Tissue-damaging exposure to reactive oxygen species (ROS) is a fact of life. These compounds are produced by our cells as a normal part of metabolism as well as environmental sources including natural radiation sources and the very air that we breathe. While initially believed to be only a toxic by-product of living in an oxygen-rich environment, scientific research has identified several ways that the body uses these ROS as a part of normal, healthy metabolism. White blood cells undergo an “oxidative burst” which releases various ROS to kill invading microorganisms. Reactive oxygen species also act as signaling molecules in many cellular pathways where they modulate cell proliferation, apoptosis (cell death), gene expression and various other physiological functions. Indeed, it is now believed that a mildly pro-oxidative balance is necessary to maintain cellular health.

However, an excessive level of ROS in the body has been linked to disease and dysfunction. Exposure to ROS is also theorized to play a major role in aging. Current research indicates that it is not simply the presence of ROS that damages cellular lipids, proteins, and DNA but the imbalance created by excessive oxidants or depleted antioxidants. This imbalance is often termed “oxidative stress.” Situations that can increase oxidative stress in the body include stress, pollution, smoking and strenuous exercise. Living organisms have a built-in defense mechanism against an overbalance of these damaging compounds that includes antioxidant enzymes and non-enzymatic antioxidants. However, antioxidant levels in the body may be depleted. A deficiency in the production of antioxidant enzymes, decreased dietary intake or reduced absorption of antioxidant compounds from foods may all lower antioxidant activity.

Oxidants are defined as substances that remove electrons from other compounds which can produce free radicals that are capable of initiating oxidative cascades. Oxidants include oxygen, hydrogen peroxide, nitric oxide and their free radicals.

Antioxidants are defined as substances that inhibit the oxidation of other compounds. Antioxidants include enzymes as well as vitamins, minerals, thiols, polyphenols and other compounds. Antioxidant enzymes include superoxide dismutase, catalase and various peroxidases.

While the body utilizes many different compounds as antioxidants to maintain a healthy balance, this article will focus on the primary antioxidant enzymes—superoxide dismutase (SOD), catalase, and peroxidases—and dietary nutrients that may support their activity. Antioxidant enzymes catalyze reduction-oxidation (redox) reactions that reduce reactive species through the oxidation of another molecule, transferring an electron to stabilize the free radical.

Figure One illustrates the redox cascade catalyzed by the primary antioxidant enzymes when exposed to oxygen free radicals.
SUPEROXIDE DISMUTASE (SOD) catalyzes the simultaneous oxidation and reduction of the superoxide radical to produce oxygen and hydrogen peroxide.

SOD is an essential enzyme that detoxifies the highly reactive superoxide radical to create hydrogen peroxide. This antioxidant enzyme is found throughout the body. In the human body, there are two forms of SOD: Cu/Zn-SOD found in the cytosol and extracellular space; and Mn-SOD found in the mitochondria. Left unchecked, the superoxide radical is capable of creating numerous other reactive species including peroxynitrite, lipid peroxyl and alkoxyl radicals which can cause destructive havoc throughout the body. The primary functions of this enzyme are to neutralize the superoxide radical and protect cellular proteins, lipids and DNA from ROS-induced destruction and maintain healthy cells, tissues, organs and bodies. Sufficient levels of this enzyme are also necessary to promote healthy aging. Environmental radiation from radon, cosmic radiation and other natural sources can induce the formation of free radicals in the human body. Research indicates that SOD protects the body from radiation-induced oxidation. SOD’s antioxidant activity helps protect the healthy individual from everyday natural radiation exposure.

Supplemental SOD is available from bovine liver as well as the vegetarian form from Cucumis melo.

CATALASE catalyzes the conversion of hydrogen peroxide to produce water and oxygen.

Often described as the “perfect catalyst”, catalase exhibits an extremely high reaction rate that is capable of decomposing millions of hydrogen peroxide molecules every second. Interestingly, the enzyme has also been reported to act as a peroxidase and is known to catalyze the conversion of short chain alcohols to their corresponding aldehydes. The enzyme’s tetrameric structure includes an iron at each active site. This structure is quite stable making the enzyme more resistant to pH, heat and proteolysis than many other enzymes.

Catalase is found in peroxisomes, red blood cells, and in the extracellular spaces. In the human body, catalase levels are highest in the liver and red blood cells and comparatively low in the heart and brain. This antioxidant enzyme serves many functions in the human body including modulating inflammation, mutagenesis, and apoptosis. Catalase protects pancreatic β-cells and nerve cells as well as the oxygen-carrying capacity of red blood cells. Hydrogen peroxide radicals can be a major source of cell injury and cell death. Catalase’s ability to neutralize these damaging ROS inhibits apoptosis and helps regulate cell proliferation. Research has also found that catalase activity in tumor cells is often low.

The major source of supplemental catalase is produced via fermentation by microorganisms such as Aspergillus niger.

PEROXIDASES
This diverse group of enzymes participates both in the immune defense against invading microorganisms and in neutralizing free radicals that initiate cellular damage. Like catalase, these enzymes catalyze the neutralization of hydrogen peroxide and help protect the body from ROS-induced tissue damage. Within this group of enzymes glutathione peroxidase is one of the most studied in mammalian systems.

GLUTATHIONE PEROXIDASE catalyzes the reduction of hydrogen peroxide while oxidizing glutathione to produce water and glutathione disulfide.

Glutathione peroxidase utilizes glutathione as an electron donor to reduce ROS. Glutathione itself is not an enzyme, but merely a substrate for the antioxidant reaction catalyzed by glutathione peroxidase. In the human body, reduced glutathione disulfide is regenerated by the action of a second enzyme, glutathione reductase. Glutathione also serves the body as an antioxidant by donating electrons to maintain the activity of other antioxidant compounds such as vitamin C and vitamin E.

Like catalase, glutathione peroxidase is a tetrameric protein but with selenium at the catalytic site. High levels of glutathione peroxidase have been shown to protect against oxidative stress in both in vitro cellular and in vivo animal studies.

A standardized glutathione peroxidase is not currently available as a dietary supplement.

Lactoperoxidase is another peroxidase found in mammalian secretions including milk and saliva. This enzyme functions in the body as part of the innate immune system. The enzyme catalyzes hydrogen peroxide through a reaction that both neutralizes the ROS potential and creates antimicrobial compounds such as hypohiociyanate.

Supplemental lactoperoxidase is currently available from cow’s milk.

ANTIOXIDANT ENZYME SUPPLEMENTATION
Antioxidant enzymes are a component of all living cells and are a natural component of the foods we eat. Unfortunately, these enzymes are often heat labile and do not survive the cooking process. In 2007, a group of researchers reported on the effect of boiling, microwaving and baking various fruits and vegetables on the activity of SOD, catalase and glutathione peroxidase. These researchers reported that the antioxidant enzyme levels were significantly diminished by heat treatment in almost all fruits and vegetables tested (except tomato). This loss of antioxidant enzyme activity reduces the antioxidant potential of these foods.

Dietary antioxidant enzymes may act to spare or renew other nutritional antioxidants. Their nature as enzyme catalysts allows them to counteract oxidative reactions repeatedly as food passes through the digestive tract. Evidence suggests that at least some SOD may survive the digestive process and be absorbed for direct systemic supplementation. Research
has also identified that combination with gliadin may further improve the gastric survival and absorption of SOD. One research team studied the effect of vegetarian SOD on oxidative cell damage in healthy volunteers when exposed to hyperbaric oxygen and found that supplementation protected against DNA damage. Antioxidant enzyme supplements may be useful to support the general antioxidant system of the body as well as providing general immune support and helping to maintain healthy skin, muscles and connective tissues.

Alternatively, various nutrients may be supplemented that can increase the body’s production or activity of antioxidant enzymes. Dietary intake of polyphenols has been shown to increase the expression of antioxidant enzymes including SOD, catalase and glutathione peroxidase. It is believed that these phytochemicals induce expression of antioxidant enzymes through the nuclear factor-erythroid-2-related factor 2 pathway (Nrf2). Furthermore, some researchers believe it is this indirect antioxidant effect, rather than the antioxidant potential of dietary polyphenols, that is most vital to their in vivo protective action. Phytochemicals that have been shown to induce antioxidant enzyme activity include resveratrol, green tea catechins, curcumin, lycopene, strawberry anthocyanins, oleuropein, and sulforaphane. Research indicates that both endogenous and supplemental melatonin enhance the level and/or activity of antioxidant enzymes including glutathione peroxidase and SOD. Supplementation of the trace minerals zinc and selenium has also been shown to increase serum antioxidant enzyme levels. Antioxidant enzyme activity is also supported by supplementation of omega-3 and omega-6 fatty acids. Likewise, the amino acid taurine has also been shown to increase the level of antioxidant enzymes including catalase, glutathione peroxidase and Mn-SOD though the mechanism is currently unknown. Supplementation of the tripeptide glutathione, or its component amino acids — glycine, glutamine, and especially cysteine — may also promote the action of glutathione peroxidase, particularly if systemic glutathione levels are depleted. Supplementation of S-adenosylmethionine (SAMe), whey protein, alpha-lipoic acid, and silymarin have also been shown to increase cellular glutathione levels. Meanwhile, clinical studies indicate that supplemental alpha-lipoic acid and SOD work synergistically to eliminate the toxic potential of ROS.

Antioxidant enzymes are a key component of the body’s natural antioxidant defense system. Maintaining adequate levels of these enzymes is vital in maintaining good health and in replenishing depletions brought on from aging, strenuous exercise and environmental conditions. Supplementation of antioxidant enzymes or nutrients that promote their expression or activity may be an important part of a dietary regimen to maintain health and wellness.

SELECTED REFERENCES:


Additional references available upon request