

# The Science of Free Radicals and Antioxidants

## What is a Free Radical?

A free radical is an atom or molecule that has an unpaired electron in its outer shell making it unstable and generally highly reactive [1].

An atom is stable when its outermost shell is full and becomes unstable when its outermost shell is not full. Because atoms naturally seek to reach a state of stability, an atom will try to fill or empty its outer shell by gaining or losing electrons. Alternatively, atoms can complete their outer shells by sharing electrons with other atoms. By sharing electrons, the atoms are bound together to create a stable molecule. Free radicals form when one of the bonds between atoms is broken and an uneven number of electrons remain. This means there is an unpaired electron, which makes the molecule unstable. It will then try to steal an electron from a nearby molecule to stabilize itself. Once a free radical forms and it succeeds in gaining another electron from a nearby molecule, its victim becomes a free radical since it is now short an electron. This unstable molecule will then try to steal an electron also. The result is referred to as a free radical cascade.

## How Do Free Radicals Form?

While there are different types of free radicals, the most common in aerobic organisms are oxygen free radicals, often referred to as reactive oxygen species (ROS), which include superoxides, hydroxyl anions, hydrogen peroxide and singlet oxygen.

ROS are formed either endogenously as a byproduct of normal metabolic processes in the human body or from other endogenous sources like mitochondria, inflammation, phagocytosis, arachidonate pathways and exercise [2]. These ROS do have roles in cell signalling and homeostasis [3]. Some exogenous sources of free radicals are cigarette smoke, environmental pollutants, radiation (eg. Ultraviolet, X-rays), certain drugs (eg. drug-induced toxicities), pesticides, industrial solvents and ozone.

## What is Oxidative Stress?

A balance between free radicals and antioxidants is necessary for proper physiological function. When ROS overwhelm the cellular antioxidant defense system, whether through an increase in ROS levels or a decrease in the cellular antioxidant capacity, oxidative stress occurs [4,5]. Short-term oxidative stress may occur in tissues injured by trauma, infection, heat injury, toxins, and excessive exercise. ROS have been implicated in carcinogenesis [6,7], diabetes mellitus, age-related eye disease, aging [8] and neurodegenerative diseases such as Parkinson's disease [9].

## How Do Free Radicals Cause Damage?

Free radical cascades in the body often terminate when a molecule that loses an electron becomes changed or cannot function without it. This causes damage to the molecule, and thus to the cell that contains it since the molecule often becomes dysfunctional. Free radicals are capable of damaging molecules such as DNA, proteins, carbohydrates, and

lipids [10] leading to cell and tissue damage. In the skin, this damage over time results in visible signs of aging including fine lines, wrinkles, discolouration, reduced firmness and even skin cancer.

## What is the Free Radical Theory of Aging?

The free radical theory of aging (FRTA) states that organisms age because cells accumulate free radical damage over time [11]. This theory was first proposed by Denham Harman in the 1950s [12]. In 1972 Harman modified his original theory to implicate mitochondria in the production of ROS [13]. This became known as the mitochondrial theory of aging [14], which proposes that ROS that are produced in the mitochondria cause damage to lipids, proteins and most importantly mitochondrial DNA [15].

Since then, the free radical theory has been expanded to include not only aging, but also age-related diseases. Free radical damage within cells has been linked to a range of disorders including cancer, arthritis, atherosclerosis, Alzheimer's disease, and diabetes [16].

## What are Antioxidants?

Antioxidants are molecules that prevent oxidative reactions by donating an electron to a free radical without becoming destabilized [17]. Antioxidants can safely interact with free radicals and terminate the cascade before vital molecules are damaged. Antioxidants are sometimes referred to as "free radical scavengers". Ascorbic acid (vitamin C), for example, can lose an electron to a free radical and remain stable itself by passing its unstable electron around the antioxidant molecule [18].

Both enzymatic and nonenzymatic antioxidants exist in the intracellular and extracellular environment to detoxify ROS [19]. There are several enzymes within the body that scavenge free radicals such as superoxide dismutase (SOD), catalase and glutathione peroxidase. Some of the nonenzymatic antioxidants, including glutathione and ubiquinol are produced during normal metabolism in the body [20]. Other antioxidants must be supplied by diet, including vitamin E ( $\alpha$ -tocopherol), vitamin C (ascorbic acid), and B-carotene [21].

Antioxidants are the skin's natural way to protect itself from free radicals. However, the effectiveness of the body's endogenous antioxidant system decreases with age [22], making supplementation essential.

Sunscreen is a must for protecting the skin from UV-induced free radicals, but it is important to remember that sunscreen only protects up to 55% of free radicals [23].

AlumierMD's skin care and sunscreen formulations are packed with antioxidants to replenish and protect the skin from free radical damage.

**References:**

- 1 Cheeseman KH, Slater TF. An introduction to free radicals chemistry. *Br Med Bull* 1993;49:481–93.
- 2 Ebadi M. Antioxidants and free radicals in health and disease: An introduction to reactive oxygen species, oxidative injury, neuronal cell death and therapy in neurodegenerative diseases. Arizona: Prominent Press 2001.
- 3 Devasagayam TPA, Tilak JC et al. Free radicals and antioxidants in human health: current status and future prospects. *Journal of Association of Physicians of India* 2004;52:794–804.
- 4 Rock CL, Jacob RA, Bowen PE. Update on biological characteristics of the antioxidant micronutrients-Vitamin C, Vitamin E and the carotenoids. *J Am Diet Assoc.* 1996;96:693–702.
- 5 Mc Cord JM. The evolution of free radicals and oxidative stress. *Am J Med.* 2000;108:652–9.
- 6 Trachootham D, Alexandre J, Huang P. *Nat Rev Drug Discov* 2009;8:579–91.
- 7 Valko M, Rhodes CJ et al. Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chem. Biol. Interact* 2006;160:1-40.
- 8 Haigis MC, Yanker BA. The Aging Stress Response. *Mol Cell* 2010;40(2):333-44.
- 9 Rao AL, Bharani M, Pallavi V. Role of antioxidants and free radicals in health and disease. *Adv Pharmacol Toxicol* 2006; 7:29–38.
- 10 Young IS, Woodside JV. Antioxidants in health and disease. *J Clin Pathol* 2001;54:176–86.
- 11 Hekimi S, Lapointe J, Wen Y. Taking a “good” look at free radicals in the aging process. *Trends in Cell Biology* 2011;21(10) 569-76.
- 12 Harman D. Aging: a theory based on free radical and radiation chemistry. *Journal of Gerontology* 1956;11(3):298-300.
- 13 Harman D. A biologic clock: the mitochondria?. *Journal of the American Geriatrics Society* 1972;20(4):145-47.
- 14 Harman D. Origin and evolution of the free radical theory of aging: a brief personal history, 1954–2009. *Biogerontology* 2009. 10(6):773–81.
- 15 Jang YC, Remmen HV. The mitochondrial theory of aging: Insight from transgenic and knockout mouse models. *Experimental Gerontology* 2009;44(4):256–60.
- 16 Harman D (2009). Origin and evolution of the free radical theory of aging: a brief personal history, 1954–2009. *Biogerontology* 2009;10(6):773–81.
- 17 Halliwell B. How to characterize an antioxidant- An update. *Biochem Soc Symp.* 1995;61:73–101.
- 18 Bagchi D et al. Oxygen free radical scavenging abilities of vitamins C and E, and a grape seed proanthocyanidin extract in vitro”. *Research Communications in Molecular Pathology and Pharmacology* 1997.
- 19 Frie B, Stocker R, Ames BN. Antioxidant defences and lipid peroxidation in human blood plasma. *Proc Natl Acad Sci.* 1988;37:569–71.
- 20 Shi HL, Noguchi N, Niki N. Comparative study on dynamics of antioxidative action of  $\alpha$ -tocopheryl hydroquinone, ubiquinol and  $\alpha$ -tocopherol, against lipid peroxidation. *Free Radic Biol Med.* 1999;27:334–46.
- 21 Levine M, Ramsey SC, Daruwara R. Criteria and recommendation for Vitamin C intake. *JAMA.* 1991;281:1415–23.
- 22 Poljsak B, Dahmane R. Free radicals and extrinsic skin aging. *Dermatol Res Pract* 2012;29.
- 23 Haywood, R., et al. *J Invest Dermatol* 2006;121:862-68.