lipids leads to the production of a diverse array of biologically active compounds, including some that influence the functional integrity of vascular cells. Among the well-characterized effects are increases in the expression of endothelial cell surface adhesion molecules that facilitate the mobilization and uptake of circulating inflammatory cells and alterations in the chemotactic properties of monocytes and monocyte-derived macrophages in a manner expected to increase their residence within the artery wall [14, 15]. Oxidation of the apolipoprotein B component alters LDL receptor recognition properties, leading to internalization of LDLs by macrophages via scavenger receptors, a key step in the formation of macrophage-derived foam cells [16].

In addition to these effects, oxidative processes are proposed to play a role in lesion maturation and the precipitation of clinical events. This may involve effects on intimal proliferation, fibrosis, calcification, endothelial function and vasoreactivity, plaque rupture, and thrombosis [17]. Oxidants are products of normal aerobic metabolism and the inflammatory response. They constitute a chemically and compartmentally diverse group, and it is presently unknown which, if any, are critical to the disease process. In addition to the different sources and types of oxidants, ambiguity in relating specific oxidants to the disease process arises from the multitude of pathophysiological events linked to oxidation, the paucity of methods for measuring these short-lived species within the sequestered environment of the artery wall, and the variable modulating effects of counteractive antioxidants. With regard to the latter, although oxidant formation is an inevitable feature of aerobic life, oxidant-mediated disease promotion is proposed to occur only under circumstances in which these agents overwhelm antioxidant defenses [18, 19].

Like oxidants, antioxidants constitute a diverse group of compounds with different properties. They operate by inhibiting oxidant formation, intercepting oxidants once they have formed, and repairing oxidant-induced injury. In terms of the coronary heart disease process, several points of antioxidant intervention have been proposed. Inhibition of LDL oxidation is the most-well characterized of these and includes effects on the concentration or reactivity of oxidants capable of modifying LDL and on the susceptibility or resistance of LDL to these oxidants [20, 21].

Although the antioxidant defense system includes both endogenously and exogenously (diet) derived compounds, dietary antioxidants including vitamin C, vitamin E, and carotenes have received the greatest attention with regard to coronary heart disease prevention [22, 23]. A number of other dietary factors are proposed to act as antioxidants and have been suggested to protect against coronary heart disease [24].

In addition to previous studies given above, our studies show that coronary plaques can be significantly regressed and/or completely eliminated in some cases by suitable antioxidant supplementation. Even in some volunteer patients, in whom no significant improvements have been observed in the angiography examination, it has been observed that hypo kinetic part of the heart due to a previous infarction gains normal function owing to revascularization after regular consumption of the antioxidant supplements. It has been reported that almost, all the subjects feel much better during the period of food supplementation. In addition to increased physical capability, their blood tensions and blood cholesterol levels have been reported to decrease significantly during this period [25-39].

ANTIOXIDANT FOODS AND CANCER

Cancer begins as a single abnormal cell that begins to multiply out of control. Groups of such cells form tumors and invade healthy tissue, often spreading to other parts of the body. Carcinogens are substances that promote the development of cancerous cells [40]. They may come from foods, from the air, or even from within the body. Most carcinogens are neutralized before damage can occur, but sometimes they attack the cell's

genetic material (DNA) and alter it. It takes years for a noticeable tumor to develop. During this time, compounds known as inhibitors can keep the cells from growing. Some vitamins in plant foods are known to be inhibitors. Dietary fat, on the other hand, is known to be a promoter that helps the abnormal cells grow quickly [41, 42].

Of the many diseases that affect people these days, cancer is among the most feared. But despite a wealth of scientific data, most people remain unaware of how they can reduce their risk of developing cancer. It has been known that, as much as 80 percent of all cancers are due to identified factors, and thus are potentially preventable. Thirty percent are due to tobacco use, and as much as 35 to 50 percent are due to foods. It is easy to control these and other risk factors [43, 44].

A high-fiber diet is known to reduce diseases of the digestive tract. It has been observed that in countries where diets are high in fiber (that is, plant-based diets), there were fewer cases of colon cancer. Around the world, this has proven true. The highest fiber intakes are found in non-industrialized nations where meat is scarce and plant foods fill the menu [45]. Animal products contain no fiber. In the countries that their diets are based upon animal products have the highest rates of colon cancer. While no one is certain exactly how fiber protects against digestive tract disorders, there are several possibilities. By definition, fiber cannot be digested by humans early in the digestive process. It moves food more quickly through the intestines, helping to eliminate carcinogens. It also draws water into the digestive tract. The water and fiber make fecal matter bulkier, so carcinogens are diluted. Fiber is also protective against other forms of cancer. Studies have shown that stomach cancer and breast cancer are less common on high-fiber diets. Fiber affects levels of estrogens in the body. Estrogens are normally secreted into the intestine, where the fiber binds with the hormone and moves it out of the body [46, 47]. Without adequate fiber, the estrogen can be reabsorbed from the intestine into the bloodstream. High levels of estrogen are linked to a higher risk of breast cancer. The best sources of fiber are whole grains, beans, peas, lentils, vegetables, and fruits. Unrefined and unpeeled natural foods are highest in fiber [48].

Cross-cultural studies have revealed that the populations with the highest levels of fat consumption are also the ones with the highest death rates from breast and colon cancer [49]. The lowest rates are in groups with the lowest consumption of fats [50]. Migration studies help to rule out the influence of genetics. Many studies indicate that fat in foods increases one's risk for cancer, and it may also adversely affect breast cancer survival rates for those who have cancer. Although the total amount of fat one eats is of concern, there is evidence that animal fat is much more harmful than vegetable fat. One study noted a 200 percent increase in breast cancer among those who consume beef or pork five to six times per week. Researchers note that meat is more closely associated with colon cancer than any other factor [51-52]. Meat and milk are also linked to both prostate and ovarian cancers. Fat has many effects within the body. It increases hormone production and thus raises breast cancer risks. It also stimulates the production of bile acids which have been linked to colon cancer [53-55].

IMPORTANCE OF VEGETABLES AND FRUITS IN CANCER

Not only are vegetables low in fat and high in fiber, they also contain many cancer-fighting substances. Carotenoids, the pigment that gives fruits and vegetables their dark colors, have been shown to help prevent cancer. Beta-carotene, present in dark green and yellow vegetables, helps protect against lung cancer and may help prevent cancers of the bladder, mouth, larynx, esophagus, breast, and other sites [56]. Vegetables such as cabbage, broccoli, kale, turnips, cauliflower, and Brussels sprouts contain flavones and indoles which are thought to have anti-cancer activities [57]. Vitamin C, found in citrus fruits and many vegetables, may lower risks for cancers of the esophagus and stomach. Vitamin C acts as an antioxidant, neutralizing cancer-causing chemicals that form in the body. It also blocks the conversion of nitrates to cancer-causing nitrosamines in the stomach. Selenium is found in whole grains and has the same antioxidant effects as vitamin C and beta-carotene. Vitamin E also has this effect [58]. However, high dose of selenium is toxic. All the evidence shows that a low-fat, high-fiber diet that includes a variety of fruits, vegetables, whole grains, and beans, is the best for cancer prevention. Not surprisingly, vegetarians, whose diets easily meet these requirements, are at the lowest risk for cancer. Vegetarians have about half the cancer risk of meat-eaters. Vegetarians have higher blood levels of beta-carotene. They consume more vitamin C, beta-carotene, indoles, and fiber than meat-eaters. Vegetarians also have stronger immune systems [59]. It has recently been discovered that vegetarians have more than twice the natural killer cell activity of meat-eaters. Natural killer cells are specialized white blood cells that attack and neutralize cancer cells. Also, vegetarians tend to eat more soy products than meat-eaters. Soybeans contain many substances that are anticarcinogens, including lignans and phytoestrogens. A diet that is rich in soybeans may be one reason for the lower incidence of breast cancer in the world [60].

A cancer prevention diet is one that is high in fiber, low in fat (especially animal fat), and includes generous portions of fruits and vegetables. It also minimizes or excludes alcohol. The best diets are pure vegetarian diets.

In our studies, we have observed that immune system is strengthened in cancer patients due to use of antioxidant food supplements. In particular, we obtained significant improvements in the patients with prostate cancer. We also observed that white blood cell count is maintained at the normal level in the cancer patients consuming these supplements during the chemotherapy [61-66].

ANTIOXIDANT FOODS AND OTHER DISEASES

Ageing

It has been argued that the "damage to cells caused by free radicals is believed to play a major role in the ageing process and in disease progression [67]. Antioxidants are our first line of defense against free radical damage, and are critical for maintaining optimum health and well-being. The need for antioxidants becomes even more critical with increased exposure to free radicals. Pollution, cigarette smoke, drugs, illness, stress, and even exercise can increase free radical exposure." Because many environmental factors contribute to what the terms, "oxidative stress", the assessment of individual susceptibility becomes important [68]. As part of a healthy lifestyle and a well-balanced, wholesome diet, antioxidant supplementation is now being recognized as an important mean of improving free radical protection.

This view is supported by many scientists who observe that "Metabolism, like other aspects of life, involves trade-offs. Oxidant by-products of normal metabolism cause extensive damage to DNA, protein, and lipid. This damage is a major contributor to ageing and to degenerative diseases of ageing such as cancer, cardiovascular disease, immune-system decline, brain dysfunction, and cataracts. Antioxidant defenses against this damage include ascorbate, tocopherol, and carotenoids. Dietary fruits and vegetables are the principal sources of ascorbate, carotenoids are tocopherol. Low dietary intake of fruits and vegetables doubles the risk of most types of cancer as compared to high intake and also markedly increases the risk of heart disease and cataracts [69-73].

Other diseases related to oxidant stress

Free radical damage to cells is now believed to contribute significantly to ageing and to degenerative ageing diseases such as cancer, cardiovascular disease, cataracts, immune system decline, and brain dysfunction. Free radicals activity has been implicated in at least 50 diseases. Antioxidants reduce free radical formation. Our modern lifestyles may limit the availability of antioxidants, allowing free radicals to cause cumulative and debilitating damage to our cells [74-78].

Some of the diseases attributed to oxidative stress include: Urinary problems including prostate hypertrophy and kidney stone formation, Migraine, Asthma, Sinusitis, Alzheimer's Disease, Macular Degeneration, Autoimmune Disease Multiple Sclerosis, Cancer Muscular Dystrophy, Cardiovascular Disease, Cataract formation, Parkinson's Disease, Diabetes, Rheumatoid Arthritis, Menstrual problems and Ischemic-Reperfusion Injury, etc.

Different antioxidants are effective against different diseases, so the science of antioxidant treatment will become quite complex. It has been stated that epidemiological studies show an inverse correlation between blood serum levels of carotenoids, tocopherols and retinol and the incidence of various cancers and other human diseases [79-81].

Lifestyles

Our 21st century technological and industrial way of life contributes significantly to an increase in the body's oxidant load. Following is the list given a number of things that increase our oxidant load [82-88]:

- Vigorous exercise, accelerating cellular metabolism,
- Chronic inflammation, infections, and other illnesses,
- Exposure to allergens, radiation, pollution,
- Exposure to drugs or toxins such as cigarette smoke, pollution, pesticides, and insecticides.

ANTIOXIDANT COMPOUNDS

Here are osome antioxidants [89-93]:

- Vitamin C, vitamin A, vitamin E,
- Low molecular weight compounds such as glutathione and lipoic acid. Glutathione is an important water-soluble antioxidant, synthesized from the amino acids glycine, glutamate, and cysteine.
- Antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase, and glutathione reductase that catalyse free radical quenching reactions.
- Antioxidant enzymes that metabolize oxidative toxic intermediates require micronutrient or trace element cofactors such as selenium iron, copper, zinc, and manganese for optimum catalytic activity,
- Metal binding proteins, such as ferritin, lactoferrin, albumin, and ceruloplasmin that sequester free iron and copper ions, capable of catalyzing oxidative reactions,
- Numerous other antioxidant phytonutrients present in a wide variety of plant foods,
- Polyphenols include bioflavonoids, organic acids and phenolic acids, and most of the antioxidant activity in foods is attributed to its polyphenol content. Another group of dietary antioxidant substances are plant-derived substances collectively termed

"phytonutrients" or "phytochemicals". About 3,000 plant-derived flavonoid substances have been described. In humans, flavonoids have antioxidant effects serving as anti-inflammatory, antiallergenic, anti-viral, anti-aging, and anti-carcinogenic activity compounds. In addition to an antioxidant effect, it has been reported that "flavonoid compounds may exert protection against heart disease through the inhibition of cyclooxygenase and lipoxygenase activities in platelets and macrophages".

Most antioxidant combinations contain a standard ingredient, namely vitamin C, vitamin E, beta-carotene, and the mineral selenium. Some combinations include new antioxidants, such as proanthocyanidins (flavonoids found in grape seed extract, pine bark, and red wine), N-acetylcysteine (NAC), alpha-lipoic acid, coenzyme Q_{10}, and zinc [94-98]. Others feature potent herbal antioxidants such as ginkgo biloba, garlic, green tea etc [99-103].

The word nutraceutical refers to foods or parts of foods that provide medical or health benefits, including the prevention and/or treatment of disease. Some examples of relationships between nutraceuticals and health benefits include the importance of calcium in preventing osteoporosis, folate in the prevention of neural tube defects in infants and the role of decreasing dietary fat and increasing fibre in the prevention of colon cancer. Phytochemicals and antioxidants are two specific types of nutraceuticals [104].

NATURAL HERBAL BALANCE AGAINST OXIDATIVE STRESS

Modern living has increased the challenges to our antioxidant defense system. The term "oxidative stress" has been coined to represent a shift towards the pro-oxidants in the pro-oxidant/antioxidant balance. This is caused by an increase in oxidative metabolism. This oxidative stress at the cellular level is caused by many factors, including exposure to alcohol, medications, trauma, cold, infections, poor diet, toxins, radiation, or strenuous physical activity. This is why very fit athletes are more prone to get "flue" and "colds" - their training regime has increased their oxidative stress. Protection against these processes requires antioxidant substances derived directly or indirectly from the diet. An inadequate diet - modern fast foods - lacking antioxidant nutrients may not allow one's full antioxidant potential, so increasing overall oxidative stress.

Diseases are proposed to be associated with oxidative stress [105-113]: Atherosclerosis, Anemia**,** Myocardial infarction, Multiple sclerosis**,** Cancer, Muscular dystrophy, Pulmonary dysfunction, Pancreatitis**,** Emphysema, Parkinson's disease, Cataracts, Alzheimer's disease**,** Macular degeneration, Neonatal lipoprotein oxidation**,** Degenerative retinal damage, Drug reactions**,** Arthritis and inflammatory diseases, Skin lesions**,** Inflammatory & immune injury, Ageing**,** Inflammatory bowel disease and colitis, Stroke**,** Diabetes, Shock, trauma, and ischemia**,** Renal disease and hemodialysis, Halogenated hydrocarbon liver injury.

The human body utilizes an integrated antioxidant system where different natural antioxidants complement each other. The reducing potential of each antioxidant within the whole defense system is enhanced when a full complement of antioxidants is available. As such, the best source of antioxidants is a natural source with a balanced mix of available antioxidants.

FOOD SELECTION CRITERIA AND MAJOR CONTENTS OF ANTIOXIDANT FOODS

We recommend following criteria for the food selection in the preparation of antioxidant foods.

- They must be non-toxic and have no side effects or drug interactions.
- General active components of their contents must be known.
- Safe daily dosages must be known.
- Mostly, their antioxidant potentials should be higher than a base line value.

Under the lights of all these explanations, it has been concluded that natural antioxidant foods can significantly support the medicinal therapies of the patients without any toxicity.

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