International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

Check for updates

Antioxidants and their applicability in neurodegenerative diseases

Jeniffer Aparecida de Morais Rodrigues *, Danilo Alves Guimarães de Moura, Lucas Oliveira Silva, Juliana Tonelli Teixeira Alvares, Renata Dos Santos Cunha and Murillo de Sousa Pinto

Centro Universitário Alfredo Nasser.

International Journal of Science and Research Archive, 2024, 13(02), 3742-3745

Publication history: Received on 16 November 2024; revised on 28 December 2024; accepted on 30 December 2024

Article DOI: https://doi.org/10.30574/ijsra.2024.13.2.2633

Abstract

Neurodegenerative diseases constitute a diverse group of pathologies that generally emerge at older ages and are strongly linked to aging. Oxidative stress is a key factor in the degeneration of the central nervous system (CNS), contributing to neurotoxicity, cell death, and senescence. Antioxidants are substances that reduce or inhibit oxidation caused by free radicals and can be of endogenous or exogenous origin. To investigate the development of antioxidant therapies that enhance the physiological antioxidant system's capacity, considering the essential role of oxidative stress in neuronal dysfunction. This is a literature review, searching for articles published in the last 5 years. Several epidemiological studies suggest that certain compounds present in the diet, which possess neurogenic properties, may positively impact brain aging and the prevention of neurodegenerative diseases. While there is evidence suggesting a potential beneficial effect of antioxidants in mitigating damages related to neurodegenerative diseases, more research and data are still needed to confirm this relationship.

Keywords: Antioxidants; Neurodegenerative diseases; Oxidative stress; Free radicals

1. Introduction

Neurodegenerative diseases constitute a diverse group of pathologies that generally emerge at older ages and are strongly linked to aging. These diseases are characterized by a progressive deterioration of cognitive functions, motor coordination difficulties, involuntary movements, and profound, irreversible changes in behavior and personality. Among the most well-known examples are Parkinson's disease (PD), Alzheimer's disease (AD), Huntington's disease (HD), and Amyotrophic Lateral Sclerosis (ALS). The clinical manifestation of these diseases varies according to the region of the brain affected by the degeneration or death of neurons. Among the most common pathological signs are brain atrophy, the formation of neurofibrillary tangles, plaques, and aggregates.

Neurodegenerative dysfunctions, predicted to become the second leading cause of death among the elderly by 2040, are a group of pathological conditions involving neuronal degeneration and microvascular dysfunction in the brain. According to the World Health Organization (WHO), approximately 50 million people currently suffer from dementia, a number expected to triple to 150 million by 2050. The increase in life expectancy, combined with unhealthy lifestyles, is directly related to the emergence of new health problems, including the growing incidence of neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and frontotemporal dementia.

Oxidative stress is a key factor in the degeneration of the central nervous system (CNS), contributing to neurotoxicity, cell death, and senescence. While playing an important role in maintaining homeostasis and cell signaling, the excessive

* Corresponding author: Jeniffer Aparecida de Morais Rodrigues

production and accumulation of reactive oxygen species (ROS) can cause harmful oxidative stress. This results in mitochondrial dysfunction and damage to critical biomolecules, such as proteins, lipids, and nucleic acids, leading to cellular senescence and aging in various tissues.

Protein alterations are correlated with oxidative stress, which arises from an imbalance between oxidative species, such as free radicals, and the body's antioxidant defenses. Substances contributing most to the generation of free radicals include oxygen (O_2) and nitric oxide (NO), which are categorized as reactive oxygen species (ROS) and reactive nitrogen species (RNS), respectively.

The brain is a particularly vulnerable organ to oxidative stress due to its high oxygen consumption and subsequent excessive formation of reactive oxygen species (ROS). This phenomenon leads to functional loss and neuronal disorganization, hallmarks of neurodegenerative diseases.

Antioxidants are substances that reduce or inhibit oxidation caused by free radicals and can be of endogenous or exogenous origin. Among endogenous antioxidants, reduced glutathione (GSH), superoxide dismutase (SOD), catalase, and glutathione peroxidase (GSH-Px) stand out. Exogenous antioxidants, which play a fundamental role in protecting the body, are obtained through the ingestion of certain foods, such as carotenoids, vitamins C and E, selenium, zinc, and flavonoids. These dietary antioxidants complement endogenous antioxidants, helping mitigate the damage caused by free radicals in the human body. To investigate the development of antioxidant therapies that enhance the physiological antioxidant system's capacity, considering the essential role of oxidative stress in neuronal dysfunction.

2. Methodology

This is a literature review, searching for articles published in the last 5 years on the Google Scholar and SciELO databases using the descriptors: antioxidants, neurodegenerative diseases, neuroprotection, oxidative stress, free radicals. Five articles in Portuguese were used in this study.

3. Literature Review

The brain is one of the organs most susceptible to oxidative stress for several reasons. Neurons exhibit accelerated metabolism and a high oxygen demand, in addition to containing significant amounts of polyunsaturated fatty acids in their membranes, which are prone to peroxidation. Furthermore, there is reduced activity of endogenous antioxidant enzymes and high levels of redox-active metals such as iron and copper, which catalyze the formation of reactive oxygen species (ROS).

Neurodegenerative diseases are clinically characterized by an insidious onset and accelerated progression, physiologically manifesting through the progressive dysfunction and death of nerve cells. Morphologically, neuronal loss is associated with gliosis and often with the abnormal folding of proteins, leading to the excessive accumulation of these proteins in both extracellular and intracellular spaces. Moreover, there is a dysregulation of the redox balance, which can occur due to excessive production of reactive oxygen species (ROS) or limited cellular antioxidant capacity, resulting in a state of oxidative stress.

The term oxidative stress was first introduced by Helmut Sies, referring to the imbalance between the generation of free radicals (reactive oxygen and nitrogen species) and the cells' ability to neutralize the excess of these reactive intermediates. This phenomenon occurs through the action of cellular antioxidant systems and can cause significant damage to biological systems.

Free radicals are physiologically generated during cellular metabolism and are tightly regulated by antioxidant systems, both enzymatic and non-enzymatic. Thus, free radicals, like inflammation, can play both beneficial and harmful roles depending on their intensity. At physiological levels, characterized as eustress, they play a significant role in various metabolic processes, acting as mediators in electron transfer, maintaining the organism's homeostasis, and responding to harmful stimuli, such as defending against infectious agents, among others. At low to moderate concentrations, they participate in cellular signaling cascades, thereby modulating the expression of genes involved in DNA repair, cell cycle control, inflammatory response, and apoptosis.

Mitochondrial dysfunction and chronic oxidative stress promote cellular aging, impacting the physiology of the central nervous system (CNS) and making it more susceptible to chronic and neurodegenerative diseases. The brain's high oxygen consumption, high levels of polyunsaturated fatty acids, neurotransmitter auto-oxidation, relatively low

antioxidant capacity, and limited cellular repair mechanisms make it especially vulnerable to the damage caused by oxidative stress. This condition can induce a state of progressive chronic inflammation, resulting in protein and lipid degradation, the expression of pro-inflammatory cytokines, physiological alterations, dysfunction in cellular processes, organelle damage, and cell death. Over time, this persistent situation can culminate in the development of various neurodegenerative diseases, including Amyotrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease (PD), Alzheimer's disease (AD), multiple sclerosis, muscular dystrophy, spinal muscular atrophy (SMA), progressive supranuclear palsy, spinocerebellar ataxias, corticobasal degeneration, frontotemporal lobar degeneration, among others.

While many brain neurons can tolerate increased oxidative stress, specific populations of neurons are particularly vulnerable to this increment. In neurodegenerative contexts, this vulnerability is referred to as selective neuronal vulnerability.

Neurotoxicity induced by harmful etiological agents can trigger disordered apoptosis in specific types of nerve cells, thus characterizing neurodegeneration. The molecular factors produced by dying cells become detrimental to neighboring cells, exposing them to pro-apoptotic elements similar to those affecting the dying cells. This phenomenon of cell death in one cell impacts the dynamics of cell death in adjacent cells. This apoptosis, referred to as "contagious" or the "kindergarten effect," is observed in all neighboring cells within specific regions associated with each pathology. In Alzheimer's disease, this effect occurs in the hippocampus and cortex; in Parkinson's disease, in the substantia nigra neurons; in Amyotrophic Lateral Sclerosis, in motor neurons; and in Hyaline Degeneration, in the basal ganglia, among others.

The control and restoration of oxidative stress (OS) balance are crucial for the treatment of various pathologies, as mild cognitive decline only becomes evident after the clinical onset of the condition. OS, generated by exposure to stressors in cell cultures, has been used in experimental models to investigate the mechanisms of neurodegeneration, with the aim of developing antioxidant and neuroprotective strategies. These studies are fundamental to identifying significant cellular factors related to cell death, which are presumably critical to the degeneration process, allowing their correlation with phenomena observed in human diseases.

Various significant neurodegenerative diseases are associated with the abnormal production of reactive oxygen species (ROS) and/or mitochondrial dysfunction, including Alzheimer's disease, Parkinson's disease, motor neuron disease, Huntington's disease, Amyotrophic Lateral Sclerosis, among others.

This relevant relationship with the toxicity of Reactive Oxygen Species (ROS) can serve as an approach for neuroprotection, helping to block one of the processes involved in the pathogenesis of these diseases.

Considering the positive effects of antioxidants and the fundamental role of oxidative stress in neuronal dysfunction, there is growing interest in the development of antioxidant therapies that can enhance the natural defensive response of the body's system. An effective approach involves adopting a balanced and healthy diet rich in compounds with antioxidant properties, such as vitamins A, E, and C, flavonoids, phenolic acids, and carotenoids.

Various antioxidants, such as vitamins E and C, which can penetrate the blood-brain barrier, are recognized for their effectiveness in protecting against neuron death caused by oxidative stress and dementia.

Antioxidants are compounds that help neutralize reactive oxygen species (ROS), reducing oxidative damage to our body. Often, these compounds are aromatic and have at least one hydroxyl group, which can be either synthetic or natural, and are widely used in the food industry. Due to their stability, antioxidants can donate electrons or protons to free radicals, neutralizing them and thus reducing their ability to damage cells.

Several epidemiological studies suggest that certain compounds present in the diet, which possess neurogenic properties, may positively impact brain aging and the prevention of neurodegenerative diseases. Among these, polyphenols stand out, including flavonoids, curcuminoids, stilbenes, phenolic acids, and carotenoids. These phytochemicals are found in a variety of foods, such as tea, red wine, herbs, seeds, and fruits, and are associated with health benefits, especially when consumed regularly in a diet rich in these components.

Research on antioxidant therapy has focused on the study of molecules with antioxidant properties that can target mitochondria, being able to cross the mitochondrial double membrane and eliminate the reactive oxygen species (ROS) generated during mitochondrial function. This could play an important role in preventing the progression of neurodegenerative diseases.

4. Conclusion

Oxidative stress plays a significant role in neurodegenerative diseases, contributing to the imbalance of the body's antioxidant defense systems. The excessive presence of free radicals can result in severe damage, highlighting the importance of including antioxidant-rich foods in the diet. These antioxidants not only help prevent the formation of free radicals but can also aid in repairing damage already caused. While there is evidence suggesting a potential beneficial effect of antioxidants in mitigating damages related to neurodegenerative diseases, more research and data are still needed to confirm this relationship. Finally, the importance of an antioxidant-rich diet can be emphasized as a promising means to reduce the risks associated with neurodegenerative diseases and promote brain health.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Matos, A. R. R., & Veríssimo, M. T. M. (2020). Oxidative stress and therapeutic strategies in the context of neurodegenerative diseases. University of Coimbra, Portugal.

[2] Oliveira, E. A. G. (2023). Evaluation of fucoxanthin against oxidative stress in the pathophysiology of neurodegenerative diseases: Integrative review. Federal University of Santa Catarina, Florianópolis.

[3] Silva, L. E. Q., Ferreira, E. D. P., Brasil, R. N. A., Limão, A. L. E., & Borella, V. C. M. (2022). A narrative review: Use of antioxidants in neurodegenerative diseases. Brazilian Journal of Development, Curitiba, 8(2), 10661–10669.

[4] Duarte, R. J. G. (2023). Potential application of bioactive compounds from marine macroalgae in the treatment and/or prevention of neurodegenerative diseases. Fernando Pessoa University, Porto.

[5] Cavalier, N. T., et al. (2023). The relationship between chronic inflammation and the development of neurodegenerative diseases. Revista Ibero-Americana de Humanidades, Ciências e Educação, São Paulo, 9(7), July.