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The Relationship Between Oxidative Stress and Selenium

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ABSTRACT

Oxidative stress is characterized by an imbalance between prooxidant molecules in cells and tissues and antioxidant molecules that try to detoxify these reactives molecules. Oxidative stress is affected by both genetic and environmental factors. Selenium (Se) is an essential trace element and inadequacy can lead to various types of diseases, such as cancer and heart disease. Foods are the main source of Se, and it is commonly found in seafood, grains, meat products, milk, vegetables and fruits. Se is an enzyme with antioxidant properties and is included in the structure of seleno enzymes. In this article, the metabolism and antioxidant properties of se are reviewed.

Oksidatif Stres ve Selenyum Arasındaki İlişki

ÖZET

Oksidatif stres, hücrelerdeki ve dokulardaki prooksidan moleküller ile bu reaktif molekülleri detoksifiye etmeye çalışan antioksidan moleküller arasındaki dengesizlik ile karakterize edilir. Oksidatif stres hem genetik hem de çevresel faktörlerden etkilenir. Selenyum esansiyel bir eser elementtir ve yetersizliği kanser ve kalp hastalığı gibi çeşitli hastalıklara yol açabilir. Selenyumun ana kaynağı besinlerdir ve genellikle deniz ürünleri, tahıllar, et ürünleri, süt, sebze ve meyvelerde bulunur. Selenyum antioksidan özelliklere sahip bir enzimdir ve seleno enzimlerinin yapısında yer alır. Bu yazıda selenyumun metabolizma ve antioksidan özellikleri gözden geçirilmiştir.

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1. INTRODUCTION

As an essential trace element, humans absorb selenium (Se) mainly through cereals and meat. According to the World Health Organization (WHO), the value for daily intake of Se value for adults is 50-70 micrograms/day for both men and women [1, 2]. Se plays an important physiological role in thyroid hormone metabolism, immunity, and antioxidant protection. Se deficiency has been reported to be effective in various types of diseases, including cardiovascular disease and cancer [3]. Se is involved in the structure of the enzyme glutathione peroxidase enzyme (GPx). This enzyme is a very important component of the antioxidant defense system of the organism, as it protects lipids, proteins and nucleic acids in the cell structure from oxidative damage [4]. This article deals with the metabolism of Se and its antioxidant role in human health and disease.

Selenium

Se is found in group 16 of the periodic table and is an essential element necessary for human and animal organisms [5]. Depending on dietary habits, the total Se intake comes from meat and fish as well as cereals. Se is widely used in photocells in industry, glass and ceramic photography, rubber industry, steel alloying, Se rectifiers, electronics industry, laser printers and photocopiers [6].

Se compounds are absorbed in the duodenum in humans. Se binds to plasma proteins and lipoproteins (Very low-density lipoprotein (VLDL), low-density lipoprotein (LDL)) in the blood. When Se is taken to meet normal needs, the organs where it is collected in the highest concentration are the liver, kidney, testes, and thyroid. Skeletal muscle accounts for most (40-50%) of the Se pool in the body [7]. The uptake, metabolism and distribution of Se in the body are shown in Figure 1. [8].

In the evaluation of daily Se intake compared with blood Se levels determined in the Turkish population, daily Se intake was calculated to be 43 µg/Lday on average [9]. Se is included in the structure of the enzyme GPx, which is an important member of the antioxidant defense mechanism. Se exerts its biological effects through selenoproteins, which mainly contain the amino acid selenocysteine. Selenocysteine, which is present in the structure of some enzymes, is formed when one of the sulfur atoms in the amino acid cysteine is replaced by a Se atom. The antioxidant properties of selenoproteins help prevent cell damage caused by free radicals. Selenocysteines are anionic at biological pH, thus enabling biological redox reactions by electron exchange [10]. Se is generally found in tissues in two forms: Selenocysteine and selenomethionine. Selenocysteine: it is the biologically active form of Se that forms the active part of enzymes that participate in oxidation and reduction reactions in prokaryotic and eukaryotic life. Selenomethionine cannot be synthesized in the body and is absorbed through the diet. Selenomethionine is believed to be a structure that stores the element Se. When the absorption of this element in the body is blocked, it acts as a source of Se for the organism. Selenocysteine is a Se-containing analog of cysteine, which is defined as the twenty-first amino acid encoded by DNA. Se-containing amino acids, selenomethionine, are derived from plant

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sources, while selenocysteine is derived from animal sources. Se is an essential element with antioxidant and anticarcinogenic properties [11, 12]. As a member of the selenoprotein family, Se has structural and enzymatic functions. The best known of its enzymatic functions is its antioxidant and catalytic role in the production of active thyroid hormone. Se acts as an oxidation-reduction center and contributes to the control of intracellular oxidation-reduction. Selenoproteins are protein structures that contain selenocysteine residues. Se deficiency is thought to cause clinical findings that are due to a disturbance in the formation of selenoproteins. At least seven isoenzymes of GPx have been identified [10, 13, 14].

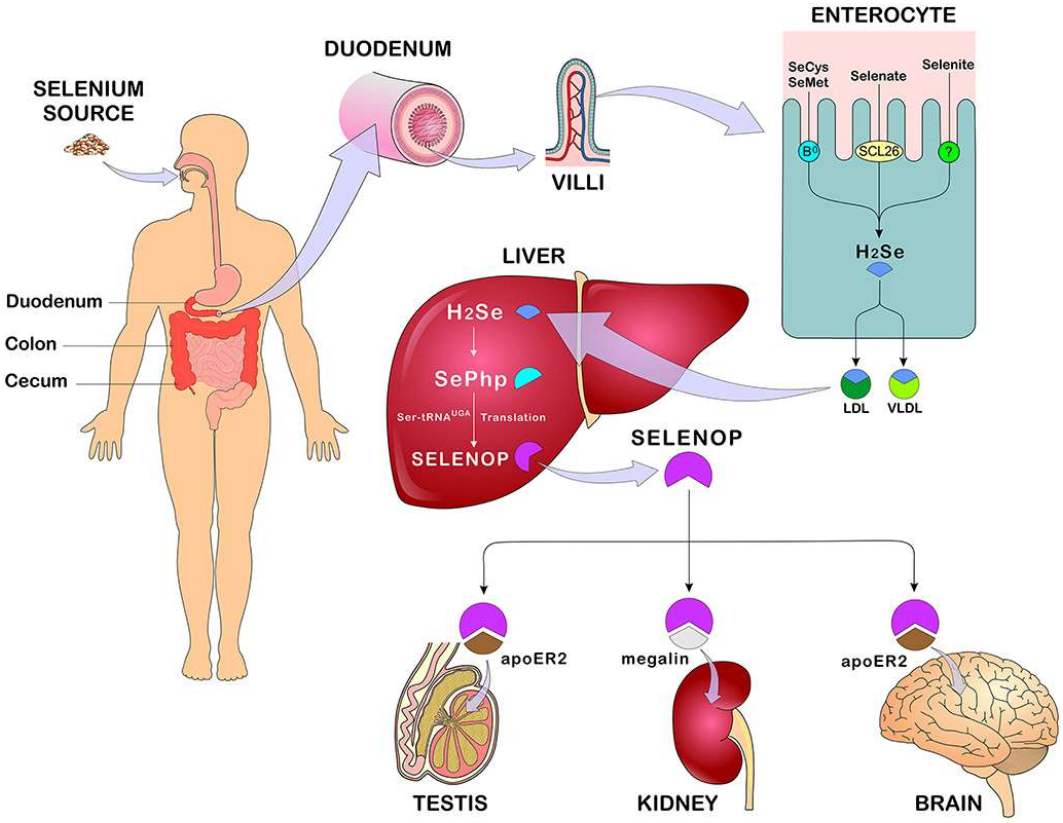

Figure 1. Se absorption, metabolism, and distribution [8]

GPx1 is the most abundant form and is found in almost all mammalian tissues. It catalyzes the reaction of conversion of hydrogen peroxide to water. Thus, it protects the organism from oxidative damage. GPx1 is an antioxidant in the cytoplasm of cells and acts as a se store. When the structure of glutathione peroxidase was studied, it was recognized that it consists of a tetrameric selenoprotein containing a selenocysteine residue. The most important functional part in the structure is the selenocysteine end, and the forms that do not contain selenocysteine are nonfunctional. Although each GPx is a different selenoprotein, they are all antioxidant enzymes that reduce potentially harmful reactive oxygen species such as hydrogen peroxide and oil hydroperoxides by oxidizing glutathione to harmless products such as water and alcohol [15].

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Oxidative stress

Oxidative stress occurs when reactive oxygen species (ROS) is formed in cells that damage or kill cells. Metal ions react with superoxide anions and hydrogen peroxide to produce highly reactive species such as free hydroxyl radicals and metal-oxygen complexes in biological systems that lead to oxidative damage. Oxidative stress occurs when there is an imbalance between the production of ROS and its detoxification (Figure 2.) [16-18].

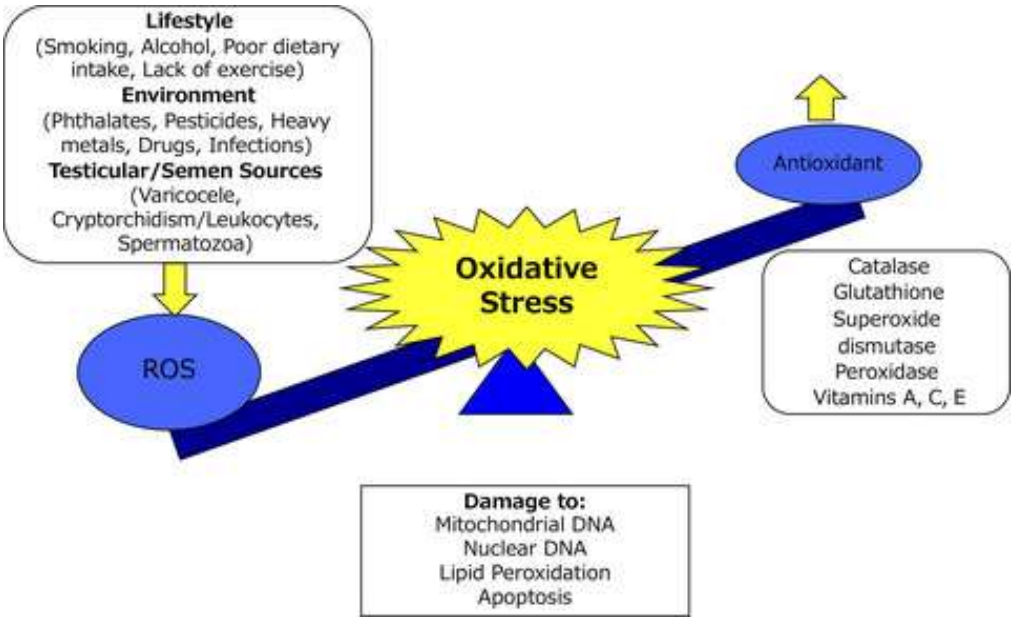

Figure 2. Oxidative stress [18]

All tissues and cells contain systems to detoxify biologically reactive intermediates and prevent or reduce cellular damage from oxidative stress. Biological antioxidants are natural molecules that protect the cell from the uncontrolled formation of free radicals and ROS or prevent them from reacting with biological structures [19]. ROS are superoxide radicals, hydrogen peroxide, and hydroxyl radicals, which are formed in small amounts during normal oxygen metabolism. ROS can initiate radical chain reactions in which various free radicals are formed and cause the formation of various free radicals such as carbon-centred organic radicals, peroxide radicals, alkoxy radicals, and sulfenyl radicals in the cell. ROS and oxygen-free radicals are often unstable and highly reactive. Radicals such as superoxide anion radical, hydroxyl radical, peroxyl radical, nitric oxide, organic peroxide radical are divided into nonradicals such as hydrogen peroxide, lipid hydroperoxide, singlet oxygen, ozone, nitrogen dioxide, and hypochlorous acid. Three major reactive oxygen species, the superoxide radical, hydrogen peroxide, and hydroxyl radical, are normal metabolites continuously produced by mitochondria in growing cells [20, 21].

Free radicals are defined as molecules with one or more unpaired electrons, short-lived, unstable, of low molecular weight and very active. They are formed by the removal of an electron from a nonradical atom or molecule or by the addition of an electron to an atom or

molecule. The radicals formed are not very reactive and are stable. They act as reducing or oxidizing agents in the body because they can donate electrons to or accept electrons from other molecules. Oxidative stress occurs when the balance between free radicals and the antioxidant defense system shifts in favor of the free radicals [22]. Free radicals have different chemical structures such as hydroxyl, superoxide, nitric oxide, and lipid peroxide radicals. The most important free radicals in biological systems are those formed from oxygen. For example, the superoxide radical, which is extremely active and damages many cells, is converted to hydrogen peroxide by superoxide dismutase. Hydrogen peroxide, which is much less effective than superoxide, is rendered harmless by being converted to water and oxygen by enzymes such as catalase and peroxidase in tissues [23]. Free radicals formed in the organism are of endogenous and exogenous origin. Endogenously, mitochondrial electron transport chain (ETZ) in mammals, oxidative reactions in phagocytic and endothelial cells, redox cycles and arachidonic acid metabolism are formed by the action of enzymes such as xanthine oxidase and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. Exogenous sources include industrial pollutants, drugs, diet, ionizing radiation, ultraviolet light and cigarette smoke. [16, 22, 24].

In the organism, there are protective mechanisms against the harmful effects of free radicals. Some of these mechanisms prevent the formation of free radicals, and others prevent the harmful effects of the formed free radicals. All substances that perform these functions are called antioxidants. Antioxidants are substances that protect cells both directly and indirectly from the adverse effects of xenobiotics, drugs, carcinogens, and toxic radical reactions. Antioxidants act in four different ways. Chain-breaking action: it stops the chemical reactions that generate free radicals, binds the oxygen free radicals to itself, breaks their chains and prevents their function. Suppressive action: it reduces the reaction rate, interacts with the oxygen free radicals and transfers a hydrogen to them, reducing their activity or converting them to an inactive form. Vitamins have this effect. Restorative action; They regenerate the biological molecular damage that occurs in structures such as lipid, protein and DNA. Enzymatic action; they show their action by increasing the synthesis of antioxidant enzymes such as SOD and non-enzymatic antioxidants in the organism.Antioxidants are substances that oxidize at low concentrations and can reduce (with electron transfer) or prevent the oxidation of another substrate, i.e. fight oxidation. Antioxidants can be of endogenous or exogenous origin [19, 22].

Selenium and oxidative stress

Oxidative stress results from the production of endogenous and exogenous ROS and an imbalance between the production of ROS and antioxidant defenses. Oxidative stress plays a role in the development mechanism of many diseases such as cardiovascular disease, acute and chronic kidney disease (CKD), diabetes, hypertension, chronic obstructive pulmonary disease (COPD), neurodegenerative diseases (NDs), biliary disease and cancer. Se is found in the structure of selenoprotein that exhibit antioxidant, anti-inflammatory, and antiviral effects [25, 26].

It has been shown in animal studies that Se supplementation increases plasma GSH levels and decreases malondialdehyde (MDA) levels, and as a biomarker of oxidative stress [26-28]. Some studies reported that Se supplementation could not affect plasma GSH and total antioxidant capacity (TAC) levels in a short time (3 weeks) [29]. Se is one of the essential components of the GPx enzyme, its task is to protect the cell from free radicals. [3, 11, 26]. Se supplementation suppresses the NF-kappa B pathway with selenoproteins. Se uptake may play a role in reducing oxidative stress through free radical inhibition by being involved in the GPx structure. [1, 8, 12].

2. CONCLUSION

Research on Se over the past few years has produced a wealth of evidence showing the important role that Se and its metabolites play in human disease. In particular, our knowledge of the functional roles of the GPx and TrxR groups as essential antioxidant selenoenzymes in protecting cells from oxidative stress has greatly increased. Until specific biomarkers that directly associate Se with disease prevention and treatment are identified, its use as a supplement in health care should be taken with caution. Se increases the levels of antioxidant biomarkers against free radicals, decreases the levels of oxidative markers and thus prevents oxidative stress. Se, oxidative stress and antioxidant status can be studied in oxidative-related diseases.

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