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Neuroprotective Role of Polyphenols in Treating Neurodegenerative Disorders: A Comprehensive Review

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Abstract

This comprehensive review investigates the neuroprotective potential of polyphenols in the treatment of neurodegenerative disorders. Polyphenols, natural compound abundantly present in plant-based foods, possess antioxidant, anti-inflammatory, and anti-apoptotic properties. Through their ability to neutralize harmful free radicals, suppress neuroinflammation, and modulate cell survival pathways, polyphenols offer a promising avenue for mitigating neurodegenerative disease progression. This review critically analyzes existing literature, including preclinical studies and clinical trials, to provide a thorough understanding of the mechanisms underlying the neuroprotective effects of polyphenols. The findings underscore the significant therapeutic promise of polyphenols as a novel approach in combating neurodegenerative disorders.

Keywords: Neuroprotective • Polyphenols • Neurodegenerative disorders

Introduction

Neurodegenerative disorders represent a growing global health concern, posing a substantial burden on affected individuals and their families. With aging populations on the rise, the prevalence of conditions such as Alzheimer's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis (ALS) continues to escalate. Despite extensive research efforts, effective treatments for these devastating conditions remain elusive. In recent years, there has been mounting interest in exploring the potential neuroprotective properties of polyphenols, a class of bioactive compounds found abundantly in plant-based foods.

This comprehensive review aims to delve into the emerging evidence surrounding the neuroprotective role of polyphenols in treating neurodegenerative disorders. Polyphenols exhibit a diverse array of antioxidant, anti-inflammatory, and anti-apoptotic properties, which have garnered considerable attention as potential therapeutic agents. Through their ability to neutralize harmful free radicals and modulate signaling pathways associated with neurodegeneration, polyphenols hold promise in mitigating disease progression and promoting neuroregeneration [1].

By systematically analyzing and synthesizing existing literature, this review seeks to shed light on the mechanisms underpinning the neuroprotective effects of polyphenols and evaluate their potential as a novel therapeutic approach in the battle against neurodegenerative diseases. The pathogenic features of neurodegenerative diseases include mitochondrial dysfunction and the generation of derived reactive oxygen species. The neural tissue is extremely sensitive to oxidative stress, which is a major cause of both chronic and acute neurodegeneration. Based on this, therapeutic strategies that use antioxidant molecules to achieve redox equilibrium have been widely used to treat a variety of brain pathologies. Polyphenols, carotenes, and vitamins are among the most common exogenous antioxidant agents that have been tested as adjunctive therapies in neurodegeneration. Other types of antioxidants, such as hormones like the widely used melatonin, are also considered neuroprotective agents and have been used in various neurodegenerative contexts.

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Literature Review

Neuroprotective role of polyphenols in treating neurodegenerative disorders reveals a substantial body of evidence supporting their potential therapeutic benefits. Polyphenols are natural compounds widely distributed in fruits, vegetables, and other plant-based sources. This review critically examines various studies and research papers to provide a comprehensive overview of the mechanisms and outcomes associated with polyphenol treatment.

One prominent mechanism by which polyphenols exert their neuroprotective effects is through their potent antioxidant properties. Oxidative stress plays a pivotal role in the pathogenesis of neurodegenerative diseases, leading to neuronal damage and cell death. Polyphenols, acting as free radical scavengers, neutralize reactive oxygen species, thus preventing oxidative damage and preserving cellular integrity. Furthermore, polyphenols exhibit anti-inflammatory actions, inhibiting pro-inflammatory cytokines and enzymes. Chronic inflammation is a hallmark of neurodegenerative disorders, contributing to the progression of neuronal loss. By suppressing inflammatory responses, polyphenols can reduce neuroinflammation and limit the neurotoxic effects associated with the release of inflammatory mediators [2].

Additionally, polyphenols have been shown to modulate intracellular signaling pathways involved in cell survival and apoptosis. These compounds can activate pro-survival pathways and inhibit apoptotic cascades, ultimately enhancing neuronal survival and promoting neuroregeneration. Through an extensive review of preclinical studies and clinical trials, this analysis highlights the promising results of polyphenol interventions in animal models and human subjects with neurodegenerative disorders. Several polyphenols, such as resveratrol, curcumin, and epigallocatechin gallate have demonstrated notable neuroprotective effects in various neurodegenerative conditions.

Discussion

Neurodegenerative diseases are a diverse group of disorders characterised by the progressive loss of function and death of specific groups of neurons, which results in the disease's clinical manifestation. Changes in specific proteins cause dysfunction of various cellular pathways, including increased numbers of reactive oxygen species resulting from mitochondrial dysfunction, excitotoxicity, and synaptic dysfunction, impairment of protein degradation

systems, endoplasmic reticulum stress, DNA damage, inflammation, and cell cycle reentry. Their complex interaction makes understanding the mechanisms that cause neurotoxicity and cell death difficult, as well as finding an effective treatment.

The human brain, which accounts for about 2% of total body weight, receives 15% of cardiac output and consumes about 20% of total basal oxygen. According to the hypothesis that neurodegeneration has a mitochondrial basis, oxidative tissues with high energy demands are the most vulnerable to oxidative phosphorylation system defects. Furthermore, the most metabolically active areas of the brain (the cortex, particularly the motor cortex and thalami, which receive three times the blood flow of white matter) are the most susceptible to hypoxic ischemic encephalopathy. According to this, antioxidant therapeutic strategies for the treatment of various brain pathologies in order to restore redox equilibrium by scavenging free ROS are a promising approach [3].

The inner mitochondrial membrane is highly folded and impervious to almost all molecules and ions, forming the mitochondrial cristae in which the OXPHOS enzymatic complexes are embedded. Through the transfer of electrons by the five mitochondrial enzymatic complexes, OXPHOS enables the synthesis of ATP coupled to oxygen consumption. Electrons flow through the mitochondrial respiratory chain via oxidation-reduction reactions, eventually arriving at complex IV, where oxygen serves as the final receptor for the electrons and is reduced to H_2O. Thus, oxygen is consumed in the OXPHOS, and an electrochemical gradient is established, driving ATP synthesis. When OXPHOS fails, intermediate reactive metabolites derived from oxygen, known as ROS, are produced, making mitochondria the primary source of ROS [3].

Under physiological conditions, all antioxidant mechanisms reduce ROS production and thus act as oxidative stress defence systems. However, in the presence of mitochondrial dysfunction, ROS production may exceed the detox threshold, jeopardising cell viability [4,5]. Furthermore, even modest endogenous antioxidant defence makes the brain more vulnerable to oxidative stress. That is, the brains comparatively low endogenous antioxidant defence in comparison to many tissues makes it vulnerable to disrupted redox homeostasis. Beyond the protective endogenous antioxidant enzymatic defence cell mechanisms, exogenous antioxidants, including those administered through diet, such as polyphenols, carotenes, and vitamins, have been widely described in the literature to play a role in redox balance, including in the context of neurodegeneration [6].

Conclusion

In conclusion, exogenous adjunctive interventions, the majority of the antioxidant agents recently tested in the randomised controlled clinical trials discussed herein belong to the polyphenol, carotenes, fatty acid, and vitamin families. However, the antioxidant and neuroprotective power of these groups is not limited to these groups, as other antioxidant molecules such as nucleosides, hydrogen gas, or hormones have been tested in clinical trials against neurodegenerative disorders, primarily Parkinson's disease, in the last year. Melatonin, a hormone, is one of the most frequently studied antioxidant molecules in a wide range of diseases, including neurodegenerative disorders. Two of the most recent randomised clinical trials using antioxidants in neurodegenerative diseases found in this review used melatonin in different neurodegenerative contexts.

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Conflict of Interest

There are no conflicts of interest by author.

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