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Oxidative Stress: Cause Mechanisms and Defense Agents

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ABSTRACT

Although oxidation is a fundamental part of cellular metabolism and is involved in energy production, regulation of cell growth, and cell defense, there may be detrimental effects related to the aggression of proteins in the tissues, enzymes, and DNA. In this context, the objective of this work is to analyze the main mechanisms that cause oxidative stress, and the most relevant agents for antioxidant defense. This work means to be descriptive in nature. The descriptive research, according to Gil (2007) has as main objective the description of the characteristics of certain populations or phenomena, aiming to describe, explain, classify, and clarify the presented problem. The methodology was given through bibliographic research initially. The research was done with theoretical basis, being sketched arguments by the researcher on the subjects treated. It was concluded that the installation of oxidative stress occurs due to an imbalance between pro-oxidant and antioxidant factors, since the mechanisms of free radical generation occur in mitochondria and cytoplasm.

Keywords

Oxidative stress, Free radicals, Antioxidant.

Introduction

The body has an antioxidant protection system that acts as a defense mechanism against free radicals that are constantly formed, but in excess causes oxidation of biological molecules [1]. Although oxidation is a fundamental part of cellular metabolism, and involved in energy production, regulation of cell growth, and cell defense, there may be detrimental effects related to the aggression of proteins in the tissues, enzymes and DNA. Oxygen during the transport of electrons in the mitochondria can be reduced in order to generate reactive oxygen species - EROs, hydrogen peroxide - H_2O_2 and free radical -OH-.

When one has the loss of balance of production and elimination of ROS, oxidative stress occurs, causing damage to DNA, RNA and lipids, besides contributing to diseases such as cancer. The mechanisms of free radicals, usually occur in the mitochondria and the cytoplasm, besides being generated in the enzymes NADPH oxidases, which has the function of transferring electrons through cell membranes. The hydroxyl radical - HO has a short half life, making it difficult to in vitro sequestration, being formed in the body by the reaction of hydrogen peroxide - H_2O_2, causing damage to DNA, RNA, lipids and cell membranes [1].

The most deleterious means of oxygen to the body is singlet oxygen, causing photoinduced toxicity of O_2 in living organisms, and can act in a beneficial way in the defense of infection, stimulating the neutrophils to produce ERO [2]. The process of oxidative stress is established when there is an imbalance between oxidative and antioxidant compounds due to the excess of free radicals. It is mentioned that the lipid component of the erythrocyte membrane is subjected to intracellular oxidative aggression [3]. Frequent diseases in old age result in oxidative stress such as Parkinson's disease, stroke, multiple sclerosis and cataract [2].

In this context, the objective is to analyze the main mechanisms that cause oxidative stress and the most relevant agents for antioxidant defense. As specific objectives: to conceptualize oxidative stress; to verify the relationship between free radicals and oxidative stress; describe the antioxidant defense.

The referring work is descriptive in nature. The descriptive research, according to Gil (2007) has as main objective the description of the characteristics of certain populations or phenomena, trying to describe, explain, classify, clarify the presented problem.

The methodology was initially based on bibliographical research, seeking academic support for the theoretical realization about the proposed theme, in an integrated way with dialectical analysis.
A bibliographic search is done with the purpose of "improving the understanding of the data and deepening the interpretations". Thus, with the bibliographic reference, selective reading of chapters, articles, and texts that would contribute to this investigation was carried out.

There was a first approximation with the material, but others took place at different times in an attempt to explain some information not understood or to make comparisons between authors. The research was done with theoretical basis, being sketched arguments by the researcher on the subjects treated.

Oxidative Stress

Doctors describe drugs to treat disease, which may be toxic to some patients, by genetic predisposition, by irrational use or inappropriate drug administration. Taniguchi et al. [4] point out that drugs considered common over-the-counter drugs can be fatal if taken at supratherapeutic doses.

Consequently, it is explained that the irregular use of drugs causes oxidative stress, where it focuses the harmful effects to the human body. This occurs because all drug molecules are metabolized by the tissues or liver, if they are damaged or functioning irregularly, it will lead to a series of problems [3].

It is noteworthy that GSH has antioxidant power, protecting against the shock lung, induced by the oxidative stress resulting from hyperoxia. When there is inactivation of an oxidizing agent, there is production of GSSG and depletion of GSH and under conditions of excess oxidizing agents there will be an imbalance between GSH consumption and GSSSG production, characterizing oxidative stress [2].

The theory of oxygen radicals, proposes that aging may be secondary to oxidative stress, leading to lipid oxidation reactions and DNA triggering slow and progressive changes in tissues and genetic codes.

It is well known the participation of oxidative stress in aging because it is a multifactorial event, taking as a theory the fact that the cellular damages caused by ROS are cumulative over time. It is questioned if oxidative stress can explain the phenomenon of aging, although there is no evidence to answer this question, there are studies that demonstrate heterogeneous behavior of the antioxidant defense system regarding aging.

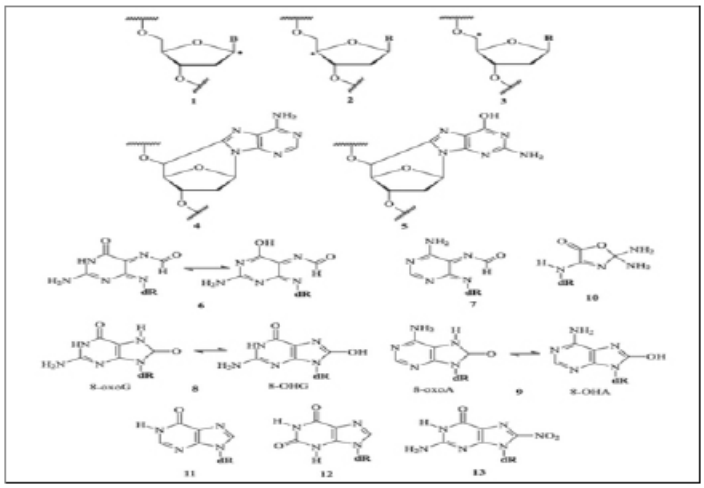
It should be emphasized that the indiscriminate use of drugs containing exogenous antioxidants should be judged in the treatment of diseases associated with oxidative stress [2]. Obesity has a mutual relationship with oxidative stress, increasing ROS and presenting inflamed cytokines, establishing oxidative stress and other chronic diseases such as insulin resistance and metabolic syndrome [3]. Silva and Jasiulionis mentions that:

Among the ERO-regulated pathways, the mitogen-activated kinase (MAPK) and phosphoinositide 3 kinase (PI3K) proteins stand out. The first has important role in tumorigenesis, mainly by activating transcription factors such as c Jun and c Fos, which regulate the expression of genes involved in cell proliferation, differentiation, transformation, inflammation, among others. On the other hand, PI3K is related to the RAS pathway, which has an important physiological role in cell survival.

The following topic addresses free radicals and oxidative stress for a better understanding of the subject.

Free Radicals and Oxidative Stress

It is explained that the cells are in constant renewal making it possible to divide the genetic information transmitted to the daughter cells through the duplication of the cellular material, including the chromosomes. Thus, the cells start to present oxidative stress, besides the loss of the capacity of cellular division.
Picture 1- Major products of DNA oxidation by ERRO and RNA
Source: André et al., 2006.



Organic and inorganic molecules, atoms with one or more electrons and independent are classified as free radicals, whose presence becomes critical for the maintenance of normal physiological functions [3]. Chorilli et al. [4], explain as follows:

Free radicals are small unstable molecules, produced from the energy received by an extremely reactive oxygen atom, which somehow lost an electron from its outermost layer. The main source of free radicals produced in the body comes from the normal metabolism of oxygen. A fraction of approximately 95% of the oxygen is metabolized to water via the electronic chain; the other 5% form free radicals which may also be useful in some physiological processes, especially phagocytosis.

When oxidative stress occurs, there is an increase in enzymatic antioxidant defenses, which generates a large amount of free radicals, and consequently damage and cell death. Once induced in cells and tissues, oxidative damage is related to diseases such as heart disease, pulmonary problems and others [6].

It is emphasized that free radicals are highly damaging, causing breakage in the DNA bases generating among other mutation and cellular apoptosis and impairment of intercellular transport. The free radicals still alter the functioning of telomerase, an enzyme that catalyzes the addition of nitrogenous bases, helping to regenerate telomeres [1].

As defense strategy is the use of antioxidants, which act to inhibit the lesions caused by free radicals. When included in the diet through fruit and vegetable consumption, they reduce the risk of developing diseases related to free radicals.

Protection against oxidation with vitamin C occurs with elimination of the peroxide radicals before initiating lipid oxidation and in the plasma as a reducing agent, by donating electrons. It also regenerates the active form of vitamin E and other antioxidants to play its role. Zinc acts on the antioxidant defense by inhibiting NADPH oxidase and participating directly in the neutralization of the hydroxyl free radical, inducing the production of metallothionines. Thus, zinc supplementation in oxidative stress markers is favorable for antioxidant defense [7]. The stress caused by ultraviolet radiation is an important risk factor for the development of skin tumors, and although melanocytes are able to suppress the increase of ROS, melanoma does not have such ability.

Treatment of melanocytes prior to each cycle of adhesion blockade with DNA demethylating agent results in the evident impairment of malignant transformation, suggesting that oxidative stress are important early events for the malignant transformation of melanocytes.

Antioxidant Defense

Protein and DNA lipid oxidation occurs in severe starvation as a response to depletion of dietary antioxidants, protein stocks and inflammation [8]. Other mechanisms may explain the role of inflammation in this context as induction of the nfkb pathway, inhibition of insulin-induced protein synthesis, and muscle loss by means of the activation of the suppository uhbine proteasome system.

Recent studies have linked inflammation to insulin resistance and its association with metabolic syndrome has been speculated. It has been shown that tnf reduces lipolysis increases which is highly related to insulin resistance, and also inhibits insulin action in muscle, liver and adipocytes both in vivo and in vitro [8].

Low circulating levels of vitamin D, decreased kloto and increased factor-F fibroblast growth factor may increase parathyroid hormone synthesis and thus contribute to the development of secondary hyperparathyroidism, which is closely related to protein loss in this population [3].

Insulin like growth factor (IGF-1) and IGF-2 are fundamental for embryological and postnatal development of skeletal muscle and other tissues. While limiting intake of sodium, phosphorus, potassium, and fluids may prevent important complications, problems grow when such restrictions are not accompanied with appropriate nutritional counseling in alternative food choices and / or strategies to ensure adequate nutrient intakes. The use of gh or growth factor -insulin like has shown a small benefit in improving sarcopenia there are doubts whether these products directly affect the skeletal muscles or if the observed effects are due to the improvement of latent heart failure.

The antioxidant defense system with the function of inhibiting the damage caused by the action of free radicals. This system is divided into enzymatic and non-enzymatic. Antioxidants are defined as substances present at lower concentrations that are capable of effectively retarding or inhibiting oxidation [9]. Based on the recommendations of Uskova et al. with some modifications the antioxidant activities will be determined in the free fraction of the cytosol in 1 g of the hepatic tissue.

In cases of intoxication, the enzymes that catalyze normal conjugation reactions (glucuronidation and sulfation pathways) become saturated, and only the cytochrome P450 enzyme complex functions as a metabolizing pathway, mainly the CYP2E1 isoenzyme, which converts the paracetamol in the NAPBQI reactive metabolite.

Carnosine has a buffering function that can act as a potent antioxidant agent, contemplating a reduction of thiobarbituric acid concentrations. Carnosine and its analogues have been shown to be efficient transitional metal chelating agents which promote the production of free radicals such as hydroxyl by the Fenton reaction.

Through chelating action, increased concentrations of carnosine may reduce the production of these radicals. The antioxidant potential of carnosine is not certain to be ergogenic and whether antioxidant supplementation can suppress the trigger for adaptations and may have an ergologic effect.

Carnosine may exert functions on the skeletal muscle that is related to the improvement in calcium release from the sarcoplasmic reticulum and the sensitivity of the calcium-binding device [1].

Isoflavones are the main phytoestrogens present in soybeans, with emphasis on genistein, daidzein and glycyte, which are non-steroid compounds with estrogen-like structures and bind to estrogen receptors.

High ingestion of soy products, rich in isoflavones, has been shown to inhibit bone loss by increasing its mineral density and improving bone microarray [10].

As a result of the presence of isoflavones, fruits, vegetables and soybean flavonoids play an important role in the health of the human being, being able to act as antioxidant, anti-inflammatory, among others [11].

Isoflavones provide reduction of coronary heart disease, delayed atherosclerosis, protection against cancer, hormonal improvement,

and therefore, several soy products have been indicated for the prevention of diseases [11].

Final Conclusion

It was verified that the installation of oxidative stress occurs by an imbalance between the pro-oxidant and antioxidant factors. Since the mechanisms of free radical generation occur in mitochondria and cytoplasm.

Supplementation study has demonstrated positive effects on specific biomarkers that diverge between the conditions of the individuals and variability aimed at the intervention of the content of the antioxidant components.

It was mentioned that among the pathological processes, there is the participation of oxidative stress in cardiovascular diseases, diabetes and cancer, in addition to several human tumors, have high levels of ROS. Thus, tumor cells are exposed to stress conditions, with imbalance in oxidative metabolism and various environmental factors.

It was concluded that environmental factors can help to modulate the level of ROS, and confirmed the participation of oxidative stress in several diseases, especially cancer in the initial stages. Antioxidants should be the target of studies in cancer prevention because there is a great interaction with oxidative stress.

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