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A Review Article: Free Radical and Replacement Synthetic Antioxidant by Natural Antioxidant

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ABSTRACT

Free radical may be responsible of several pathophysiology disease for threatening human life, and they are produced from endogenous and exogenous sources. Using the balanced amount of nutritious diet lead to a good health, may be neutralizing or scavenging free radicals by antioxidants compounds. daily diet have large number of vitamin A, E and C, carotenoids, polyphenols, etc. as natural antioxidants, the main bases of them are fruits, cereals, vegetables, and beverages. Enzymatic and non-enzymatic antioxidant substances are two different kinds that lessen the reactions of free radicals. In order to protect itself from reactive oxygen species, the human body uses an enzyme antioxidant. The two kinds of non-enzymatic antioxidants are natural antioxidants and synthetic antioxidants. The aim of this review is to knowledge a reasons which causes the free radical and balance them by natural antioxidant constituents, and replacement synthetic antioxidant by natural antioxidant, due to daily diet have large amounts from natural antioxidants, and natural antioxidants more effective than synthetic antioxidants, in additional they occurrence in nature and more inexpensive.

Keywords- Free radicals, Natural antioxidants, medicinal plants, fruits and vegetables.

I. INTRODUCTION

Free Radicals are an unpaired electron molecules. These molecules are extremely reactive because the occurrence free unpaired electron, they are intermediated in the natural processes including cytotoxicity (Khan *et al.*, 2018). Biochemical activities generate free radicals, which can cause DNA damage and membrane lipid breakdown (Khan et al., 2018). Excessive production of reactive nitrogen species (RNS) and reactive oxygen species (ROS) caused by alcohol intake, cigarette smoking, environmental pollutants, and radiation disrupts the stability of oxidation and anti-oxidation. and cause some illnesses to persist and deteriorate (Li et al., 2015; Zhou et al., 2016).

The oxidation of lipids, proteins, and DNA was induced by reactive nitrogen species RNS and ROS as hydroxyl and nitric oxide superoxide radicals (Li et al., 2015). Free radicals have been linked to several neurological diseases, including Alzheimer's and Huntington's disease. (Khan *et al.*, 2018).

Natural anti-oxidants found in food and therapeutic plants, such as carotenoids and polyphenols, have a broad diversity of biological properties, with anti-aging, anti-inflammatory, anti-cancer, and anti-atherosclerosis (Xu *et al.*, 2017). The exogenous antioxidants chiefly occurrences in vegetables, fruits, mushrooms, cereals, flowers spices and traditional medicine herbal (Li *et al.*, 2016; Zhang *et al.*, 2016). Natural protectors include main polyphenols (flavonoids, phenolic acids, anthocyanins, lignans, and stilbenes), carotenoids (xanthophylls and carotenes), and vitamins E and C obtained from plant components (Li *et al.*, 2016; Zhang *et al.*, 2016; Deng *et al.*, 2012). Increasing natural antioxidants intake would improve the harm produced by oxidative stress by oxidative chain reaction, performing as free radical reducer (Baiano and del Nobile, 2015). The aim of this review is to knowledge a reasons which

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causes the free radical and balance them by natural antioxidant constituents, replacement synthetic antioxidant by natural antioxidant.

II. FREE RADICALS' SOURCES

Free radicals may be created from endogenous and exogenous sources. The endogenous sources of free radicals contain diverse cellular organs as endoplasmic reticulum, peroxisomes, mitochondria, and where the oxygen intake is great (Finkel and Holbrook, 2000). Various exogenous sources of free radicals as water pollution, smoking, heavy metals**,** drugs**,** pesticides, ultraviolet light, and industrial solvents **(**Pham-Huy *et al.,* 2008**)**.

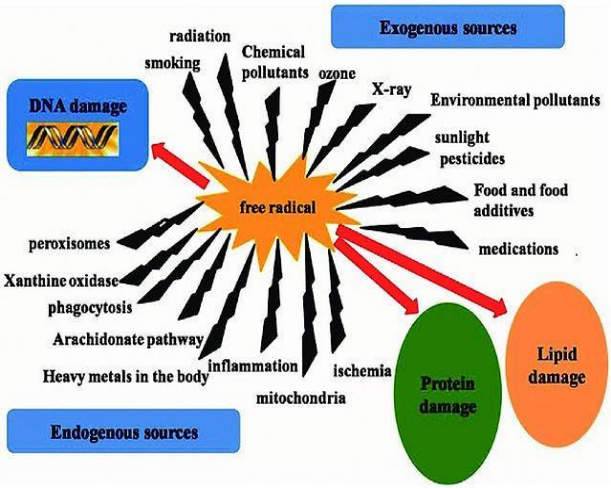

Figure 1: Exogenous and endogenous sources of free radicals (Ahmad *et al.*, 2017)

III. FREE RADICAL TARGETS

Deoxyribonucleic Acid (DNA)

Hydrogen peroxide, $O2^{\cdot-}$ dioxygen, and $OH^{\cdot}$ functional group are formed by oxygen metabolism (H_2O_2). Because of its high sensitivity, the $OH^{\cdot}$ interacts with organic compounds like proteins, lipids, and DNA and changes their chemical composition. Numerous studies have documented the DNA oxidative damage caused by OH (Halliwell and Gutteridge, 2007; Von Sonntag, 2006). The $OH^{\cdot}$ reacts with DNA basepairs in a number of ways, producing oxidative harm to the sugar and heterocyclic moiety in oligonucleotides. This particular type of DNA oxidative damage is closely related to metabolic processes like mutagenesis, aging, and cancer (Dizdaroglu, 1992; Breen and Murphy, 1995).

Proteins

The oxidative damage of protein may be created through radical species such as peroxyl, OH•, $O2^{\bullet-}$, alkoxyl, hydroperoxyl, in addition to the H_2O_2 non-radical species, HOCl, O3, OONO-, singlet oxygen (Dean *et al.*,1997). Amino acids of the proteins, oxidization by ROS producing creation of protein–protein cross linkages, producing in the loss and denaturing of proteins function, loss of receptors function and transport proteins, loss of enzyme activity (Butterfield et al., 1998). Amino acids which containing the sulphur as cysteine and methionine are more sensitive to ROS oxidation and are changed to methionine sulphoxide and disulphides (Brodie and Reed, 1990; Pryor *et al.*, 1994) respectively. Only these two proteins can be converted from their oxidized versions to their natural states in living systems thanks to two different enzymes called methionine sulfoxide and disulfide reductases (Berlett and Stadtman, 1997; Kikugawa *et al.*, 1994).

Lipids

The lipids of membrane, particularly the poly-unsaturated fatty acid remains of phospholipids are high sensitive to free radicals oxidation (Siems *et al.*, 1995). Lipid peroxidation impairs membrane function by inactivating membrane-bound enzymes, sensors, and permeability (Bast, 1993). Aldehydes are constantly broken down by lipid hydroperoxides. Aldehydes are physiologically active substances that can diffuse from the place of an attack and feast to other cell parts (Devasgayam *et al*.,2003). Lipid peroxidation has frequently been linked to illnesses and tissue injury (Esterbauer *et al.*, 1991).

IV. NATURAL ANTIOXIDANTS IN FRUITS AND VEGETABLES

Antioxidants are compounds that inhibit free radical-induced processes or prevent cell damage (Young and Woodside, 2001). Antioxidants can exist in both enzyme and non-enzymatic types in both the external and intracellular surroundings. ROS and RNS are made as a consequence of regular biochemical interactions and greater atmospheric exposure (Bagchi and Puri, 1998). Superoxide dismutase (SOD) and reduced glutathione (GSH) are examples of endogenous antioxidants, while vitamin E and C, as well as carotenoids, are examples of external antioxidants (Halliwel, 2011; Amber *et al*., 2013). Balance between free radicals produced by metabolism and antioxidant molecules is one of the antioxidants' functions (Poljsa *et al*., 2011).

There are four main categories of natural antioxidants (non-enzymatic) that can be used to categorize the antioxidants present in fruits and vegetables: carotenoids, polyphenols, vitamins, and minerals. Two major categories can be used to classify polyphenols: Flavonoids and phenolic compounds (Ariasal et al., 2022). Consuming fruit and vegetables which have vitamins and minerals in suitable amounts improves the immune system and avoid sicknesses as heart disease, diabetes, obesity, and cancer (Ariasal et al., 2022).

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Carotenoids are found as acyclic molecules or as α- and β-carotene chain with six-carbon rings at each end, in veggies and fruits (Bohn *et al*., 2019). Carotenes are great antioxidants because of their capability to decrease the formation of free radicals (Fiedor and Burda, 2014; Perera and Yen, 2007). Furthermore, eating carotene-rich foods increases immunological response, lowers cardiovascular risk, reduces cell growth, cancer, and has neuroprotective and hepatoprotective properties (Chiu *et al*., 2019; Ikonne *et al*., 2020; Sun *et al*., 2020). Vitamins are important compounds in a variety of biochemical and metabolic processes in the human body. Fruits and veggies contain vitamins A, E, and C, three of the many essential vitamins (Noh and Mustar, 2019), they may stop the progression of illnesses like some types of cancer, cardiovascular, neurological, and cell degenerative diseases that are caused by oxidative stress and free radicals (Gelain *et al.,* 2012). Phenolic acids commonly occurrence in vegetables and fruits have great antioxidant potential (Süntar and Yakıncı, 2020; Thakur *et al.,*2020). Plants produce phenolic acids as secondary compounds. They are made up of an aromatic ring called benzene in which hydroxyl groups or carboxylic acids replace the hydrogen atoms (Chen *et al.,* 2020). Comparing phenolic acids to flavonoids, their primary benefit is that they are in free state, which makes them easier to dissolve, translate, and absorb by the digestive system (Chen *et al.,* 2020).

The minerals found in the highest parts in fruits and vegetables are selenium, magnesium, copper, and zinc. Selenium is found in glutathione peroxidase, an antioxidant enzyme that catalyzes the reduction of hydrogen peroxide and peroxide radicals (Fanucchi, 2014). Numerous health properties of selenium have been described, involving hormone biosynthesis, cellular and molecular defense, and diseases prevention as atherosclerosis, cardiovascular, some kinds of cancer, and coronary risks (Prashanth *et al.,* 2015; VA and EN, 2004). For more than 300 enzymes and more than 2000 regulatory factors, zinc serves as a crucial coenzyme (Marreiro *et al*., 2017). It aids in a number of antioxidant processes, including the protection of proteins from oxidation damage, the promotion of enzyme development, and the inhibition of enzymes that cause lipid peroxidation products, nitric acid synthase, and NADPH oxidase to experience oxidative reactions (Prasad, 2014). When used in thiol groups, zinc can immediately act as an antioxidant and prevent ROS and RNS such as hydroxyl radicals, hydrogen peroxide, peroxynitrites, and superoxide anions (Olechnowicz *et al.,* 2017). Due to the role that magnesium plays in a wide range of enzyme processes, a number of its health benefits have been identified (Szenthmih ´alyi *et al.,* 2014). The main enzyme, manganese superoxide dismutase, has antioxidant functions that are critical for preventing oxidative harm to mitochondria during ATP synthesis, which generates a superoxide radical at the same time (Erikson and Aschner, 2019). It too functions as a coenzyme in the ATP biochemical procedure (Castellanos-Guti'errez *et al*., 2018). Copper is an essential component because a dearth of it has been exposed to raise cellular oxidative harm. Its existence is essential since it can function as a cofactor in a number of oxidative procedures that change ROS to water. (Nimse and Pal, 2015). In addition to antioxidant defense, copper is essential for a variety of metabolic and cellular processes including enzyme stimulation, immune function, iron metabolism, and molecule formation (Bost *et al.,* 2016).

V. FREE RADICALS' MODULATION THROUGH NATURAL ANTIOXIDANTS

Antioxidants occurrences in two types are the enzymatic and non-enzymatic antioxidants which reduce the free radical reactions. Human body keeps himself from reactive oxygen species through utilizing enzymatic antioxidant mechanisms (Moncanda *et al.,* 1991). Superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase (CAT), and peroxiredoxin are enzymes that catalyze the transformation of $O2^{\bullet -}$ into H_2O_2 and oxygen using metal ions as cofactors, such as manganese (Mn), copper (Cu), and zinc (Zn) (Gough and Cotter, 2011). The peroxisome contains the enzyme CAT, which converts H_2O_2 to oxygen and water (Stone and Yang, 2006). The enzyme GPX are accrue in together the extracellular and cytoplasm in nearly all human tissue which converts H_2O_2 into the water (Cabiscol *etal.,*2000). Peroxyredoxin enzyme promote the decrease of organic hydroperoxides, H_2O_2, and the peroxynitrite (Valko *et al.,* 2006).

Antioxidants the non-enzymatic are two kinds, the synthetic and natural antioxidants. a-tocopherol (vitamin E) is an effective antioxidant which lipid soluble, it functions as break down a chain through lipid peroxidation in various lipid particles and cell membranes including low-density lipoprotein (LDL) (Morli`ere *et al.,* 2012; Stocker *et al.,*1991). Vitamin E's antioxidant properties reduce fatty peroxyl radicals in both in vitro and in vivo systems (Niki, 2014).

Ascorbic acid, or vitamin C, is a water-soluble antioxidant and anti-free radical. Furthermore, Vitamin C modifies the ascorbate radical by adding an electron to the lipid radical, thereby halting the lipid peroxidation chain reaction (Retsky *et al.,*1993; Oh *et al.,* 2010). Monaghan and Schmitt (1932) showed that vitamin A may keep lipids against rancidity.

Bioflavonoids commonly spread in vegetables and fruits, are showed to have several biological properties involving free radical-reducing activity (Rubens de Souza *et al.,*2004).

Compared to any other reactive oxygen species, carotenoids are antioxidant compounds that help to decrease the peroxyl radicals that are expertly added. The peroxyl radicals made by the development of lipid

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peroxidation, which may damage the lipids in cell walls. They may disrupt the metabolic plan and prevent cellular lipid harm by scavenging. Because of their peroxyl radical reducing action, carotenoids are recognized to play a key role in protecting cellular membranes and lipoproteins from other reactive oxygen species (Sies and Stahl,1995; Stahl and Sies, 2003).

VI. REPLACING SYNTHETIC ANTIOXIDANTS WITH NATURAL ANTIOXIDANTS

Synthetic antioxidants are manufactured artificially through mixtures of many chemical compounds inside the laboratory (Anbudhasan *et al.*, 2014). According to some accounts about their mutagenicity and carcinogenicity, these compounds that are not naturally occurring are added to foods as preservatives to prevent lipid oxidation (Atta et al., 2017). As a result, natural antioxidants are used in their stead (Uzombah, 2022).

Due to the fact that the average western diet contains close to 1 g of natural antioxidants, humans prefer to substitute synthetic antioxidants with natural ones. Fruits, cereals, veggies, and drinks are the main sources of natural antioxidants. Natural antioxidants must be added to the food in greater amounts than manufactured antioxidants because natural antioxidants are more active (Pokorný, 2007). Food manufacturing is leading for their replacement synthetic antioxidants with natural antioxidants due to increase the human prefer the natural antioxidants in additional, not only more inexpensive but are ecofriendly (Rashmi and Disha, 2011). The choice of natural antioxidants mainly occurrence in diet products is controlled by the international standards or regulatory laws of particular countries. Synthetic antioxidants have been utilized in place with natural antioxidants, generally due to they current higher stability, low costs, performance, and wide availability (Saad *et al.*, 2007; Xiu-Qin *et al.*, 2009).

VII. CONCLUSION

Both natural and exogenous sources can create free radicals, which antioxidant substances can either scavenge or neutralize. There are two kinds of antioxidant compounds: enzyme and non-enzymatic. The human body uses enzyme antioxidants to protect itself from ROS. There are two types of non-enzymatic antioxidants: natural and manufactured antioxidants. Increasing fruit, vegetables, cereals, and medicinal plants due to have large number of antioxidants compounds at different levels, and these compounds which neutralizing free radicals, and treating several diseases caused by oxidative stress, and replacement synthetic antioxidant by natural antioxidant due to they are more effective than synthetic antioxidants, in additional they occurrence in nature and more inexpensive.

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