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A neuroprotective approach towards nature's goods for nervous system disorders: Current update

Pushpendra D. Pratap [1] and Sharique Ahmad [2,*]

[1] *Department of Biochemistry, Era's Lucknow Medical College and Hospital, ERA University, Lucknow Uttar Pradesh India.*
[2] *Department of Pathology, Era's Lucknow Medical College and Hospital, ERA University, Lucknow Uttar Pradesh India.*

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Abstract

A wide spectrum of progressive neurological disorders with a multifactorial etiology that contributes to the pathophysiology of the disease are collectively referred to as nervous system disorders (NSDs). A number of molecular and cellular processes, including oxidative stress, mitochondrial malfunction, protein misfolding, excitotoxicity, and inflammation, are involved in this intricate process. One current method of studying the degenerative process of the disease is to investigate the role of genes, as genetic forms of degenerative diseases are rather uncommon. Thus, it has been hypothesized that close interactions between genetic and environmental factors are responsible for idiopathic forms of the diseases; the genetic component may favor or even protect against the disease process. Owing to their wide range of biological and pharmacological activities, natural compounds may be suitable options for the treatment of these complex morbidities. Nevertheless, their low bioavailability and consequently inadequate brain delivery have limited their therapeutic potential against neurodegenerative diseases. An overview of the molecular mechanisms underlying the neuroprotective effects of natural compounds is given in this article.

Keywords: ROS; NSDs; CNS; Alzheimer's; Parkinson's

1. Introduction

Individuals between 60 to 80 years are expected to increase by roughly 50% by 2030 as a result of increased longevity among individuals and an upsurge in the percentage of elderly persons [1]. As a result, one-third of the population will be aged older than 65 and a quarter will be older than eighty. Despite these reasons, the number of people suffering from nervous system disorders (NSDs) having chronic cognitive decline and dementia is rapidly increasing, posing a crucial global health issue [2]. NSDs are a class of central nervous system (CNS) diseases that include ensembles of neurons that gradually lose functionalities and connectivity, leading to sensory and motor impairments as well as cognitive impairment [2, 3]. The most prevalent NDs are extrapyramidal and pyramidal movement deviations as well as cognitive or behavioral impairments [2]. NSDs are neurodegenerative accumulation of proteins diseases [4]. Neurodegeneration is described as a gradual demise of neurons and associated mechanisms, accompanied by a progressive deterioration in neural function [5]. Neurobiology advancements have revealed fresh insights on NSD, emphasizing their numerous similar traits [6]. Most prevalent NSD over the age of 65 is Alzheimer's disease (AD), posing an imminent threat to public health and the frequency of AD doubles every 5 years affecting up to 50 % of individuals over the age of 85 [7]. Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) are both diseases associated with ageing that are becoming more common as the population ages [8, 9]. NSD includes progressive supranuclear palsy (PSP), frontotemporal dementia (FTD), corticobasal degeneration (CBD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA), Huntington's disease (HD), chronic traumatic encephalopathy (CTE), spinocerebellar ataxias,

* Corresponding author: Sharique Ahmad

and a number of further uncommon proteinopathies [10]. Autophagy dysfunction, accumulation of proteins, inflammation, oxidative damage, mitochondrial dysfunction, genomic and epigenetic characteristics, apoptosis, diminished growth factor impacts, and loss of synaptic plasticity are all contributing factors to NSDs [11]. Different NSD phenotypes represent regional CNS patho-geographies depending on the molecular features of the accumulating protein as well as genetic and environmental effects. The substantia nigra and accompanying regional abnormalities are connected with Parkinson's disease; FTD with asymmetric frontal and temporal modifications; HD with striatal impact; and AD with first medial temporal effects [12]. The course of NDD is becoming better understood in terms of prion-like protein transmission via disease-relevant pathways [12].

2. Factors leading to NSDs

Misfolding and aggregation of neurotoxic proteins are promoted by genetic variables and natural ageing processes [13, 14], resulting in a dysregulated brain inflammatory response [15, 16]. This neuroinflammatory activity is associated with a state of chronic oxidative stress [16], both known as hallmarks of NSDs (Mittal et al., 2014), which stimulates activation of microglia along with astrocytes [17, 18, 15, 16]. Peripheral myeloid cell infiltration occurs at a later stage of neuroinflammation when the blood brain barrier (BBB) begins to break down, which ultimately results in progressive tissue damage over time [18, 16]. Differentiating autoimmune inflammatory disorders of the Central Nervous System (CNS) from other non-inflammatory diseases (NIDs) is crucial. The adaptive immune system—specifically, T- and B-lymphocytes—involves the CNS autoimmune illnesses, including MS and ALS, at an early stage and plays a causal role. Innate immune responses are present in Parkinson's disease (PD) and Alzheimer's disease (AD) as a protective mechanism. But in addition to aberrant astrocyte and microglia activity, the exacerbation of persistent proinflammatory triggers [19], [20], [16], plays a critical role in neuronal loss and dysfunction that leads to neurodegeneration [18], [16]. The pathophysiology of NSDs, like that of most multifactorial illnesses, is characterized by a complicated development wherein a variety of genetic, environmental, and behavioral factors play causative roles depicted in Figure 1 [21]. There are additional variables influencing the development of disease in addition to the hereditary component. The biggest risk factor is acknowledged to be aging naturally [13, 14, 22]. Metabolic diseases, including hyperlipidemia and type 2 diabetes mellitus (T2DM) [14, 22, 23], are recognized risk factors linked to the advancement of non-disordered diabetes. Presented with such massive evolve, investigations into the disease's causes, hazards, early detection, and prevention, as well as appropriate care, require immediate attention for the affected people. In order to prevent deterioration and age-associated disorders, including NSDs, a thorough investigation of plant based compounds is being encouraged by the search for natural ways to promote healthy aging. Consequently, the therapeutic activity of these compounds in the brain and their beneficial effects in different NSDs will be discussed in this study.

3. Neuroprotective effects of natural compounds in NSDs

Because medicinal plants contain a variety of chemical components that can act either singly or in combination, they offer a therapeutic alternative with a range of pharmacological properties. Furthermore, they are renowned for having negligible or no adverse effects [24], [25]. Natural compounds particularly polyphenols are big phytochemicals occurring naturally in plant foods, fruits, cereals, spices, legumes, and beverages including tea, coffee, red wine, spices, and herbs, as well as other critical elements in the human diet [26] [27], [28]. Polyphenols are plentiful in the human diet, with more than 1 mg of polyphenol content per serving and up to 1 g of median total polyphenol intake per day [29]. Additionally, they contribute to food's bitterness, colour, flavour, odour, astringency, and oxidative stability [30], [31]. Plant polyphenols also defend the plant against reactive oxygen species (ROS), ultraviolet (UV) radiation, diseases, parasites, and plant predators [32]. Numerous studies have been conducted on plant secondary metabolites for the maintenance of health as well as the prevention, diagnosis, treatment, or amelioration of mental and physical illnesses [33], [34]. They are especially fascinating to the pharmaceutical industry because they are either used as drugs or to develop new drugs [33].

Many phenolic compounds have been identified, either as pure compounds or as specific ratios of various plant extracts. Examining the impact of these natural compounds on health poses a significant challenge in the field of modern medicine [35]. The most prevalent phenolic compounds are called flavonoids, and they are divided into subclasses such as flavones (like luteolin), anthocyanins, proanthocyanidins (like cyanidin, pelargonidin), flavonols (like rutin, quercetin), flavanones (like naringin, hesperidin), isoflavones (like daudzein, genistein), and flavonols (like catechin). These substances are well known for having potent antioxidant properties [36], [37], [38]. It has been demonstrated that a variety of phenolic compounds have protective effects on cells, preventing or attenuating damage to cells and mitochondria caused by oxysterols like 7-ketocholesterol [39]. Resveratrol, apigenin, and quercetin are examples of antioxidants that can control the production of reactive oxygen species (ROS) from oxysterols [40].

Using a variety of scavenging assays, phenolic compounds including flavonoids, rosmarinic acid, ferulic acid, caffeic acid, vanillic, p-hydroxybenzoic acid, protocatechuic acid, and p-coumaric acid were found to contribute to the antioxidant potential [41], [42]. Numerous studies have shown that consuming polyphenolic substances reduces the risk of developing NSDs, cancers, and CVDs.

In vitro research was done to examine the inhibitory effects of a plant species called Sesamia cretica extract on these enzymes (AChE and BChE and α-amylase and α-glucosidase). Strong activity was shown by the extract against the main enzymes linked to AD and type II diabetes [43]. Twelve phenolic compounds, including kaempferol, hesperidin, chlorogenic acid, benzoic acid, and apelin, were found in the S. cretica extract. These compounds demonstrated the ability to chelate metal ions and scavenge radicals. Another similar study focused on the phenolic compounds found in Senecio biafrae leaf extract, specifically caffeic acid, chlorogenic acid, gallic acid, rutin, kaempferol, and quercetin. Additionally, this extract showed inhibition of important enzymes associated with AD and T2DM [44].

Because they have the ability to withstand oxidative stress, dietary phenolic compounds are potent phyto-compounds that have a long therapeutic history for PD. In the 6-OHDA-induced PD model, the study sought to determine whether the naturally occurring phenolic compounds quercetin, naringenin, curcumin, and fisetin could act as neuroprotective agents. The ability of naringenin and curcumin to cross the blood-brain barrier and offer neuroprotection may be associated with their respective high levels of antioxidants [45].

4. Conclusion

Given the growing number of elderly people worldwide and their longer lifespans, it is expected that NSDs—complex brain disorders marked by a variety of dysfunctional pathways—will become more common in the future. One expected consequence is the onset of dementia, the most common age-related brain disorder. Appropriate actions, such as cognitive training, physical activity, and dietary interventions, can be taken to postpone the detection of cognitive and memory deficits in the preclinical stage can lead to the onset of NDDs. Investigating dietary therapies appears to be a helpful tactic for reducing inflammation, preventing or delaying the onset of the disease, and slowing the disease's progression, especially in light of the increased attention being paid to the factors that contribute to NDDs. Individuals with non-degenerative diseases (NDDs) may experience dietary modifications that enhance or maintain normal brain functions in both younger and older populations. The use of natural products and the powerful bioactive substances they contain is essential for the non-invasive treatment and prevention of a variety of neurodegenerative diseases.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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