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Free radicals v/s Antioxidants: The deadly Demons v/s the friendly scavengers: A review

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Introduction

Biological combustion produces harmful intermediates called free radicals. A free radical is simply defined as any species capable of independent existence that contains one or more unpaired electron that is alone in an orbital. There are two major types of free radicals Nitrogen Oxygen species (NOS) and Reactive Oxygen species (ROS)[1]. Free radicals are continuously produced by the body's aerobic life and our metabolism. Free radicals are also generated through environmental pollutants like cigarette smoke, radiation, air pollutants, pesticides etc. so these free radicals are an integral part of our daily life and in fact there appears no escape from them[2]. Nitric oxide acts on a variety of tissues normally but too much of it can be toxic. It has bee associated with lots of diseases. Exposure to this free radical is highly toxic[3].

ROS are formed during the reduction of oxygen to water. About 98% of inspired oxygen is reduced to water during lipolysis, inflammatory processes, production of chemical energy and several other biological processes. Remaining 2% of inspired oxygen leads to the formation of major ROS i.e. super oxide ion (O_2) Hydrogen peroxide (H_2O_2) and Hydroxyl ion (OH).

Besides these, two minor classes Trichloro methyl (CCL^3) a carbon centered radical thiyl (RS) a sulphur – centered radical etc. are also produced during different biochemical processes. All these free radicals are generated in the body and they become stable by "stealing" electrons from nucleic acids, lipids or any near by molecule by a process called reduction.

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The molecule that picks up an electron is reduced or stabilized and the molecule that loses an electron is oxidized. If this stealing of electron is left unchecked by the body's defense system the creation of free radical launches a chain reaction that results in cellular damage and various diseases[1-5].

Free radical management by body's defense system

Antioxidants are the substances, which act against oxidative compounds. They have been defined as substances that are capable of preventing oxidation of easily oxidizable materials[6]. Antioxidants may exert their effects by different mechanisms such as suppressing the formation of active species (ROS, NOS) scavenging active free radicals, repairing the damage and biosynthesis of other antioxidants or defense enzymes[7].

Under normal conditions the body's antioxidants convert ROS to H2O2 to prevent the over production of free radicals. The four main antioxidants in the body are Catalase, Super oxide dismutase (SOD), Glutathione peroxidase and Glutathione reductase[8]. The body's complex antioxidant enzyme system is influenced by two of the most familiar antioxidants i.e. vitamin E and C. Studies have shown that vitamin C and Vitamin E effectively scavenge free radicals and decrease lipid peroxidation[9]. Flavonoides are substances of vegetable origin also found to act as effective antioxidants.

In our body when level of free radicals exceeds the capacity of antioxidants to detoxify them then it results in "oxidative stress". This leads to several diseases, which regardless of their initiating pathological events share a series of steps that lead to a common mechanistic pathway of oxidative stress through regulatory oxidative signals[10].

Free radicals play a major role in Aging

Aging is the decline in physiologic functions of the living organisms that occurs over time. For all organisms the ultimate culmination of aging is same i. e. Death. Several theories of aging have been propounded from time. Among them Harman proposed "The free radical theory of aging" in Nov. 1954[11]. Human studies have also shown a strong connection between the radical/ oxidative damage and aging.Oxidative damage to DNA is an ongoing process in our body and it tends to increase with age. Several age dependent markers have been documented for this, which provide evidence of oxidative damage to DNA in human aging[12].

Free radicals and disorders

Atherosclerosis_– Oxidative stress especially oxidation of low density lipoproteins (LDL) has long been suspected to play a critical role in atherogenesis that leads to accumulation of cholesterol in the atherosclerotic lesion[13]. Many

observations support the view that hyperlipidemia is merely a risk factor and oxidative stress is the root cause of atherogenesis[14]**.** It was observed that high fat diet affects 32 genes; however only three genes were observed to be related to atherogenesis and some showing decreased expression were those of free radical scavenging enzymes resulting in increased oxidative stress. This experiment also showed that oxidative stress induces atherogenesis[15].

Alzheimer – Recent evidence in the field of Alzheimer disease research has highlighted the importance of oxidative process in the pathogenesis[16].Alzheimer disease is the commonest form of dementia in women and men aged 60-69 years[17]. However the initial source of oxidative stress in Alzheimer disease is still unclear. Recent research reveals that dietary antioxidants may have promising therapeutic potential in delaying the onset as well as preventing the aging population with Alzheimer disease and its related complications[18].

Neurodegenerative Diseases- The role of antioxidants has been studied in neurological disorders also. Patients of Amyotrophic lateral sclerosis (ALS) and Down's syndrome show decreased level of SOD. After many studies it has been concluded that a deterioration of the antioxidant defense system contributes to neuronal death and we can consider free radicals as the first cause of neurodegenerative disorders[19,20].

Cancer – The process of development of cancer can be divided in to three stages. The first stage is initiation, second is promotion and third is progression. Free radicals play the role of mediators in carcinogensis especially in the stage of initiation and promotion. Each stage involves both genetic and epigenetic changes[21]. Sequence specificity of DNA damage plays a key role in the mutagenic process. Endogenous DNA damage arises from a verity of intermediates of oxygen reduction and several free radicals are now known to take part in this process by various mechanisms. Apart from these actions, antioxidants have also been documented as anticancer agents[22].

Diabetes and diabetic complications- Considerable evidence supports the fact that hyperglycemia results in the generation of ROS. One major consequence of this is the expression of gene products that cause cellular damage and are ultimately responsible for late complications of diabetes[23]. The ability of antioxidants / free radical scavengers to protect from the effects of hyperglycemia and free fatty acids along with clinical benefits following antioxidants therapy indirectly proves the role of oxidative stress in causing these abnormalities[24].

Stroke- It's the leading cause of death and disability in the USA. In the general population

incidence of stroke is 1/1000 individuals; however incidence doubles in individuals who are 80 years and above of age[25]. The newer developments also support views that agents that scavenge free radicals or prevent their production may be able to prolong the therapeutic time window. Several antioxidants and free radical scavenging based therapeutics have been recently launched and are under development for treatment purpose[26].

Having explored in various ways the universe of free radicals, their formation, their role in our body, and their implication in disease we conclude that an increase in free radicals or reduction in antioxidant defense system leads to oxidative stress. This causes many complications which means to say that antioxidants can be used to treat oxidative stress generated disorders. However as always the dictum of "prevention is better than cure" should be followed and a complete diet should be the rule rather than an exception. Although supplementary antioxidants can be useful but should not be used as a replacement for a wholesome diet and other lifestyle factors known to prevent diseases. Consumption of fresh fruits and vegetables, regular exercise and smoking cessation are all – important for reducing the risk of disease.

Presented below is a summary of the salient features of the Free radicals, their effects and antioxidants in **poetry form:**

H_2O_2, O_2 and OH----Deadly all three,
Commonly known they are as radicals free.

Electrons they steal and become stable,
Of causing oxidative stress, they are capable.

Antioxidants---the friendly scavengers,
Function they, as the body's avengers.

SOD and Catalase we have got,
Glutathiones also forget we should not.

Aging—the free radicals cause and induce,
Creases and wrinkles in everyone they produce.

Oxidative damage to DNA---a major event,
Try as much one might, but cannot prevent.

Atherogenesis—the killer deadly but mute.
Oxidative stress is present at its root.

Alzheimer—the curse of Mankind,
Dig deep and free radicals you find.

Causing damage neuronal is their creed,
To Amyotrophic Lateral Sclerosis and down's they lead.
Initiation and Promotion in cancers seen,
Attributed to free radicals it has been.

Mutation around DNA damage revolves,

Action by most free radicals, that involves.

Diabetes and its complications known and unknown,
To them, oxidative stress makes the patient prone.

Stroke disability or death is the effect,
If antioxidant mechanism has a defect.

With antioxidants Mother Nature does abound,
In most fresh fruits and vegetables found.

Consume them aplenty and keep stress at bay,
Lead a disease free and healthy life you may.

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