International Journal of Biological and Pharmaceutical Sciences Archive

ISSN: 0799-6616 (Online)

Journal homepage: https://ijbpsa.com/

(REVIEW ARTICLE)

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The Role of Antioxidants in Biochemistry

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International Journal of Biological and Pharmaceutical Sciences Archive, 2024, 08(01), 135-141

Publication history: Received on 05 June 2024; revised on 29 August 2024; accepted on 31 August 2024

Article DOI: https://doi.org/10.53771/ijbpsa.2024.8.1.0059

Abstract

Antioxidants play a critical role in mitigating oxidative stress by neutralizing reactive oxygen species (ROS) and preventing cellular damage. This review explores the biochemical mechanisms of antioxidants, classifying them into enzymatic and non-enzymatic categories, and highlights their essential functions in maintaining cellular homeostasis. The role of antioxidants in disease prevention, particularly in neurodegenerative disorders, cardiovascular diseases, and cancer, is discussed in detail. Additionally, the interplay between ROS generation and antioxidant defense mechanisms is examined, providing insight into the delicate balance required for optimal physiological function. While dietary and synthetic antioxidants offer promising therapeutic potential, challenges such as bioavailability, dosage optimization, and potential adverse effects remain areas of active research. This review also outlines future directions in antioxidant research, emphasizing the need for further studies to elucidate synergistic interactions and novel therapeutic applications.

Keywords: Antioxidants; Oxidative Stress; Reactive Oxygen Species; Disease Prevention; Biochemical Mechanisms

1. Introduction

Antioxidants are molecules that prevent the onset of chain reactions by reducing free radicals within biological systems, such as lipid peroxidation, which is involved in the aging processes and many diseases. Numerous and different antioxidants, internal and external to the organism, can suppress and inhibit these free radicals to lessen the damage done to the cellular components; this fact shows the importance of antioxidants in health and disease (Kalam et al., 2012) (Engwa et al.2022). Free radicals generally have one or more unpaired electrons, thereby making them a reactive species. In cells, the largest contributor to free radical production is respiration, particularly in the mitochondria. After the water and oxygen molecules are split, the single unpaired electron formed by the reaction can bind with oxygen to create the very damaging superoxide anion. Additionally, the binding of carbon dioxide and nitrogen dioxide gas, as well as the binding of double bonds near the respiratory chain, can be potential sites of attack. The superoxide anion will then lose an electron through a dismutation reaction to either hydrogen peroxide or the immensely damaging hydroxyl radical (Martemucci et al.2022)(Napolitano et al., 2021). Antioxidants quench or scavenge free radicals by binding to some of these molecules. They are particularly good at donating an electron to a free radical without themselves becoming reactive. An increase in these oxygen free radicals can lead to chain reactions targeting lipids, either on individual molecules as parts of larger macromolecular structures, as in the lysosomal membranes. The carbocations formed are extremely reactive and will then have a domino effect in roping in other lipids to continue the reaction. Since lysosomes contain hydrolysing enzymes, the cell's autolysis can result. In addition, because lipids are an important component of the plasma membrane, their peroxidation can decrease membrane fluidity and increase the activation energy required for metabolism (Engwa et al.2022)(Angelé-Martínez et al.2022).

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1.1. Definition and Classification of Antioxidants

Antioxidants encompass natural and synthetic compounds used in pharmaceuticals, cosmetics, and foodstuffs. The term "antioxidant" concerns a broad set of substances with varied chemical structures that quench reactive species through chemical (chain-breaking) or biological (enzyme-inducing) mechanisms. Antioxidants are distinct in nature and mechanism of action, making simple definition challenging. Nonetheless, a clear picture is essential to understand how such compounds might interact with reactive species, leading either to beneficial (e.g., stabilisation of polyunsaturated lipids in a diet) or detrimental (tissue damage in pathologies) effects (Halliwell, 2024). Accordingly, some definitions and classifications will be proposed in an attempt to render the complexity of the issue in an easily assimilable manner. In fact, a compound also might switch its antioxidant properties according to the surrounding conditions. Hence, few cut-and-dried categories exist. Yet in numerous didactic formats simple classifications remain useful. Here, antioxidants are categorised according to their source, mechanism of action, or some properties they share and contrasted (Bensid et al.2022)(Shen et al., 2022). Commonly antioxidants are described as either enzymatic or non-enzymatic. The former catalyse reactions in which free radicals are either directly neutralised or transformed into less reactive species. The latter readily trap free radicals, and are classified as either hydrophilic (e.g., ascorbate, glutathione, urate, or thiols) squared schemes. This class is expanded to include compounds oxidised during redox cycling reactions (e.g., quinol and metal ions, Trolox, or sodium bisulfite) (Stoia & Oancea, 2022). A second class of non-enzymatic antioxidants includes compounds capable of being inactivated throughout reactions with hydroperoxides, or chelating pro-oxidant metal ions (e.g., phytic acid, or protein-bound sulphur compounds). Many interesting compounds found in foodstuffs and supplements belong to this broad, but poorly defined, class of antioxidants (Engwa et al.2022)(Rudenko et al.2023). For instance, xanthophylls, flavonoids, lignans, or polyphenols. Moreover, compounds such as tocotrienols, -lipoic acid, carotenoids, phytosterols, and ubiquinones interfere at some stage with the free radical cascade, or scavenge less toxic lipid peroxidation end-products. Bioavailability, a critical aspect of the dietary intake of antioxidants might influence the effectiveness of these compounds (exogenous antioxidants are distinct in e.g., ion trapping or radical quenching actions) (Rudrapal et al.2024)(Bešlo et al., 2023).

2. Reactive Oxygen Species (ROS) and Oxidative Stress

Oxygen consumption mediated by cellular metabolism results in the generation of reactive oxygen species (ROS) as natural byproducts, including the superoxide, hydroxyl radical, and hydrogen peroxide. Mainly attributed to mitochondrial activity, superoxide is produced when electrons escape the electron transport chain to react with molecular oxygen. Additionally, NADPH oxidases, peroxisomes, and some enzymes also generate superoxide (Zandi & Schnug, 2022)(Juan et al.2021). This type of ROS can act as a signaling molecule, subsequently promoting mitogenic responses and restricting pathogen invasion. Through the Fenton reaction, superoxide is converted into hydroxyl radicals which are known for their oxidative damage on nucleotides, amino acids, and lipids. Similarly, hydrogen peroxide can be generated directly by reactions with molecular oxygen or indirectly through the enzymatic dismutation of superoxide by superoxide dismutase (Liu et al., 2021)(Fujii et al., 2022).

In biological systems, the deleterious consequence of ROS on various cellular components is referred to as oxidative stress. It results from an imbalance between the production of ROS and the cellular antioxidant defense, including reducing compounds and enzymatic systems. This kind of stress can manifest itself in two separate ways: on one hand, mitochondrial cytochrome c release can initiate apoptosis and on the other, the progressive accumulation of oxidative damage induces necrosis (Saleh et al.2023)(Demirci-Çekiç et al.2022). In either case, oxidative stress may lead to chronic inflammation and the onset of various chronic diseases including neurodegenerative pathologies and cancer. Besides contributing largely to degenerative diseases, oxidative stress is also critically involved in aging. Indeed, aging is associated with a gradual loss of regenerative capacity and increase in oxidation-induced cellular fitness damage, cardiac tissue being particularly susceptible, especially in pathologies involving such stress (Jomova et al.2023)(Leyane et al.2022).

2.1. Generation of ROS in Biological Systems

The generation of reactive oxygen species (ROS) is constant in biological systems. ROS are continuously generated through cellular respiration, by various metabolic pathways, and due to many environmental factors (Zhang et al., 2019). Most living organisms contain antioxidant systems to prevent cellular damage. However, the ROS levels can be greatly elevated under many physiological and pathological conditions. Under simple physiologic conditions, ROS can be produced by factors such as inflammation and exposure to various toxins (A. Alfadda & M. Sallam, 2012). Here, it is emphasized how various living organisms generate ROS, and what physiologic and pathologic impacts they can have. Attention is drawn to what is particularly known about ROS and antioxidant functions in animals and plants, and also the different functions of cellular ROS. The complex physiology of ROS generation and their relevance to antioxidant function are understood. The circumstances under which antioxidants become necessary can be understood with a broad knowledge (Sies et al.2022)(Jomova et al.2023).

ROS generation and the defense mechanism against them are quite complex in nature, and there has been increasing interest in the interplay between them in both biomedical sciences and elsewhere. One obvious theme of the ROS/antioxidant interplay is the relation between the degree of ROS production and the magnitude of antioxidant defenses: one often observes an increase in the latter where there is an increase in the former. This may be observed, for instance, following cellular exposure to toxic agents (Fujita & Hasanuzzaman, 2022)(Zhang et al.2022). A second is the primary role that certain antioxidant compounds may play against particular oxidant species. Many orders have considered the role of glutathione in detoxifying peroxides, for example. There is also much current interest in the role of ascorbic acid in protecting against superoxide free radicals. A third theme is the sources of ROS in living organisms, notably the mitochondrion and peroxisome, and their corresponding antioxidant defense mechanisms (Dumanović et al.2021)(Pisoschi et al.2021).

3. Mechanisms of Antioxidant Action

Antioxidants are compounds that inhibit oxidation, which is a process involving a transfer of electrons, to cell membranes or other components of metabolic reactions. Therefore they reduce or eliminate the adverse effects of reactive oxygen species (ROS) and some nitrogen species, which form frequently when living organisms use oxygen. An imbalance between antioxidants and oxidants leads to oxidative stress that damages cells and their contents (Jomova et al.2023). Antioxidants play a pivotal role both in wipes cellular protective mechanisms and in protective systems that the body uses to defend against diseases. Plants containing antioxidants are likely to be consumed and substances, usually not synthesized by the body, are essential to health. Antioxidants are generally not harmful, but the overuse of antioxidants as dietary supplements in excessive doses should be avoided. Antioxidants operate through interrupting the involvement of free radicals or other ROS in chain reactions (Halliwell, 2024). Each antioxidant has a different and versatile mechanism of action, and respective antioxidants can act in combination. Besides, antioxidants are capable of protecting DNA from free radical-induced damage and of repairing oxidative damage. The mechanism of action of each antioxidant dependents on, but is not limited to, the physical and chemical nature of the damaging substances, the cellular site or lipid membrane in which an antagonist can interrupt the chain reaction, the rate of antagonist depletion, and the influence of the lipid environment on free radical chain reactions. In biological systems, the principal antioxidants are superoxide dismutase, catalase, and glutathione peroxidase (Chandimali et al.2025)(Ahmad et al.2024). These enzymes break down ROS to non-radical or less harmful molecules. Superoxide dismutase offers a remarkable efficiency, and, within one second, it can eliminate nearly all superoxide radicals in the intermembrane space. Catalase is very effective at protecting the cell membrane by decomposing the most dangerous hydrogen peroxide formed by superoxide anions. Other non-enzymatic antioxidants interrupt chain reactions by collecting single electrons or hydrogen atoms from ROS process. Assorted antioxidants, including tocohperols, carotenoids, ubiquinol, bilirubin, uric acid, melatonin and flavonoids, also exhibit notable efficiency in neutralizing free radicals (Fujii et al., 2022)(Zheng et al., 2023)(Andrés et al.2023). The triglyceride structure, which is highly susceptible to oxidation, can be safeguarded by α-tocopherol, whilst ascorbate is a preventive agent that battles against membrane oxidation and can repair α-tocopherol. It is highlighted that antioxidants are often effective as a group because they scavenge many types of free radicals and can quench for another to regenerate their original state. The balance of this text will focus on the protection of membrane lipids (Martemucci et al.2022)(Jaganjac et al.2022).

3.1. Enzymatic Antioxidants

Antioxidants are compounds that inhibit the oxidation of other molecules by preventing the initiation or propagation of oxidative chain reactions. They work to interact with and stabilize free radicals, which in large quantities can cause significant damage to living organisms. The resulting cellular damage can lead to a variety of health problems, most commonly associated with issues related to aging (Jomova et al.2024). To combat oxidative stress, enzymatic antioxidants are produced within the body to defend its cells and vital molecules. These enzymes function to terminate the propagation of free radical chain reactions by removing the radical intermediates and other oxidation products (Jomova et al.2024)(Roy et al.2023). The enzymes accomplish this task by converting harmful oxidants into less reactive, non-radical forms or even repairing the damage that they cause. Present within the human body are various enzymes that protect against the harmful effects of ROS: superoxide dismutase (SOD), catalase, and various peroxidases of which glutathione peroxidase (GSH-Px) is the most well-known (V. Maksimenko & V. Vavaev, 2012). SOD is responsible for converting superoxide radicals to oxygen and hydrogen peroxide, which are less damaging to cells, while catalase is used to convert hydrogen peroxide to oxygen and water. Catalase in cells essentially ‘mops up’ any hydrogen peroxide formed (Luisa Racchi, 2013).

4. Health Implications of Antioxidants

Antioxidants act as defensive mechanisms against bacteria and viruses, as well as against harmful radicals and other toxic substances found within blood and lymph. Their role maintains health and life by donating missing electron to these molecular structures. For instance, Vitamin E, or Tocieferol, is fat-soluble and localizes in cell membrane in the liver protecting the liver (Unsal et al., 2021). When the liver cell membrane encounters a harmful toxin range of effect, it donates one of its own electrons to dispose off that toxin avoiding it from penetrating into the cell membrane. This in turn results in a third-generation compound called Tocieferoxyl. However, this third-generation compound that was formed in the process itself transforms a toxin. Additionally, the Vitamin E, coming from the adventitial blood, recycles itself when it gains two electrons and drops it in the cell membrane; since this compound called transitional Tocieferol gives enough time to the cell membrane to debar the harmful toxin (Trevithick et al.2023)(Bhandari et al.2024). Antioxidants are the agents capable of stabilizing or deactivating free radicals before they attack cells or stabilize the cells that have been damaged by free radicals already. It is generally a broad group of compounds that are essential for maintaining optimum health or optimum well-being. The consumption of high oxygen consuming processed foods and the new set of lifestyle have increased the efficiency of free radicals. Among different metabolic processes are the most cytotoxic species and destroy the cellular compounds, the main metabolites are derived from mitochondrial respiration i.e.; iminoquinone, hydrogen peroxide and free radicals (Engwa et al.2022)(Abdulrahman et al.2024). Free radicals are highly labile compounds because their electrons are unpaired which make them very reactive for their attack to the other molecules. Epidemiologically, it has been found that blood creatinine levels increase in direct proportion to environment exposure. It can be due to complex activities between free radicals and antioxidants. Combustion of fuel, consumption of edible oils and tree-borne leaf are the potential sources of exposure. Commercial crop-prepared food supplements are the potential source of free radicals. Random supplementary food is consumed in the form of tea (Kalam et al., 2012) (Martemucci et al.2022)(Jalil et al.2023).

4.1. Antioxidants in Disease Prevention and Treatment

This is a broad subject area and this document is only intended to provide an introduction to information sources relating to some key aspects of Antioxidants. It focuses on a relatively new area of study in the field of biochemistry and one that has potentially important implications for health and health care (Losada-Barreiro et al.2022). The selected reading for this article begins with a point of relevance for postgraduates considering future research projects, before reviewing works on the potential implications of antioxidants in free radical pathology, general biochemical investigations of antioxidants and free radicals, and finally the measurement of free radicals in vivo, particularly by electron spin resonance spectroscopy. While mainly grouped in the health science categories, the works reviewed are drawn from an inter-disciplinary field of study and are from a wide range of journals (Chaudhary et al.2023)(Sadiq, 2023).

Antioxidants are substances that may prevent potentially disease-producing cell damage produced by unstable molecules known as free radicals. While many clinical studies support the ability of antioxidants in the reduction of the risks of chronic diseases, such as cancer and heart disease, claims for preventative or treatment role in diseases have sometimes not been supported. Rather than damaging the target cell as such, it is assumed that the oxidation-related damage may affect the ability of cellular components to perform their characteristic functions (Cerasuolo et al.2023)(Garewal, 2024). This, in turn, may contribute to a number of disease processes. Treatment protocols involving the administration of controlled levels of select antioxidants, which aim to exert a specific pharmacological action, are discussed. Caveats regarding the use of antioxidants in healthcare are expressed, including the difficulty in establishing and maintaining appropriate dosage levels and limitations on the use of antioxidants due to interactions between the agents and with other medications (Aghemo et al.2022)(Bukowska & Duchnowicz, 2022).

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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