NUTRI NEWS

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ANTIOXIDANTS

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Nowadays you can't read or hear anything related to health without coming across the term "antioxidant." Almost every new product is in some way touted for its beneficial antioxidant properties. However, this claim raises many questions. What really is an antioxidant? Are antioxidants truly related to health benefits? Do I need more antioxidants? While the subject of antioxidants is extensive, considering a few of these basic questions can help you determine just what role antioxidants have in providing you with significant health benefits.

What are free radicals?

First we need to understand a few important chemical processes. Key to an understanding of antioxidants is the concept of "free radicals." Technically speaking, a free radical can be defined as "any chemical species capable of existence that contains one or more unpaired electrons." Simply speaking, all molecules are composed of atoms and all atoms have a nucleus around which electrons orbit. Due to various energetic principles, these electrons generally orbit their respective nuclei in pairs. However, various circumstances can cause a molecule to either loose an electron, or gain an extra electron. The result is a molecule with an unpaired electron. A molecule with an unpaired electron is considered a free radical. Because the free radical state is by definition unbalanced (extra or missing electrons), the free radical is highly reactive, meaning it will try to combine with other molecules to "steal" an electron and return to a stable state. This, of course, makes the molecule that has lost an electron a free radical as well. So, this newly formed free radical must regain its lost electron from another molecule, in turn creating yet another free radical. This becomes a self-perpetuating process, as each time a free radical attacks a molecule, a new free radical is formed.

Where do free radicals come from?

Essential to understanding the chemistry of free radicals is the role played by oxygen. The simple act of breathing in oxygen to produce ATP (energy molecules) for use in our metabolism results in the production of free radicals. So, one source of free radical production is the oxidative metabolism involved in the body's production of energy. A second source of free radicals is found in certain types of white blood cells (phagocytic cells). These cells are responsible in part for destroying unwanted microbes and other infectious invaders. One way in which these cells achieve their destructive ability is by the production of free radicals. This demonstrates both the dangerous power of free radicals as well as their practical utility within the body.

Free radicals are also a result of enzymatic production. Enzymes that comprise the cytochrome P450 system (enzymes involved in various oxidative reactions including drug detoxification) produce free radicals as a by-product. Additionally, the activity of the enzyme xanthine oxidase can result in the production of free radicals that are in part involved in the tissue damage that occurs during surgery that involves ischemia followed by reperfusion. Finally, sources as simple as cigarette smoke and sunlight can also result in the formation of free radicals.

Are free radicals harmful?

Excessive production of free radicals can cause damage. Fats, proteins, carbohydrates, and DNA are all subject to free radical damage. Once damaged, a tissue may no longer function properly. For example, membranes lose their ability to properly transport nutrients, lipoproteins particles (composed of both fat and protein) become altered and more atherogenic, and damaged DNA can lead to potential mutations. Free radical damage is associated with almost every disease, including arthritis, heart disease, cancer, cataract, Alzheimer's, and Parkinson's. What remains unclear is the degree to which free radical production precipitates or results from the disease pathology.

Antioxidants protect against free radical damage

Fortunately, our bodies have protective mechanisms against free radical damage. These mechanisms take the form of antioxidants. Antioxidants can be grouped into many categories; however, the easiest way to categorize them is into one of the following groups: antioxidant enzymes or low molecular weight antioxidants.

Antioxidant enzymes

Antioxidant enzymes include:

- **Superoxide dismutase**
  Superoxide dismutase converts a highly reactive form of oxygen called superoxide to hydrogen peroxide, with the help of copper and zinc or manganese. Superoxide is formed in the body through various processes, including oxidative metabolism.
- **Catalase**
  While hydrogen peroxide is technically not a free radical, it is considered a reactive oxygen species. In other words, under the proper conditions hydrogen peroxide can contribute to the formation of free radicals. Consequently, catalase is designed to convert the hydrogen peroxide formed by superoxide dismutase as well as other superoxide within the body to oxygen and water.
- **Glutathione peroxidase**
  Like catalase, glutathione peroxidase removes peroxides that can contribute to the formation of free radicals. With the help of glutathione, glutathione peroxidase converts molecules such as lipid peroxides (peroxides formed on fatty acids as a result of free radical damage) to less reactive molecules.

Low molecular weight antioxidants

Other than enzymes, antioxidants take the form of individual molecules. In general terms, they are considered antioxidants due to their ability to donate one of their electrons to a free radical, thereby "quenching" and eliminating the radical. While the antioxidant itself becomes a free radical, it is usually much less reactive than the original radical being quenched. Consequently, the antioxidant radical does not result in further damage. In fact, many antioxidants do not function independently, but rather synergistically to help recycle other antioxidants, thereby allowing for optimal antioxidant activity. For example, once vitamin E functions as an antioxidant and donates its electron, it cannot function again until it is "recharged" with its missing electron. Vitamin C donates its electron to vitamin E, allowing it to function again. What develops is a complex network or partnership of antioxidants that not only fights free radicals, but also serves to regenerate one another.

Vitamin E

Arguably the most well know antioxidant, vitamin E, is not a single compound, but technically a family of compounds including both alpha, beta, gamma, and delta tocopherols and tocotrienols. However, when referring to vitamin E, most people are speaking of alpha-tocopherol or a mixture of the four tocopherol isomers. Vitamin E is lipid soluble and is transported within the body primarily in low density lipoprotein cholesterol particles (LDL), where it functions to help prevent the oxidation of the fatty acids and proteins that comprise the LDL particle. If LDL particles are not protected from free radical damage they can become modified by oxidative processes, which results in the particle becoming more atherogenic. Oxidized LDL particles are selectively taken up by macrophages and contribute to the formation of fatty streaks and ultimately atherosclerotic plaques. It stands to reason that if oxidized LDL particles are involved in the progression of atherosclerosis and if vitamin E protects LDL particles from oxidation, then vitamin E may have a significant application in preventing heart disease. Research has demonstrated that supplementation with vitamin E protects LDL particles from oxidation and that people who consume diets high in vitamin E have a reduced risk for developing atherosclerosis. Additionally, within the past five years a number of clinical trials have demonstrated that vitamin E supplementation (~ 400 IU/d) can reduce the rate of restenosis in coronary vessels, as well as reduce the risk for suffering a non-fatal heart attack in certain individuals. Although vitamin E is a fat soluble vitamin, it is not stored in the liver to the extent that vitamin A and D are stored. Consequently, toxicity from excess intake of vitamin E is rare.

Natural versus synthetic vitamin E

For most vitamins, the synthetically produced version of the molecule is identical to the natural form. Alpha-tocopherol occurs as one isomer in nature (denoted RRR-alpha-tocopherol, or d-alpha-tocopherol). However, when alpha-tocopherol is made synthetically, the process generates seven additional isomers. They are all considered alpha-tocopherol, but their 3-dimensional structures differ. Interestingly enough, the liver contains a transfer protein that is able to discriminate between the natural and synthetic forms and selectively puts the natural isomer in lipoprotein particles more readily than the seven other isomers. While synthetic vitamin E is not inherently bad, if equal amounts of synthetic and natural vitamin E are consumed, over time supplementation with natural vitamin E will result in almost two-fold greater plasma and tissue concentrations.

Carotenoids

The carotenoids are a group of greater than 500 hundred different pigments found in plants. However, there are only a small number of carotenoids in significant amounts in human blood and tissues, including alpha carotene, beta-carotene, cryptoxanthin, lutein, lycopene, and zeaxanthin. Carotenoids function as antioxidants, but perform a bit differently from other antioxidants. Certain carotenoids are able to destroy a particularly damaging form of oxygen termed singlet oxygen. A significant body of research supports the hypothesis that a diet rich in carotenoids is related to reductions in the risk for many diseases, including cancer, heart disease, and age-related macular degeneration.

Recently, much attention has been given to the carotenoids lutein and zeaxanthin. While zeaxanthin is not yet available as an individual carotenoid, it can be found in supplements containing natural beta-carotene. Lutein and zeaxanthin are the only two carotenoids found in the macula of the eye and may play a significant role in the prevention of age-related macular degeneration (AMD). People who consume diets rich in lutein and zeaxanthin-containing foods (spinach, and other greens) have a reduced risk for developing AMD.

Vitamin C

Ascorbic acid is probably the most well-known water soluble antioxidant. Unlike vitamin E and beta-carotene, vitamin C is not transported in lipoprotein particles but rather circulates freely in plasma. In addition to many of vitamin C's functions as a coenzyme, it is a strikingly powerful reducing agent. In other words, it gives up electrons exceedingly well, and therefore serves as an excellent antioxidant. Vitamin C is crucial for the role it plays in the recycling of vitamin E and other antioxidants. It is particularly important for immune function, eye health, cancer and cardiovascular disease prevention, as well as other diseases in which free radicals are suspected to play a role. Smoking is particularly detrimental to vitamin C metabolism, which is why smokers have lower plasma vitamin C levels as well higher levels of oxidative stress. Therefore, vitamin C supplementation appears to be of some benefit to smokers.

Glutathione

Glutathione (GSH) is a tripeptide consisting of the amino acids glutamic acid, cysteine, and glycine. GSH acts as a substrate for a number of enzymes including the peroxide-removing enzyme glutathione peroxidase. In addition, GSH has the ability to scavenge free radicals directly. Cellular GSH levels are high in many tissues, including the eye and the liver where GSH acts to prevent damage from radicals and detoxify dangerous compounds. Decreased GSH levels are found in numerous disease states, which may have either resulted from or predisposed the individual to the condition. Supplementation with GSH and/or its precursor cysteine is beneficial to maintaining optimal antioxidant status. GSH also helps recycle vitamin C as well as other antioxidants.

Lipoic Acid

Alpha-lipoic acid, (also known as thioctic acid) is a unique antioxidant because it possesses both water and fat-soluble characteristics. Lipoic acid functions as a cofactor in dehydrogenase enzyme complexes, such as the mitochondrial pyruvate dehydrogenase system. Consequently, lipoic acid plays an important role in the conversion of glucose to energy. More recently, it has been observed that lipoic acid can function independently from its role as a cofactor. Lipoic acid is able to directly scavenge free radicals and, like vitamin E, can help prevent lipid peroxidation. However, due to its dual solubility, it can also scavenge free radicals not located in lipid membranes. This also allows lipoic acid to help regenerate other antioxidants in the complex web of antioxidant interactions. Research demonstrates that lipoic acid can play an important role in diabetes. Like many other diseases, diabetes is associated with increased oxidative stress, which may contribute to the progression of pathologies associated with the disease. Supplementation with at least 600 mg/d of lipoic acid has been shown to significantly improve glucose metabolism. Research currently underway may help to determine the effect of lipoic acid on long term diabetic complications.

Bioflavonoids

Bioflavonoids, also known as flavonoids, are phenolic compounds (many of which have phytoestrogenic effects) that occur naturally in many plants. Flavonoids are an extremely complex group of compounds. Briefly, they are generally divided into six categories:

Isoflavones - found predominantly in soy,
Flavonols - found in onions, kale and broccoli,
Flavones - found in greens, including thyme and parsley,
Flavonones - found in citrus fruits,
Catechins - found in tea and apples,
Anthocyanidins/Proanthocyanidins - found in grapes, cherries, strawberry and other colored fruits.

Many of these flavonoids exhibit potent antioxidant activity and interact with other antioxidants to help fight free radicals. Interestingly, cultures that consume diets high in flavonoid-containing foods have significantly lower incidences of certain

diseases. Recent studies indicate that flavonoids have the ability to inhibit tumor growth in vitro, increase capillary function, improve venous insufficiency, reduce the susceptibility of LDL to oxidation, as well improve other parameters associated with free radical damage. Given the complexity of this family of compounds, scientists still have a great deal to learn in terms of the exact mechanisms by which these compounds may offer protection against disease.

Minerals

Certain minerals play an important role in antioxidant protection. The most notable antioxidant minerals are selenium, zinc, copper, and manganese. While these minerals do not possess antioxidant activity on their own, their functions are as cofactors for various antioxidant enzymes and support their classification as antioxidants. The enzyme superoxide dismutase catalyzes the conversion of superoxide to hydrogen peroxide. The cytosolic form of this enzyme requires copper and zinc as cofactors, while the mitochondrial form of superoxide dismutase requires manganese. Likewise, glutathione peroxidase requires selenium to function properly in the removal of peroxides. Deficiencies in any of these minerals can reduce the enzyme effectiveness in protecting against free radical damage. In fact, the consumption of certain minerals, such as selenium, is inversely correlated with the risk for developing cancer. Consequently, many antioxidant supplements include these minerals.

Providing balanced protection

There is a constant battle between the production of free radicals and the body's attempt to remove these radicals. This can be pictured as a balance with free radicals production on one side and antioxidant nutrients on the other. Data continue to emerge that show a role for antioxidants from both food as well as dietary supplements in disease treatment and prevention. Although optimal intakes of antioxidants have yet to be determined, science continues to learn more each day about this fascinating area of nutrition.

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