



УДК 614.9:579. 62:613

**FUNCTIONS OF THE ANTIOXIDANT SYSTEM IN THE ANIMAL BODY
ФУНКЦІЇ АНТИОКСИДАНТНОЇ СИСТЕМИ В ОРГАНІЗМІ ТВАРИН****Рыліпко Т.М. / Приліпко Т.М.,***d.a.s., prof. / д.с.н., проф.*

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Publons: AAF-5445-2019

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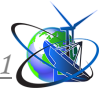
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Abstract. Free radicals are dangerous because they can easily interact with other biomolecules, including nucleic acids, proteins and free amino acids, lipids and carbohydrates. Such interactions can lead to disruption of cell membrane function, metabolic processes, and genetic expression. In situations where the defense forces do not cope, as a result of increased oxygen concentration or a decrease in antioxidant defense mechanisms, a state of oxidative stress occurs. This can lead to either immediate cell death or more subtle and chronic damage, such as the development of malignant neoplasms. There is now increasing evidence that the tissue damage that accompanies the aging process is caused by the formation of free radicals. Based on the available evidence, it has been suggested that life expectancy can be increased by five years or more through dietary modifications. To protect the body from RFK, animals and humans have developed a very powerful and complex antioxidant defense system. It includes various components of endogenous and exogenous origin.

Key words: animals, free radicals, oxygen concentration, antioxidant defense mechanisms, aging process, nutritional modification.

The topic of antioxidant enzymes occupies a central place in cell biology and medicine. The study of antioxidant enzymes is of great importance not only for the interpretation of cellular defense, but also for understanding the mechanisms leading to the action of drugs [1,4]. As a result of increased oxidation reactions, a mass of reactive forms of oxygen — free radicals and peroxides — is formed. They also occur with direct damage to cell membranes and walls. Activation of free radical oxidation and lipid peroxidation is a mandatory component of the cellular response to stress factors. This is the general link of the mechanism of stress induction, in which the effects of various stressogenic factors converge [4]. During the vital activity of the organism, free radicals are constantly formed in the cell - metabolically active compounds that disrupt the metabolism. Free radical oxidation (FRO) plays an important role for the body: on the one hand, it is necessary for the renewal of cell membranes and the synthesis of a number of biologically active substances, and on the other hand, FRO is a universal mechanism of damage to biomembranes in various pathological conditions [7]. Stress is an integral part of our lives [5]. It can lead to both adaptation and its disruption, the development of various diseases [1,6,8]. Growth and development, changes in the physiological state, physical exertion, adaptation, and stress are accompanied by changes in the intensity of free radical oxidation processes in the body [1,4, 8]. Within the physiological norm, BPO is maintained due to the coordinated action of the enzymes of the antioxidant system.

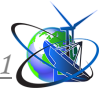


Free radicals are electrically charged molecules that have an unpaired electron in their molecular structure. Such an unpaired electron causes molecules to seek and capture electrons from other substances in order to self-neutralize. The initial attack by free radicals causes the body to neutralize them, which in the process leads to the formation of another free radical. Thus, a continuous chain reaction is formed, during which thousands of free radical reactions can occur within a few seconds, regardless of the deactivation of a part of the radicals [2]. Free radicals are dangerous because they can easily interact with other biomolecules, including nucleic acids, proteins and free amino acids, lipids and carbohydrates. Such interactions can lead to disruption of cell membrane function, metabolic processes, and genetic expression. In situations where the defense forces fail, as a result of increased oxygen concentration or a decrease in antioxidant defense mechanisms, a state of oxidative stress occurs. This can lead to either immediate cell death or more subtle and chronic damage, such as the development of malignancies [1,4].

There is now increasing evidence that tissue damage accompanying the aging process is caused by the formation of free radicals [1,2]. Based on the available evidence, it has been suggested that life expectancy can be increased by five years or more through dietary modifications. For example, in the field of human cancer research, interventions aimed at blocking the formation of free radicals or intercepting them before they interact with biomolecules may be attractive and effective proposals for protection against malignancy [1,9]. In the body of animals and humans, molecular oxygen is the main source of oxidation. The electron configuration of an oxygen molecule in its ground state has two unpaired electrons in its outer shell. Despite the fact that the reactions between oxygen, which is in the ground state ($3O_2$), and biological molecules are thermodynamically favorable, they occur slowly due to the high value of the activation energy. One of the ways to activate triplet oxygen is its transfer from the basic ($3O_2$) to the excited singlet state ($1O_2$). Singlet oxygen is not a radical, an electrophile, an extremely reactive and short-lived particle [1,4]. Reactive forms of oxygen (ROS) formed as a result of the restoration of its triplet state include: superoxide anion radical ($O_2^{\bullet-}$), its conjugate acid (HO_2^{\bullet}) (perhydroxyl radical), hydrogen peroxide (H_2O_2), hydroxyl radical OH^{\bullet} , hypochlorite acid $HOSl$ and peroxyxynitrite $ONOO^-$. The strongest electrophiles and the most reactive forms of oxygen are $1O_2$ and OH^{\bullet} [131]. RFK occur in different ways [7]: - under the action of ionizing, ultra-high-frequency UV radiation, powerful electromagnetic fields, thermal energy, and other physical factors; - in the processes of normal vital activity of the body, for example, during peroxidation of lipids; - as a result of activation of macrophages in inflammatory processes of an infectious or non-infectious nature; - in a state of acute and chronic stress; - in reactions of transition metals with hydroperoxides [1,2,7]. As a rule, the uniform reduction of oxygen during cellular respiration is limited by cytochrome oxidase in the mitochondrial electron transport chain. This chain reduces O_2 to a water molecule without releasing superoxide or hydrogen peroxide. However, superoxide is invariably produced in respiratory cells. This is due to the lack of one electron in a specific section of the mitochondrial electron transport chain. When the electron transport chain is strongly shortened and the respiration rate depends on the presence



of ADP, the amount of electron release at the ubisemiquinone and ubiquinone sites increases, leading to the production of superoxide and hydrogen peroxide [1]. Cytochrome P450, P450-reductases and cytochrome b5-reductases affect the formation of hydrogen peroxide during the catabolic cycle of xanthine oxidase in the endoplasmic reticulum [1,5]. The presence of a trace amount of hydrogen peroxide and Fe²⁺ is necessary for the formation of the hydroxyl radical ([°]OH). An exception is anomalous exposure to ionizing radiation [1,5,7]. Therefore, the aerobic type of cellular respiration always threatens the formation of ROS, as oxygen (O₂) is a highly reactive atom capable of becoming part of potentially harmful molecules called free radicals or reactive forms of oxygen. About 5% or more of inhaled O₂ is converted to ROS, such as superoxide, hydrogen peroxide, and hydroxyl radicals by monovalent oxidation of O₂ [159]. To protect the body from RFK, animals and humans have developed a very powerful and complex antioxidant defense system. It includes various components of endogenous and exogenous origin [161]. It is known that significant changes in the physiological functions of birds occur after their hatching during the period of adaptation to new conditions of existence in an oxygen environment. An important role in maintaining the homeostasis of the bird's body belongs to the system of antioxidant protection. It ensures the inactivation of lipid peroxide oxidation products and prevents their accumulation in tissues [9, 12]. So, for example, it has been proven that in the tissues of geese with a high level of oxygen consumption - the brain and myocardium - from the middle of the embryonic period, a genetically programmed increase in the power of their antioxidant defense system occurs [1,6]. The antioxidant system (AOS) is a powerful protective mechanism that prevents the development of avalanche-like free radical and peroxide reactions in the body. This system of body cells works due to the presence of compounds - antioxidants, which contain a mobile hydrogen atom that is not very strongly connected to carbon (C-H) or sulfur (C-H). As a result of the reactions of antioxidant molecules and free radicals, antioxidant radicals are formed, which are not powerful oxidizers and cannot continue the course of free-radical oxidation reactions. In this way, chains of free-radical reactions are broken. Radicals of antioxidant molecules are removed in the form of end products, which are the result of interaction with molecules of other antioxidants [6]. Antioxidants can neutralize free radicals even before their destructive effect is realized. Thus, the main task of the antioxidant system is to reduce the number of free radicals to the minimum possible level. All components of the body's antioxidant system are conditionally divided into several groups: 1. Enzymatic link of the antioxidant system; 2. Macromolecular non-enzymatic compounds (metal-binding proteins); 3. Low-molecular non-enzymatic compounds (fat-soluble and water-soluble antioxidants) [6,8]. The enzymatic link of the AOZ system includes: superoxide dismutase (SOD), catalase (KAT), glutathione peroxidase (GLP), cysteine and many others. The key enzyme of antiradical protection is superoxide dismutase. It dismutates superoxide radical to less toxic hydrogen peroxide. Superoxide dismutase represents the first line of defense of the body against the action of 39 RFK [1,81]. There are several isoforms of this enzyme. Depending on the trace element included in the active center, Fe-, Cu-, Zn- and Mn-dependent superoxide dismutase are isolated. According to localization in body



tissues, Fe-dependent superoxide dismutase is mainly found in erythrocytes, Zn, Cu-dependent in cytoplasm, and Mn-dependent in mitochondria [61]. All types are present in plants, animals and humans. Prokaryotic Mn-SOD, Fe-SOD, and eukaryotic Cu / Zn-SOD are dimers, while mitochondrial Mn-SOD are tetramers [1,11]. In the molecule of the enzyme Cu / Zn - SOD, copper and zinc ions, interacting with each other, are in such a close relationship that any changes around one ion affect the environment of the other. Zinc ions perform only a structural role [50] in contrast to copper ions, which are required for the catalytic activity of the enzyme [2,3]. In the formation of the antioxidant effect, the glutathione system of antioxidant protection of the body, which is formed by glutathione, glutathione peroxidase, glutathione transferase, glutathione reductase, etc., is of great importance. Glutathione is the main component of this system, which inactivates hydrogen peroxide and inhibits reactive oxygen species [8]. It has been proven that the formation of an adaptive response to oxidative stress in the heart muscles of geese occurs due to the activation of glutathione peroxidase and the resources of vitamin E and β -carotene [3]. Glutathione participates in the metabolism of xenobiotics, regulates cell proliferation, affects the synthesis of nucleic acids and proteins, as well as the activity of enzymes. Deficiency of glutathione in cells leads to activation of lipoperoxidation processes [8]. Glutathione peroxidase is a selenium-containing enzyme that catalyzes the breakdown of lipid hydroperoxides in a non-radical way using reduced glutathione. GLP is a tetramer consisting of four identical spherical subunits. Each subunit contains one selenium atom [7]. It is selenium that stimulates the conversion of methionine into cysteine, as well as the synthesis of glutathione, which, together with the amino acids glycine, glutamate, and cysteine, synthesizes HLP [5,6]. Glutathione peroxidase is localized mainly in the cytosol (about 70%) and only 30% in the matrix of mitochondria. Selenium deficiency, caused by its low content in the diet, leads to violations of the optimal vital activity of the body, which is accompanied by a decrease in the activity of glutathione peroxidase, activation of lipoperoxidation processes, and the development of oxidative stress [3]. o, for example, domestic birds are characterized by periods of tension in the antioxidant defense system and intensification of lipoperoxidation processes, associated with the restructuring of the body's physiological functions and the action of adverse environmental factors [2]. Glutathione peroxidase provides protection of cell membranes from the destructive action of peroxide radicals, catalyzes the decomposition of hydrogen peroxide and oxidizes glutathione, and catalyzes the reaction of restoring unstable organic hydroperoxides with glutathione [7]. The affinity of HLP for hydrogen peroxide is much higher than that of catalase, so the former works more efficiently even at low concentrations of H₂O₂. At the same time, catalase plays a key role in protecting cells from oxidative stress caused by high concentrations of H₂O₂ [4]. Catalase is a heme-containing enzyme that converts hydrogen peroxide into water and oxygen. It is present in almost all aerobic organisms tested to date [8]. The highest concentration of catalase is in the liver. In hepatocyte peroxisomes, catalase accounts for 40% of all proteins [7]. Mitochondria and endoplasmic reticulum contain little CAT. In the cell, it is localized mainly in peroxisomes, where it plays an important role in the removal of H₂O₂ formed by

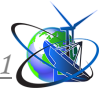


oxidases involved in β -oxidation of fatty acids, respiration and purine catabolism. Thus, intracellular hydrogen peroxide cannot be eliminated unless it spreads to peroxisomes [8]. It is known that catalase contains the highest reversible rate of reactions among all known enzymes. One molecule of CAT can convert approximately 6 million molecules of hydrogen peroxide into water and oxygen per minute. The catalase reaction can occur in two stages: α and β -phase [10, 11].

The α -41 phase works catalytically, breaking down hydrogen peroxide into water and oxygen molecules without the formation of free radicals. The reaction proceeds in two di-electron reactions. First, the H_2O_2 molecule oxidizes heme to compound I, removing one oxidation equivalent from trivalent ferrum, forming oxoferyl groups, and another from the porphyrin ring, forming a porphyrin cation radical. Second, H_2O_2 then reduces compound I to regenerate the free (ferrite) enzyme, releasing H_2O and molecular O_2 [132]. I. $KAT(Por-Fe^{3+}) + H_2O_2 \rightarrow (Por^{+\bullet} -Fe^{4+=O}) + H_2O$ II. $(Por^{+\bullet} -Fe^{4+=O}) + H_2O_2 \rightarrow KAT(Por-Fe^{3+}) + H_2O + O_2$ At peak H_2O_2 concentrations, catalases can undergo one-electron reduction with the inactive intermediate compound II, which can then be converted into another inactive form, with union III. $(Por^{+\bullet} -Fe^{4+=O}) + HA \rightarrow (Por^{+\bullet} -Fe^{4+=OH}) + A^{\bullet}$ III. $(Por^{+\bullet} -Fe^{4+=OH}) + H_2O_2 \rightarrow (Por-Fe^{2+} =OOH) + H_2O$ B-phase works peroxidically, removing H_2O_2 with oxidizing alcohols, formic acid salt - formate (RH_2), or nitrate, thereby releasing O_2 and natural enzyme [10, 11]. Although catalase is not essential for some cell types under normal conditions, it plays an important role in the acquisition of tolerance to oxidative stress in the adaptive response of cells. Thus, the survival of rats under the influence of 100% oxygen increased when liposomes containing SOD and CAT were administered intravenously before and during exposure [10].

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***Анотація.** Вільні радикали небезпечні, оскільки вони здатні легко взаємодіяти з іншими біомолекулами, включаючи нуклеїнові кислоти, білки та вільні амінокислоти, ліпіди та вуглеводи. Такі взаємодії можуть призвести до порушення функції клітинної мембрани, обмінних процесів та генетичної експресії. У ситуаціях, коли захисні сили не справляються, внаслідок підвищеної концентрації кисню або зниження антиоксидантних захисних механізмів, виникає стан окисного стресу. Це може призвести або до негайної загибелі клітин, або до більш тонких і хронічних пошкоджень, таких як розвиток злоякісних новоутворень. Зараз збільшується кількість доказів того, що пошкодження тканин, які супроводжують процес старіння, відбувається через утворення вільних радикалів. На основі наявних даних було стверджено, що тривалість життя може бути збільшена на п'ять років і більше за допомогою модифікацій харчування. Для захисту організму від РФК тварини та людина розвинули дуже потужну і складну антиоксидантну систему захисту. Вона включає різні компоненти ендogenousого і екзогенного походження.*



Ключові слова: тварини, вільні радикали, концентрація кисню, антиоксидантний захисних механізмів, процес старіння, модифікація харчування.