World Journal of Pharmacy and Biotechnology

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Review Article **Open Access**

Antioxidative Strength for Vigour and Vitality

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A B S T R A C T

The demand for natural antioxidant is increasing due to its unquestionable advantages compared with the addition of antioxidants directly to the food. There is consistent evidence from human and animal studies that strenuous physical exercise may induce a state wherein the antioxidant defenses of several tissues are overwhelmed by excess reactive oxygen. There has recently been a remarkable increment in scientific articles dealing with oxidative stress. Polyphenolic compounds have been identified in various plant species and reported to possess many useful properties including antiallergic, antiinflammatory, antimicrobial, antiviral, antioxidant, oestrogenic, enzyme inhibition, vascular and cytotoxic anti- tumor activity. Brassica vegetables, which include different genus of cabbage, broccoli, cauliflower, Brussels sprouts, and kale, are consumed all over the world. While use of synthetic antioxidants (viz. butylated hydroxytoluene and butylated hydroxyl anisole) to maintain the quality of ready-to-eat food products has become commonplace, consumer concern regarding their safety has motivated the food industry to seek natural alternatives. Plant extracts, generally used for their flavoring characteristics, often have strong H-donating activity thus making them extremely effective antioxidants. This antioxidant activity is most often due to phenolic acids (gallic, protocatechuic, caffeic and rosmarinic acids), phenolic diterpenes, flavonoids and volatile oils. Anthocyanin and anthocyanidin can chelate metals and donate H to oxygen radicals' thus slowing oxidation via 2 mechanisms. Tea and extracts of grape seeds and skins contain catechins, epicatechins, phenolic acids, proanthocyanidins & resveratrol, all of which contribute to their antioxidative activity. The objective of this article is to provide an impending overview of clinical manifestation resulted due to overload of free radicals & natural antioxidants, their mechanisms of action, nutritional prophylaxis & imminent therapeutic applicability.

Keywords: Self-micro emulsifying drug delivery systems (SMEDDSs), Lipophillic / hydrophobic compound, Aqueous solubility, Droplet Size, Oral Bioavailability.

A R T I C L E I N F O

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Article History: Received 10 March 2015, **Accepted** 24 April 2015, **Available Online** 29 June 2015

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Manuscript ID: WJPBT2105

PAPER-QR CODE

Citation: Raaz K Maheshwari, *et al.* Antioxidative Strength for Vigour and Vitality. *W. J. Pharm. Biotech.*, 2015, 2(1): 47-56.

1. Introduction

It is well known that many botanicals possess natural antioxidants with high antioxidant activity and investigations on these were initiated based on their uses in traditional folkloric medicines. Antioxidants are the nutritional equivalents and are loyal protectors and nurturers of our cells, repelling disease, and promoting good health. Antioxidants can come from healthy eating or in the form of supplements, and they include a family of naturally formed components like vitamin A, β-carotene, lycopene, vitamin E, and more. They are believed to protect cells from free radicals, harmful oxygen molecules thought to damage cells that result in cancer, atherosclerosis, Alzheimer's disease and rheumatoid arthritis, and they may be the underlying reason why we age. In nature due to instinctive oxidation process - an apple slice turns brown; fish becomes rancid; a cut on skin is raw and inflamed. All of these result from a natural process called oxidation.

Figure 1

It happens to all cells in nature, including the ones in your body. To help your body protect itself from the rigors of oxidation, Mother Nature provides thousands of different antioxidants in various amounts in fruits, vegetables, whole grains, nuts, and legumes. When your body needs to put up its best defense, especially true in today's environment, antioxidants are crucial to your health. As oxygen interacts with cells of any type - an apple slice or, in your body, the cells lining your lungs or in a cut on your skin -- oxidation occurs. This produces some type of change in those cells. They may pass away, such as with rotting fruit. In the case of cut skin, dead cells are replaced in time by fresh, new cells, resulting in a healed cut. This birth and death of cells in the body goes on continuously, 24 hours a day. It is a process that is necessary to keep the body healthy.

Oxidation is a very natural process that happens during normal cellular functions. Yet there is a downside. While the body metabolizes oxygen very efficiently, 1% or 2% of cells will get damaged in the process and turn into free radicals. "Free radicals" is a term often used to describe damaged cells that can be problematic. They are "free" because they are missing a critical molecule, which sends them on a rampage to pair with another molecule. "These molecules will rob any molecule to quench that need. When free radicals are on the attack, they don't just kill cells to acquire their missing molecule. "If free radicals simply killed a cell, it wouldn't be so bad… the body could just regenerate another one," he says. "The problem is, free radicals often injure the cell, damaging the DNA, which creates the seed for disease." When a cell's DNA changes, the cell becomes mutated. It grows abnormally and reproduces abnormally -- and quickly. Normal cell functions produce a small percentage of free radicals, much like a car engine that emits fumes. But those free radicals are generally not a big problem. They are kept under control by antioxidants that the body produces naturally. External toxins, especially cigarette smoke and air pollution, are "free radical generators. Cigarette smoke is a huge source of free radicals. In fact, our food and water also harbor free radicals in the form of pesticides and other toxins. Drinking excessive amounts of alcohol also triggers substantial free radical production. Free radicals trigger a damaging chain reaction, and that's the crux of the problem. Epidemiological studies and a substantial body of evidence have linked the production of free radicals with the occurrence of cardiovascular diseases, carcinogenesis, rheumatoid arthritis and denegerative processes associated with aging. Antioxidants aid in the prevention by scavenging the excess free radicals, hence preventing the formation of reactive oxygen species in the body The use of synthetic antioxidants such as butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone and propyl gallate has been negatively perceived by consumers due to safety and health effects. Hence, there is an increasing interest in the search of natural antioxidants from plant sources. Most of the potentially harmful effects of oxygen are due to the formation and activity of a number of chemical compounds, known as ROS, which have a tendency to donate oxygen to other substances. Free radicals and antioxidants have become commonly used terms in modern discussions of disease mechanisms. Free radicals are formed naturally in the body, but their production is increased by factors such as smoking, alcohol, air pollution, infection, stress, excessive sunlight, and toxins like radiation and asbestos.

Carotenoids gets involved in an entire antioxidant network of physiological systems of the body. A number of nutrients must come together in synergy to afford effective antioxidant protection. Carotenois are sacrificial antioxidants and help save other antioxidants by means of absorbing free radical hits. One mole of carotenoid absorb up to ~ 15 attacks, facilitating redox reaxtion continuing without uninterrupted mode of action. Weakness of one antioxidant moiety results collapse of entire network.

Oxidative Stress & Free Radicals Versus Antioxidants

We are exposed to electromagnetic radiation from the environment, both natural and from man-made sources. Low-wavelength electromagnetic radiation (e. g., γ- rays) can split water in the body to generate hydroxyl radical, OH*. This fearsomely-reactive radical, once generated, attacks whatever it is next to. Its lifetime *in vivo* is vanishingly small because hydroxyl radical reacts at its site of formation, usually leaving behind a legacy in the form of propagating free-radical chain reactions.The body makes another oxygen radical (ie, the unpaired electron is located on oxygen), superoxide (0;-). Superoxide is made by adding one electron to the oxygen molecule. It is generally poorly reactive. Some superoxide is made by "accidents of chemistry", in that many molecules in the body react directly with oxygen to make superoxide. Examples include the catecholamines, tetrahydrofolates, and some constituents of mitochondrial and other electron-transport chains. Activated phagocytes (neutrophils, monocytes, macrophages, eosinophils) generate large amounts of superoxide as part of the mechanism by which foreign organisms are subsided. During chronic inflammations, this normal protective mechanism may become damaging. About 1-3% of the oxygen we breathe in is used to make superoxide. Since human beings consume a lot of oxygen. Another physiological free radical is nitric oxide (NO*), which is made by vascular endothelium as a relaxing factor, and also by phagocytes and in the brain. Nitric oxide has many useful physiological functions, but excess NO can be toxic.

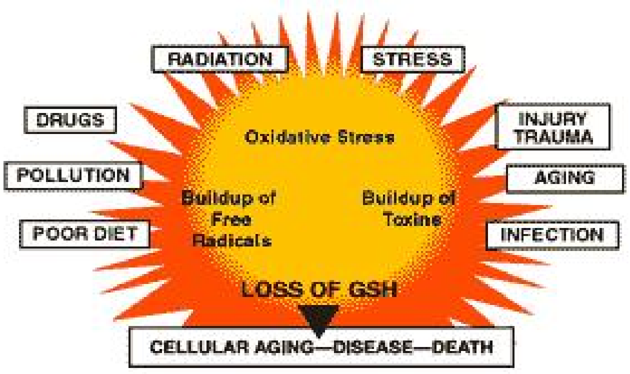

Figure 2

Neither superoxide nor NO is highly reactive chemically, but under certain circumstances they can generate more toxic products. Free radicals are dangerous because they don't just damage one molecule. One free radical can set off a whole chain reaction. When a free radical oxidizes a fatty acid, it changes that fatty acid into a free radical, which then damages another fatty acid. It's a very rapid chain reaction." These external attacks can overwhelm the body's natural free-radical defense system. In time, and with repeated free radical attacks that the body cannot stop, that damage can lead to a host of chronic diseases, including cancer, heart disease, Alzheimer's disease, and Parkinson's disease. Oxidative damage in skin cells is caused by cumulative sunlight. But if free radicals are in an internal organ - for example, if asbestos is in your lungs -- it stimulates free radical reactions in lung tissue. Cigarette smoke has active free radical generators. That's why stopping smoking is the biggest step anyone can take to preserving their health. In the 21st century, people need to get more antioxidants in their diet to offset all these assaults. These toxins are ubiquitous in the environment.The oxidative burden on the body is much, much, much higher than it was 200 years ago, in dweller of a city. It's a fact of modern life, so we have to take that into consideration. Someone compensate for the effects of environmental toxins if consume multiple servings of fruits and veggies. Body simply doesn't produce enough antioxidants to do all that. What exactly do they do? Antioxidants work to stop this damaging, disease-causing chain reaction that free radicals have started. Each type of antioxidant works either to prevent the chain reaction or stop it after it's started. For example, the role of vitamin C is to stop the chain reaction before it starts. It captures the free radical and neutralizes it. Vitamin E is a chain-breaking antioxidant. Wherever it finds sit in a membrane, it breaks the chain reaction.

Flavonoids are the biggest class of antioxidants. Some 5,000 flavonoids in various foods have identified in various veggies, cereals, fruits and spices. Polyphenols are a smaller class of antioxidants, which often refer to as "phenols". We have clear science about antioxidants, that our bodies need a NADN (Natural Antioxidant Defense Network), for lack of a better term. like a country needs a military system, the human body needs defense workers at all levels -- lieutenants, corporals, generals, staff sergeants - in the form of antioxidants. The body needs a mix of vitamins and minerals, such as vitamins A, C, E, and beta-carotene, to neutralize this free radical assault. We can't rely on a few blockbuster foods to do the job," says Blumberg. "You can't eat nine servings of broccoli a day and expect it to do it all. We need to eat many different foods. Each type works in different tissues of the body, in different parts of cells. Some are good at quenching some free radicals, some are better at quenching others. When you have appropriate amounts of different antioxidants, you're doing what you can to protect yourself. Multivitamins and vitamin supplements can provide the body with an antioxidant boost. Yet getting too much of some supplements, like vitamin E, can be harmful. Fruits, vegetables, whole grains, legumes, and nuts contain complex mixes of antioxidants, and therein lies the benefit of eating a variety of healthy foods. Researchers continue delving into the mysteries of fruits and vegetables, identifying the complex antioxidants they contain. Quercetin, luteolin, hesperetin, catetchin, even (-)-epigallocetechin are some of the the blockbuster flavonoids in our foods.

Oxidative damage results when the critical balance between free radical generation and antioxidant defenses is unfavorable. Oxidative stress, arising as a result of an imbalance between free radical production and antioxidant defenses, is associated with damage to a wide range of molecular species including lipids, proteins, and nucleic acids. Short-term oxidative stress may occur in tissues injured by trauma, infection, heat injury, hypertoxia, toxins, and excessive exercise. These injured tissues produce increased radical generating enzymes (e.g., xanthine oxidase, lipogenase, cyclooxygenase) activation of phagocytes, release of free iron, copper ions, or a disruption of the electron transport chains of oxidative phosphorylation, producing excess ROS. The initiation, promotion, and progression of cancer, as well as the side-effects of radiation and chemotherapy, have been linked to the imbalance between ROS and the antioxidant defense system. ROS have been implicated in the induction and complications of diabetes mellitus, age-related eye disease, and neurodegenerative diseases such as Parkinson's disease. A role of oxidative stress has been postulated in many conditions, including anthersclerosis, inflammatory condition, certain cancers, and the process of aging. Oxidative stress is now thought to make a significant contribution to all inflammatory diseases (arthritis, vasculitis, glomerulonephritis, lupus erythematous, adult respiratory diseases syndrome), ischemic diseases (heart diseases, stroke, intestinal ischema), hemochromatosis, AIDS (acquired immunodeficiency syndrome), emphysema, organ transplantation, gastric ulcers, hypertension and preeclampsia, neurological disorder (Alzheimer's disease, Parkinson's disease, muscular dystrophy), alcoholism, smoking-related diseases, and many others.

Heart diseases continue to be the biggest killer, responsible for about half of all the deaths. The oxidative events may affect cardiovascular diseases therefore; it has potential to provide enormous benefits to the health and lifespan. Poly unsaturated fatty acids occur as a major part of the low density lipoproteins (LDL) in blood and oxidation of these lipid components in LDL play a vital role in atherosclerosis. The 3 most important cell types in the vessel wall are endothelial cells; smooth muscle cell and macrophage can release free radical, which affect lipid peroxidation. With continued high level of oxidized lipids, blood vessel damage to the reaction process continues and can lead to generation of foam cells and plaque the symptoms of atherosclerosis. Oxidized LDL is antherogenic and is thought to be important in the formation of anthersclerosis plaques. Furthermore, oxidized LDL is cytotoxic and can directly damage endothelial cells. Antioxidants like β-carotene or vitamin E play a vital role in the prevention of various cardiovascular diseases. Reactive oxygen and nitrogen species, such as super oxide anion, H_2O_2, hydroxyl radical, and NO and their biological metabolites also play an important role in carcinogenesis. ROS induce DNA damage, as the reaction of free radicals with DNA includes strand break base modification and DNA protein cross-links. Numerous investigators have proposed participation of free radicals in carcinogenesis, mutation, and transformation; it is clear that their presence in biosystem could lead to mutation, transformation, and ultimately cancer. Induction of mutagenesis, the best known of the biological effect of radiation, occurs mainly through damage of DNA by the $HO^{\cdot}$ Radical and other species are produced by the radiolysis, and also by direct radiation effect on DNA, the reaction effects on DNA. The reaction of $HO^{\cdot}$ Radicals is mainly addition to double bond of pyrimidine bases and abstraction of H from the sugar moiety resulting in chain reaction of DNA. These effects cause cell mutagenesis and carcinogenesis lipid peroxides are also responsible for the activation of carcinogens. Antioxidants can decrease oxidative stress induced carcinogenesis by a direct scavenging of ROS and/or by inhibiting cell proliferation secondary to the protein phosphorylation. β-carotene may be protective against cancer through its antioxidant function, because oxidative products can cause genetic damage. Thus, the photo protective properties of B-carotene may protect against UV light induced carcinogenesis. Immunoenhancement of β-carotene may contribute to cancer protection. β-carotene may also have anticarcinogenic effect by altering the liver metabolism effects of carcinogens. Vitamin C may be helpful in preventing cancer. The possible mechanisms by which vitamin C may affect carcinogenesis include antioxidant effects, blocking of formation of nitrosanimes, enhancement of the immune response, and acceleration of detoxification of liver enzymes. Vitamin E, an important antioxidant, plays a role in immunocompetence by increasing humoral antibody protection, resistance to bacterial infections, cell-mediated immunity, the T-lymphocytes tumor necrosis factor production, inhibition of mutagen formation, repair of membranes in DNA, and blocking micro cell line formation. Hence vitamin E may be useful in cancer prevention and inhibit carcinogenesis by the stimulation of the immune system. The administration of a mixture of the above three antioxidant reveled the highest reduction in risk of developing cardiac cancer. The human body is in constant battle to keep from aging.

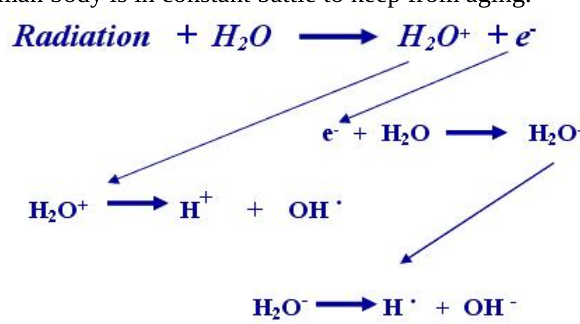

Figure 3

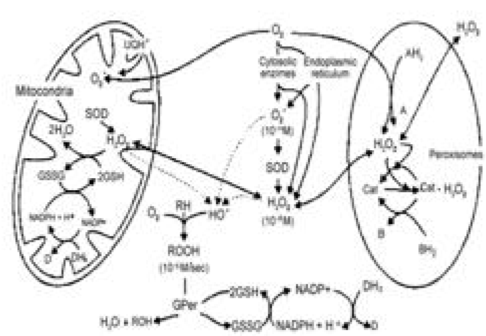

Figure 4

Research suggests that free radical damage to cells leads to the pathological changes associated with aging. An increasing number of diseases or disorders, as well as aging process itself, demonstrate link either directly or indirectly to these reactive and potentially destructive molecules. The major mechanism of aging attributes to DNA or the accumulation of cellular and functional damage. Reduction of free radicals or decreasing their rate of production may delay aging. Some of the nutritional antioxidants will retard the aging process and prevent disease. Based on these studies, it appears that increased oxidative stress commonly occurs during the aging process, and antioxidant status may significantly influence the effects of oxidative damage associated with advancing age. Research suggests that free radicals have a significant influence on aging, that free radical damage can be controlled with adequate antioxidant defense, and that optimal intake of antioxidant nutrient may contribute to enhanced quality of life.

Figure 5

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Recent research indicates that antioxidant may even positively influence life span. Proteins can be oxidatively modified in three ways: oxidative modification of specific amino acid, free radical mediated peptide cleavage, and formation of protein cross-linkage due to reaction with lipid peroxidation products. Protein containing amino acids such as methionine, cystein, arginine, and histidine seem to be the most vulnerable to oxidation. Free radical mediated protein modification increases susceptibility to enzyme proteolysis. Oxidative damage to protein products may affect the activity of enzymes, receptors, and membrane transport. Oxidatively damaged protein products may contain very reactive groups that may contribute to damage to membrane and many cellular functions. Peroxyl radical is usually considered to be free radical species for the oxidation of proteins. ROS can damage proteins and produce carbonyls and other amino acids modification including formation of methionine sulfoxide and protein carbonyls and other amino acids modification including formation of methionine sulfoxide and protein peroxide. Protein oxidation affects the alteration of signal transduction mechanism, enzyme activity, heat stability, and proteolysis susceptibility, which leads to aging.

Oxidative stress and oxidative modification of biomolecules are involved in a number of physiological and pathophysiological processes such as aging, artheroscleosis, inflammation and carcinogenesis, and drug toxicity. Early research on the role of antioxidants in biology focused on their use in preventing the oxidation of unsaturated fats, which is the cause of rancidity. Antioxidant activity could be measured simply by placing the fat in a closed container with oxygen and measuring the rate of oxygen consumption. However, it was the identification of vitamins A, C, and E as antioxidants that revolutionized the field and led to the realization of the importance of antioxidants in the biochemistry of living organisms. The possible mechanisms of action of antioxidants were first explored when it was recognized that a substance with antioxidative activity is likely to be one that is itself readily oxidized. Research into how vitamin E prevents the process of lipid peroxidation led to the identification of antioxidants as reducing agents that prevent oxidative reactions, often by scavenging ROS before they can damage cells. Antioxidants act as radical scavenger, hydrogen donor, electron donor, peroxide decomposer, singlet oxygen quencher, enzyme inhibitor, synergist, and metal-chelating agents. Both enzymatic and nonenzymatic antioxidants exist in the intracellular and extracellular environment to detoxify ROS.

Catalase is a common enzyme found in nearly all living organisms, which are exposed to oxygen, where it functions to catalyze the decomposition of hydrogen peroxide to water and oxygen. Hydrogen peroxide (H_2O_2) is a harmful by-product of many normal metabolic processes: to prevent damage, it must be quickly converted into other, less dangerous substances. To this end, catalase is frequently used by cells to rapidly catalyze the decomposition of H_2O_2 into less reactive gaseous O_2 & H_2O molecules. All known animals use catalase in every organ, with particularly high concentrations occurring in the liver. The glutathione system includes glutathione, glutathione reductase, glutathione peroxidases, and glutathione S-transferases. This system is found in animals, plants, and microorganisms. Glutathione peroxidase is an enzyme containing four selenium-cofactors that catalyze the breakdown of hydrogen peroxide and organic hydroperoxides.

Ascorbic acid or "vitamin C" is a monosaccharide antioxidant found in both animals and plants. As it cannot be synthesized in humans and must be obtained from the diet, it is a vitamin. Most other animals are able to produce this compound in their bodies and do not require it in their diets. In cells, it is maintained in its reduced form by reaction with glutathione, which can be catalyzed by protein disulfide isomerase and glutaredoxins. Ascorbic acid is a reducing agent and can reduce and thereby neutralize ROS such as hydrogen peroxide. In addition to its direct antioxidant effects, ascorbic acid is also a substrate for the antioxidant enzyme ascorbate peroxidase, a function that is particularly important in stress resistance in plants. Glutathione is a cysteine-containing peptide found in mostforms of aerobic life. It is not required in the diet and is instead synthesized in cells from its constituent amino acids. Glutathione has antioxidant properties since the thiol group in its cysteine moiety is a reducing agent and can be reversibly oxidized and reduced. In cells, glutathione is maintained in the reduced form by the enzyme glutathione reductase and in turn reduces other metabolites and enzyme systems as well as reacting directly with oxidants.

If 2 free radicals meet, they can join their unpaired electrons and make a covalent bond (a shared pair of electrons). Thus superoxide and nitric oxide combine:

$O_2{*}^{-} + NO^{\cdot} \longrightarrow ONOO^{-}$ (peroxynitrite)

At physiological pH, peroxynitrite damages proteins directly, and decomposes into toxic products that include nitrogen dioxide gas ($N0_2$), hydroxyl radical, and nitronium ion ($N0_2{}^{+}$). Hence at least somes of the toxicity of excess nitric oxide may involve its interaction with superoxide. In addition, superoxide can react with iron and Cu- ions, eventually to made hydroxyl radical. Radical plus non-radical Most molecules in the body are not radicals. Hence any reactive free radical generated is likely to react with a non-radical. When a free radical reacts with a non-radical, a free-radical chain reaction results and new radicals are formed. Attack of reactive radicals on membranes or lipoproteins starts lipid peroxidation, which is particularly implicated in the development of atherosclerosis. If hydroxyl radicals are generated close to DNA, they can attack the purine and pyrimidine bases and cause mutations. For example, guanine is converted into 8-hydroxyguanine and other products. Superoxide dismutases (SOD) convert superoxide to hydrogen peroxide (H_20_2):

$2O_2{}^{*} + 2H^{+} \longrightarrow H_2 + O_2$

2. Free Radical Generation at the Forefront

A free radical can be defined as any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital. The presence of an unpaired electron results in certain common properties that are shared by most radicals. Many radicals are unstable and highly reactive. They can either donate an electron to or accept an electron from other molecules, therefore behaving as oxidants or reductants. The most important oxygen-containing free radicals in many disease states are hydroxyl radical, superoxide anion radical, H_2O_2 oxygen singlet, hypochlorite, nitric oxide radical, and peroxynitrite radical. These are highly reactive species, capable in the nucleus, and in the membranes of cells of damaging biologically relevant molecules such as DNA, proteins, carbohydrates, and lipids. Free radicals attack important macromolecules leading to cell damage and homeostatic disruption. Targets of free radicals include all kinds of molecules in the body. Among them, lipids, nucleic acids, and proteins are the major targets. Free radicals and other ROS 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.Free radical formation occurs continuously in the cells as a consequence of both enzymatic and nonenzymatic reactions. Enzymatic reactions, which serve as source of free radicals, include those involved in the respiratory chain, in phagocytosis, in prostaglandin synthesis, and in the cytochrome P-450 system. Free radicals can also be formed in nonenzymatic reactions of oxygen with organic compounds as well as those initiated by ionizing reactions.

Figure 6

Figure 7

Exercise appears to increase reactive oxygen species, which can result in damage to cells. Exercise results in increased amounts of malondialdehyde in blood and pentane in breath; both serve as indirect indicators of lipid peroxidation. However, not all studies report increases; these equivocal results may be due to the large inter subject variability in response or the nonspecificity of the assays. Some studies have reported that supplementation with vitamins C and E, other antioxidants, or antioxidant mixtures can reduce symptoms or indicators of oxidative stress as a result of exercise. However, these supplements appear to have no beneficial effect on performance. Exercise training seems to reduce the oxidative stress of exercise, such that trained athletes show less evidence of lipid peroxidation for a given bout of exercise and an enhanced defense system in relation to untrained subjects. Whether the body's natural antioxidant defense system is sufficient to counteract the increase in reactive oxygen species with exercise or whether additional exogenous supplements are needed is not known, although trained athletes who received antioxidant supplements show evidence of reduced oxidative stress. Until research fully substantiates that the long-term use of antioxidants is safe and effective, the prudent recommendation for physically active individuals is to ingest a diet rich in antioxidants. An antioxidant is a molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage. These antioxidants delay or inhibit cellular damage mainly through their free radical scavenging property.

These low-molecular-weight antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Some of such antioxidants, including glutathione, ubiquinol, and uric acid, are produced during normal metabolism in the body. Other lighter antioxidants are found in the diet. Although there are several enzymes system within the body that scavenge free radicals, the principle micronutrient (vitamins) antioxidants are vitamin E (α-tocopherol), vitamin C (ascorbic acid), and B-carotene. The body cannot manufacture these micronutrients, so they must be supplied in the diet.

3. Antioxidants of Natural & Synthetic Origin

Synthetic and natural foodantioxidants are used routinely in foods and medicine especially those containing oils and fats to protect the food against oxidation. There are a number of synthetic phenolic antioxidants, butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) being prominent examples. These compounds have been widely uses as antioxidants in food industry, cosmetics, and therapeutic industry. However, some physical properties of BHT and BHA such as their high volatility and instability at elevated temperature, strict legislation on the use of synthetic food additives, carcinogenic nature of some synthetic antioxidants, and consumer preferences have shifted the attention of manufacturers from synthetic to natural antioxidants. In view of increasing risk factors of human to various deadly diseases, there has been a global trend toward the use of natural substance present in medicinal plants and dietary plats as therapeutic antioxidants. It has been reported that there is an inverse relationship between the dietary intake of antioxidant-rich food and medicinal plants and incidence of human diseases. The use of natural antioxidants in food, cosmetic, and therapeutic industry would be promising alternative for synthetic antioxidants in respect of low cost, highly compatible with dietary intake and no harmful effects inside the human body.

Many antioxidant compounds, naturally occurring in plant sources have been identified as free radical or active oxygen scavengers. Attempts have been made to study the antioxidant potential of a wide variety of vegetables like potato, spinach, tomatoes, and legumes. There are several reports showing antioxidant potential of fruits. Strong antioxidants activities have been found in berries, cherries, citrus, prunes, and olives. Green and black teas have been extensively studied in the recent past for antioxidant properties since they contain up to 30% of the dry weight as phenolic compounds.

Apart from the dietary sources, Indian medicinal plants also provide antioxidants and these include (with common/ayurvedic names in brackets) *Acacia catechu* (kair), *Aegle marmelos* (Bengal quince, Bel), *Allium cepa* (Onion), *A. sativum* (Garlic, Lahasuna), *Aleo vera* (Indain aloe, Ghritkumari), *Amomum subulatum* (Greater cardamom, Bari elachi), *Andrographis paniculata* (Kiryat), *Asparagusrecemosus* (Shatavari), *Azad irachta indica* (Neem, Nimba), *Bacopa monniera* (Brahmi), *Butea monosperma* (Palas, Dhak), *Camellia sinensis* (Green tea), *Cinnamomum verum* (Cinnamon), *Cinnamomum tamala* (Tejpat), *Curcma longa* (Turmeric, Haridra), *Emblica officinalis* (Inhian gooseberry, Amlaki), *Glycyrrhiza glapra* (Yashtimudhu), *Hemidesmus indicus* (Indian Sarasparilla, Anantamul), *Indigofera tinctoria, Mangifera indica* (Mango, Amra), *Momordica charantia* (Bitter gourd), *Murraya koenigii* (Curry leaf), *Nigella sativa* (Black cumin), *Ocimum sanctum* (Holy basil, Tusil), *Onosma echioides* (Ratanjyot), *Picrorrhiza kurroa* (Katuka), Piper beetle, *Plumbago zeylancia* (Chitrak), *Sesamum indicum, Sida cordifolia,Spirulina fusiformis* (Alga), Swertia decursata, Syzigium cumini (Jamun), *Terminalia ariuna* (Arjun), *Terminalia bellarica* (Beheda), *Tinospora cordifolia*(Heart leaved moonseed, Guduchi), *Trigonella foenum-graecium* (Fenugreek), *Withania somifera* (Winter cherry, Ashwangandha), and *Zingiber officinalis* (Ginger).

Whole foods represent the simplest example of functional food. Broccoli, carrots, and tomatoes are considered functional foods because of their high contents of physiologically active components (sulforaphen, β-carotene, and lycopene, respectively). Green vegetables and spices like mustard and turmeric, used extensively in Indian cuisine, also can fall under this category. "Nutraceutical" is a term coined in 1979 by Stephen DeFelice. It is defined "as a food or parts of food that provide medical or health benefits, including the prevention and treatment of disease." Nutraceuticals may range from isolated nutrients, dietary supplements, and diets to genetically engineered "designer" food, herbal products, and processed products such as cereals, soups, and beverages. A nutraceutical is any nontoxic food extract supplement that has scientifically proven health benefits for both the treatment and prevention of disease. The increasing interest in nutraceuticals reflects the fact that consumers hear about epidemiological studies indicating that a specific diet or component of the diet is associated with a lower risk for a certain disease. The major active nutraceutical ingredients in plants are flavonoids. As is typical for phenolic compounds, they can act as potent antioxidants and metal chelators. They also have long been recognized to possess anti-inflammatory, antiallergic, hepatoprotective, antithrombotic, antiviral, anticarcinogenic activities.

Ingredients that make food functional are dietary fibers, vitamins, minerals, antioxidants, oligosaccharides, essential fatty acids (µ-3), lactic acid bacteria cultures, and lignins. Many of these are present in medicinal plants. Indian systems of medicine believe that complex diseases can be treated with complex combination of botanicals unlike in west, with single drugs. Whole foods are hence used in India as functional foods rather than supplements. Some medicinal plants and dietary constituents having functional attributes are spices such as onion, garlic, mustard, red chilies, turmeric, clove, cinnamon, saffron, curry leaf, fenugreek, and ginger. Some herbs as Bixa orellana and vegetables like amla, wheat grass, soyabean, and Gracinia cambogia have antitumor effects. Other medicinal plants with functional properties include A.marmelos, A. cepa, Aloe vera, A. paniculata, Azadirachta india, and Brassica juncea.

The vitamin E family consists of 8 isomers known as α-, β-, γ- & λ -tocopherols and α-, β-, γ- & λ-tocotrienols. Numerous studies focused on the health benefits of these isomers have been performed since the discovery of vitamin E in 1922. Recent discoveries on the potential therapeutic applications of tocotrienols have revolutionized vitamin E research. Nevertheless, despite the abundance of literature, only 1% of vitamin E research has been conducted on tocotrienols. Many new advances suggest that the use of tocotrienols for health improvement or therapeutic purposes is promising. Although the mechanisms of action of tocotrienols in certain disease conditions have been explored, more detailed investigations into the fundamentals of the health-promoting effects of these molecules must be elucidated before they can be recommended for health improvement or for the treatment or prevention of disease. Furthermore, many of the studies on the effects of tocotrienols have been carried out using cell lines and animal models. The effects in humans must be well established before tocotrienols are used as therapeutic agents in various disease conditions, hence the need for more evidence-based human clinical trials.

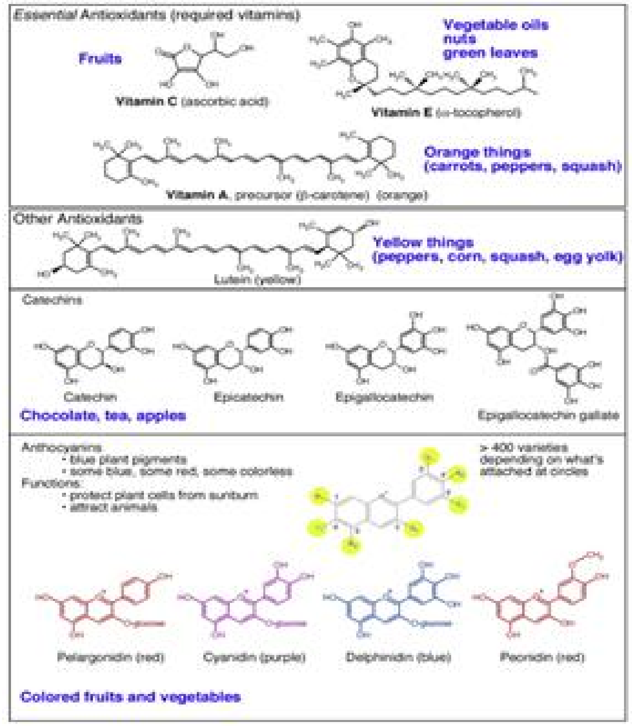

Figure 8

4. Conclusion

Free radicals damage contributes to the etiology of many chronic health problems such as cardiovascular and inflammatory disease, cataract, and cancer. Antioxidants prevent free radical induced tissue damage by preventing the formation of radicals, scavenging them, or by promoting their decomposition. Synthetic antioxidants are recently reported to be dangerous to human health. Thus the search for effective, nontoxic natural compounds with antioxidative activity has been intensified in recent years. In addition to endogenous antioxidant defense systems, consumption of dietary and plant-derived antioxidants appears to be a suitable alternative. Dietary and other components of plants form a major source of antioxidants.

The traditional Indian diet, spices, and medicinal plants are rich sources of natural antioxidants; higher intake of foods with functional attributes including high level of antioxidants in antioxidants in functional foods is one strategy that is gaining importance. Newer approaches utilizing collaborative research and modern technology in combination with established traditional health principles will yield dividends in near future in improving health, especially among people who do not have access to the use of costlier western systems of medicine. One of the most important steps you can take to prevent heart disease, cancer, Alzheimer's, and Parkinson's disease is to eat plenty of antioxidant-rich foods. Antioxidants are bounteous in plant foods, particularly those that have bright colours. The highest ranked foods in four major categories are as follows -Fruits: blueberries, cranberries, and blackberries; Vegetables: beans, , and surprisingly, russet potatoes; nuts: pecans, walnuts, and hazelnutsp; Spices: cinnamon, oregano, and ground cloves.

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