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REVIEW ARTICLE

Protective effects of natural products in neurodegeneration: A narrative review.

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ABSTRACT… This systematic review aims to analyze published studies from databases such as PUBMED, Google Scholar and Research Gate, while focusing on the role of bioactive components found in the natural medicinal products in Grape, Honey, Pomegranate juice and Moringa Oleifera in neuroprotection. The literature search was done from 2019 till 2025 with key words of natural products, neuroprotections and neurodegeneration and more than 50 full articles were included. This review highlights the therapeutic potential of natural products and their bioactive compounds in providing neuroprotective effects against the pathologies associated with neurodegenerative diseases. Neurodegenerative diseases of the nervous system manifested through various syndromes, with progressive dementia being the predominant symptom in mostly cases. The bioactive compounds include vitamins, minerals, carotenoids, polyunsaturated fatty acids, and polyphenols, alkaloids, and some other compounds found, will be the primary focus of this document. This document provides the evidence basis to determine the nutritional benefits of these medicinal products in improving the health and well-being of various groups.

Key words: Natural Products, Neuroinflammation, Neurodegeneration, Neuroprotection.

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INTRODUCTION

Natural products play a pivotal role in supporting dietary interventions for neurodegenerative conditions. Due to their potential therapeutic effects, functional foods imbued with biologically active compounds have attracted interest. Indeed, one such group of compounds, polyphenols which are found in plants, appear to be promising due to their antioxidant and wide range of biological activity which could help to prevent the neurodegenerative processes.[1] The term 'neurodegenerative diseases' refers to a group of progressive disorders that affect the nervous system and involve the irreversible degeneration of neurons.[2] These conditions impact millions of peoples globally, resulted in the significant challenges for the healthcare systems and society due to their chronic nature. Age-related diseases are very common and caused by cumulative neural cell death which is accompanied by loss of brain functions.[3] Other research has shown that the prevalence of dementia was highest in populations aged 60 years and older and it was revealed that around 44 million population has been affected by dementia specifically in Alzheimer's and predicted that the numbers will be tripled globally up to 2050.[4] It refers to a group of diseases that have a similar trait, which is an increase in the rate of deterioration of the person's mental function. A lot of different research has suggested the great potential that unfolding natural products would serve regarding a variety of neurological and neurodegenerative processes. Such an effect would include the managing of elderly depression and other geriatric disorders like Alzheimer's (AD) and Parkinson's disease (PD).[5] Natural products have also been associated with protecting from degeneration of peripheral nerves, muscular sclerosis (MS), motor neuron disease (MND) or amyotrophic lateral sclerosis (ALS) and neurotoxicity.[6]

The natural compounds seem to be aimed to act on specific enzymes in the nervous system which include acetylcholinesterase that has an impact on neurotransmitter regulation, as well as monoamine oxidase, an important mood and behavior regulator.

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This review will concentrate on those products which are effective in reducing the impact of Parkinson's Disease (PD), Alzheimer's Disease (AD), prion diseases and Multiple Sclerosis (MS). The complexity underscores for further research to unravel the underlying molecular mechanisms driving these conditions and to identify effective pharmacological targets that can address their multifaceted causes.

Neurodegenerative disorders (NDD) and Molecular Mechanism Involved in Neurodegeneration:

Neurodegenerative diseases manifested clinically in one of three patterns, includes deficits in cognition, dementia as well as impairment of higher-order brain functions, reflecting involvement of the hippocampus, entorhinal cortex, limbic system and neocortical areas.[6] The other pattern involves movement disorders, which could be hyperkinetic, hypokinetic, cerebellar disorder, or upper and lower motor neuron dysfunction. These symptoms indicate damage to areas for instance the brainstem nuclei, thalamus, basal ganglia, motor cortical regions, cerebellar cortex and nuclei and the spinal cord's lower motor neurons.[3] Neurodegenerative diseases have a molecular pathological basis that included the identification of synaptic, intracellular and extracellular protein accumulations. The precise subcellular location of intracellular deposits, such as in the nucleus, cytoplasm, or cellular processes, plays a significant role in this categorization. Innovations in immunohistochemistry, particularly with the development of new antibodies, have uncovered unique immunostaining patterns, providing deeper insights into the underlying pathology of these diseases.[6] The mainstream of intermittent and genetic adult-onset neurodegenerative diseases (NDDs) are associated with specific proteins, including: (1) Amyloid-beta (Aβ), (2) α-synuclein, (3) Prion protein (PrP), (4) Tau (5) Transactive response DNA-binding protein 43 (TDP-43), implicated in several NDDs.[7] Among all these Amyloid-beta (Aβ) is one of the most commonly identified proteins associated with neurodegenerative diseases, prominently accumulating in Alzheimer's disease (AD) alongside tau protein.[8] The pathological accumulation of these proteins is characterized by distinct immunoreactive morphologies observed in various proteinopathies, reflecting their role in disease progression.[9]

Oxidative Stress is a Key Modulator of Neurodegenerative Disorders

Neurodegeneration is associated with a range of biological mechanisms, including; oxidative stress, neuroinflammation, excitotoxicity, mitochondria dysfunction, proteins abnormal folding and aggregation, and even apoptosis. Oxidative stress (OS) refers to something that results from biochemical imbalance of oxidants and antioxidants. Such imbalance takes place with overproduction of reactive oxygen species (ROS) or malfunction of antioxidant defense system.[10] Oxygen is considered detrimental because of its univalent metabolic reduction, and unbending the ROS.

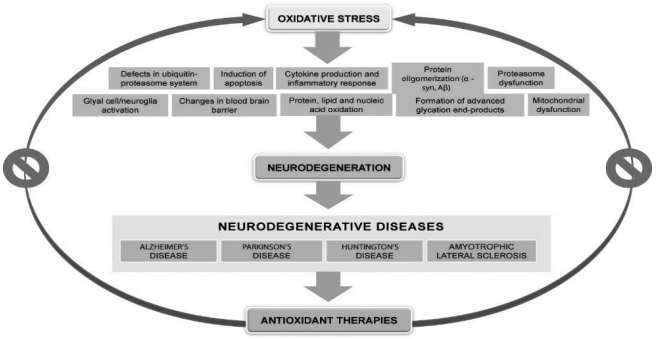

Figure1: Represent the oxidative stress phenomena and neurodegeneration results in PD—Parkinson's disease; AD—Alzheimer's disease; HD—Huntington's disease protected with antioxidant therapy.[11]

This review endeavors to consolidate current knowledge on the mechanisms and causes of neurodegenerative diseases, highlighting the significant role of oxidative stress (OS) in their progression as well as the advances in therapeutic strategies designed to combat these debilitating conditions.

Role of Natural Products in Different Neurodegenerative Diseases

Grape Seed Oil and Leaf Extracts

Natural foodstuff , due to their countless active composites have beneficial effects over the various defense mechanisms resulted in the progressive reduction of oxidative stress, leads to the reduced level of ROS establishment and eventual suppresses

the oxidation of biomolecules and progression to the cell injury.[10,11] Various natural products have been identified that provides protection in neurodegeneration and their components of a widely used natural leaf extracts, seed powder and seed oil resulted in the reduction of dementia rate.[12]

Grape seeds (Vitis vinifera L.) have been extensively studied for their bioactive properties, as they are rich in phenolic compounds, flavonoids and phenolic acids.[12] Large numbers of studies revealed that Grape oil is one of them, have the promising effect in the reduction of dementia and provide neuroprotection in the other neurodegenerative diseases.[13] The compounds present in Vitis vinifera seeds exhibit a wide range of biological effects, including antioxidant, free radical scavenging, anti-inflammatory, antihypertensive, antimutagenic, antineoplastic, antiviral, antibacterial, anti-ulcer, anti-tumor, wound healing, antihyperglycemic, cardioprotective, anti-hepatotoxic, anti-cataract, and sunscreen properties.[14,15] These effects are largely attributed to the reactivity of the phenol groups within the seeds' bioactive compounds. These properties have been extensively studied and validated through in vitro, in vivo, animal and human research.[13] The neuroprotective effects of grape seeds have been attributed to several proposed mechanisms, including their ability to search for the free radicals in the body and decreasing lipid peroxidation, also revealing more antioxidant activity, constraining DNA oxidative damage and inhibiting the cell death signaling pathways. Their oil is characterized by a diverse composition of both saturated and unsaturated fatty acids, including linoleic acid (65%), linolenic acid (1.5%), oleic acid (17%), palmitic acid (8.0%), stearic acid (4.4%) and arachidonic acid (0.6%).[13,15] Another study, exploring the effect of grape seed oil (GSO) on spatial memory function in an Alzheimer's disease (AD) model induced by scopolamine revealed that cognitive impairment caused by scopolamine results from disrupted cholinergic neurotransmission and increased oxidative stress. These results established that interventions of using the bioactive components of GSO resulted in mitigating the effects on the cholinergic system and that could be beneficial to increase the treatment options in AD. The findings indicated that GSO has potential as a well as preventive, rather than curative, agent in managing the AD.[16] The studies revealed that oil extracted from Vitis vinifera seeds contains resveratrol, a compound known for its neuroprotective properties. Resveratrol inhibits nuclear factor κB (NF-κB), a key factor involved in the toxicity of β-amyloid, which is a major contributor to the development and progression of Alzheimer's disease.[16]

Another in vitro study in which brain tissue model showed the neuroprotective effects of Vitis vinifera extract by the administration of the extract at a dose of 400 mg/kg (p.o.) for 45 days demonstrated its ability to protect brain tissue from aluminum-induced neurotoxicity (toxic dose of 100 mg/kg per/oral for 45 days). Another study conducted in PD models revealed that supplementation with grape polyphenols (GPC) significantly decreased α-synuclein accumulation and reduced the expression of neuroinflammatory markers in the frontal cortex. These effects highlighted the potentials of GPC in mitigating key pathological features of neurodegenerative diseases, such as Parkinson's disease, by targeting protein aggregation and neuroinflammatory pathways.[17]

The evidence demonstrating the potent anti-inflammatory properties of grape polyphenols (GPPs). These compounds are capable to provide the effects as 1. Downregulating the manifestation of pro-inflammatory transcription factors, such as nuclear factor kappa B (NF-κB). 2. Reducing the discharge of pro-inflammatory cytokines from peripheral leukocytes, microglia, and astrocytes.3.Inhibiting microglial priming triggered by the activation of toll-like receptors (TLRs).4.Preventing the formation of neurotoxins.[18]

Neuroprotection by Honey

Honey a natural sweetener produced by bees, have renowned therapeutic and nutritional values. Honey is rich in bioactive compounds with antioxidants, particularly polyphenols, which contributed to its health-promoting properties.[19,20] These compounds play a significant role in combating oxidative stress and supporting overall well-being, making honey a valuable functional food. Honey has been extensively studied for its wide-ranging health benefits, including its gastroprotective, hepatoprotive,

reproductive, hypoglycemic, antioxidant, antihypertensive, antibacterial, antifungal, anti-inflammatory, immunomodulatory, wound healing, cardioprotective and antitumor activities.[21] These bioactive molecules provide neuroprotection by neutralizing free radicals and combating the oxidative stress, reducing neuroinflammation by downregulating pro-inflammatory cytokines and inhibiting the aggregation of misfolded proteins such as β-amyloid and α-synuclein, thereby slowing the disease progression.[22] Many studies have been conducted in vivo as well as in vitro to see the neuroprotection of honey against the definite and indefinite neurodegenerative disorders. A systemic study shown that an in vitro study using the microglia BV2 cell line, galangin, a polyphenol found in honey and propolis, was observed to prevent the production of pro-inflammatory cytokines and nitric oxide (NO).[23] The capability of galangin to adapt this response recommends its potential mediator for the neuroprotection, dropping the sternness of brain damage and neurodegenerative diseases.[23] Another review showed examining neuroprotection in certain neurodegenerative diseases such as AD, that all polyphenols and flavonoids in honey were connected with acetylcholinesterase (AChE) inhibitory effect. Acetylcholinesterase (AChE) inhibition is significant for enhancing cholinergic neurotransmission, which is regularly affected in neurodegenerative diseases such as Alzheimer's disease AD.[24] The honey contains a rich source of antioxidants which helps to combat oxidative stress and neuroprotective agents that helps in the preservation of vital processes in the brain that are associated with memory, learning, and controlling emotions.[25,26] A study included in- vitro experimentation of SH-SY5Y cell line resulted in necrotic neuronal cell death induced by the oxidative stress due to exposure of tert-butyl hydroperoxide and when treated with the Chrysin a bioactive compound of Honey act antioxidant, tert-butyl hydroperoxide mitigate its necrotic injury while in the same study in-vivo model showed antioxidant and neuroprotective effects when treated with Chrysin in chronic exposure of AlCl3 induced neurodegeneration, with the improvement of their cognitive impairment suggesting that chrysin contributed to the prevent and delay the progression of neurodegeneration.[27] Another systemic review also focused that the polyphenols compound found in honey offers neuroprotective benefits by improving cognitive performance, reducing oxidative stress and alleviating the symptoms of neurological diseases like Alzheimer's disease (AD) due to polyphenolic and total antioxidant capacity (TAC) of these bioactive substance.[28] Baranowska et al. (2020) highlighted the cholinesterase inhibitory properties of 47 Polish honey types, with phenolic content ranging from 0–1267.96 mg GAE/100 g and significant inhibition of acetylcholinesterase (AChE) and butyrylcholinesterase, suggesting honey as a potential source of cholinesterase inhibitors.[29,30] The study by Zaidi et al. (2019) evaluated 31 Algerian honey types and they observed AChE inhibition ranging from 20.69% to 76.04%, with flavonoid content and antioxidant activity varying based on floral and geographical origins.[31,32] Arshad et al. (2020) found that Kelulut honey improved spatial memory and preserved hippocampal morphology in rats with metabolic syndrome.[33] Yaacob et al. (2020) showed that Tualang honey restored spatial and recognition memory in rats with LPS-induced neuroinflammation, highlighting its neuroprotective potential.

Neuroprotection and Neurodegeneration Mitigation by Pomegranate

Pomegranate (Punica granatum L.) a fruit rich in polyphenols, has been extensively utilized in traditional medicine for its medicinal properties.[34] Native to central Asia, particularly regions of Iran, pomegranate is an economically significant fruit that has spread globally due to its therapeutic potential and versatility most wide considered as blood tonic.[35] There are several studies revealed the medicinal effect of Pomegranate in various diseases, here we only considered Punicalagin (PUN) as a neuroprotective bioactive compounds of Pomegranate. This review summarizes the neuroprotective effects of Punicalagin (PUN) Bioactive compound of Pomegranate juice with its neuroprotection in various in-vitro as well as in –vivo studies.

In Vitro Studies

Cell Line/ Model	Condition/Model	Punicalagin (PUN) Dose	Duration	Findings	References
Pheochromocytoma 12 Cells line	Oxidative stress H_2O_2-induced	0.5, 1, 5, 10, 20 μM	24 hrs	Resulted in reduction in the cell apoptosis, cell viability; mitochondrial membrane potential increased with reduction in ROS production	[36]
Mouse neuronal cell line of HT22 Cells	oxidative stress induced by Glutamate	6.25 and 50 μM	24 hrs	Increased cell viability due to the reduced in cellular cytotoxicity; improved mitochondrial function as well as reduction in ROS	[37]
SH-SY5Y Cells	6-OHDA-induced damage	50, 100, 200 μM	2 hrs	Improved mitochondrial function; reduced ROS and apoptosis; increased ATP levels and AMPK activity.	[38]
Primary Microglia	LPS-induced neuroinflammation	5–40 μM	24 hrs	Reduced TNF-α, PGE2, and COX-2; inhibited NF-kB, p38, and MAPK signaling.	[39]
BV2 Cell Line		25, 50, 75, 100 μM	24 hrs	Reduced IL-6, IL-1β, and NO production; inhibited NF-kB and MAPK activation.	[40]

In Vivo Studies

Animal Model	Condition	Punicalagin (PUN) Dose	Duration	Findings	References
APP/PS1 Transgenic Mice	Alzheimer's Disease (AD)	12.5, 25, 50 mg/kg (oral)	45 days	Improved learning and memory; reduced Aβ deposition and tau phosphorylation.	[41]
Sprague Dawley Rats	Manganese-induced Parkinson's Disease	2.5 mg/kg (oral)	35 days	Enhanced motor function; decreased neuroinflammation and acetylcholinesterase activity.	[42]
Wistar Rats	Cerebral ischemia-reperfusion injury	15 and 30 mg/kg (oral)	7 days	Reduced infarct volume and neurological deficits; improved BBB integrity and reduced inflammation.	[43]
C57BL/6 Mice	High-fat diet-induced diabetes	50 and 100 mg/kg (oral)	8 weeks	Ameliorated cognitive dysfunction; reduced neuronal apoptosis.	[44]
Embryonic Mice	High-glucose-induced neural tube defects	10 and 20 μmol/L	24 hrs	Reduced neural tube defects; suppressed caspase 3 and 8 cleavage.	[45]

Moringa Oliefera as A neuroprotective Phytochemical

While experts define Moringa oleifera (Lam) as a tree with various organs utilized for nutrition, medicine, and other purposes, in Indonesia it is known as Kelor. The tree is peculiarly belong to the Moringaceae family in Southeast Asia, and for that matter, Kelor used for nutritional and medicinal uses.[46] Moringa has many attributes, and researches have shown its impacts on environmental science, medicine, health, nutrition, and phytochemistry.[47] Moringa leaves are known to be a rich source of phytochemicals and because of such they are potent sources of antioxidants. Some of the prominent ones are quercetin, gallic acid, chlorogenic acid, p-coumaric acid, ferulic acid, and sinapinic acid, which independently and together provides medicinal protection. Khalid et al. (2023) have reported some of the important ones found with its strong antioxidant effects.[48] Health promoting effects of M. oleifera are multifaceted, showcasing nutritional value that goes beyond its potent anti-inflammation activity.[49] A particular animal study looked into the antioxidant and nootropic activities of Moringa leaf extract with a consideration of its ability to improve memory and provide neuroprotection. Their findings claimed that the extract improves memory and reduces neurodegeneration in the CA1, CA2, and CA3

regions and the dentate gyrus of the hippocampus. Di(2-ethylhexyl) dicarboxylate (DEHP), a plasticizer associated to neurotoxic effects, offers neurons protection inside SH-SY5Y cells. According to Jaafaru et al., glucosinolate isothioacyanate GMG-ITC is produced when Moringa oleifera glucosinolate GMG is hydrolyzed.[50] Studies have shown that the neuroprotective effects of Moringa are exerted through its glucosinolates, particularly R,S-sulforaphane (SFN), which is hydrolyzed to isothiocyanates (ITCs). SFN initiates the mitogen-activated protein kinase (MAPK) pathway that, in turn, phosphorylates Kelch-like ECH-associated protein 1 (Keap1).[51] This is followed by the degradation of nuclear erythroid 2-associated factor 2 (Nrf2), which is an anti-oxidation transcription factor. ITC widens this effect by covalently binding to the Keap1 sulfhydryl group, enabling the translocation of Nrf2 to the nucleus and triggering the Nrf2/ARE pathway. This pathway increases the expression of antioxidant proteins, including heme oxygenase 1 (HO1) and quinone oxidoreductase (NQO1), which are responsible for mitigating oxidative damage and neurodegeneration.[52] Studies were conducted to evaluate whether Moringa oleifera seed oil (MOO) or Moringa oleifera leaf aqueous extract (MOE) could reduce scopolamine (Sco)-induced damage in rats. This study also included phytochemical analysis of both formulations. In this experiment, MOO (2 ml/kg body weight) and MOE (500 mg/kg body weight) were administered orally for 28 days to induce mental illness, and Sco (1 mg/kg) was injected intraperitoneally on days 22 to 28. The results showed that the Sco group was significantly poorer in Y-maze recall and novel object recognition. This group also showed strong acetylcholinesterase (AChE) activity in hippocampal tissue ($p < 0.0001$) and increased total antioxidant capacity (TAOC) in blood.[52] However, in the Sco + MOO treatment group, scopolamine-induced memory impairments were reversed supported by the previous study and AChE flares were completely attenuated ($p < 0.0001$), while TAOC levels remained similar between groups.[53] Mechanistically, protein expressions of tropomyosin receptor kinase B (TrkB), a receptor for brain-derived neurotrophic factor, and nuclear factor-kappa-light-chain-enhancer of activated B cells (NF-κB) were elevated in the hippocampus of the Sco group. Pretreatment with MOO, but not MOE, significantly reduced TrkB and NF-κB expression levels ($p < 0.05$ and $p = 0.09$). These revealed that MOO is more effective than MOE as a neuroprotective agent, primarily by improving memory impairment through AChE and NF-κB inhibition and modulation of TrkB expression as supported by the previous observations.[54,55]

Another experimentation focuses on the neuroprotective effects of Moringa Oleifera (MO) against nicotine-induced cerebellar degeneration and neurobehavioral disturbances. Nicotine, a neuro-stimulant associated with numerous neurodegenerative diseases, induces oxidative stress, histological alterations in cerebellar morphology, and behavioral deficits, as evidenced in rodent models.[56] MO prevent cerebellar chromatolysis and maintained the histoarchitecture of the cerebellar layers. It also enhanced locomotor activity, increased SOD levels, and decreased MDA expression in the cerebellum, demonstrating its ability to combat oxidative stress. The antioxidant properties of MO, which are linked to its phytochemical components like flavonoids, phenolics, and arotenoids, were identified as the main mechanisms behind its protective effects. It was suggest that Moringa Oleifera possibly will serve as a potential therapeutic agent for preventing nicotine-induced neurotoxicity and for preserving cerebellar function through its antioxidant and neuroprotective properties.[57]

CONCLUSION

Natural products have significant contribution in neuroprotection and in preventing the development of neurodegenerative diseases, helping protect the brain from disease. The results highlight the bio modulation of bioactive material in nature products e.g. grape seed oil, pomegranate juice, honey, and Moringa Oleifera. They counteract oxidative stress, neuroinflammation, protein aggregation, and mitochondrial dysfunction – key contributors to neurodegenerative diseases. What is more this study highlighted the value of these natural agents on enhancing cognitive ability, protecting neuron cells from damage as well as providing complementary alternatives to conventional pharmacological therapies. Additionally, assessment of these natural compounds could concrete the

way for innovative therapies for neurodegenerative disorders, eventually enhancing the quality of life for those affected by these conditions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Mohd Sairazi NS, Sirajudeen KN. **Natural products and their bioactive compounds: neuroprotective potentials against neurodegenerative diseases.** Evidence-Based Complementary and Alternative Medicine. 2020; (1):6565396.
2. Singh A, Kukreti R, Saso L, Kukreti S. **Oxidative stress: A key modulator in neurodegenerative diseases.** Molecules. 2019; 24(8):1583.
3. Chen WW, Zhang XI, Huang WJ. **Role of neuroinflammation in neurodegenerative diseases.** Molecular Medicine Reports. 2016; 13(4):3391-6.
4. Prince MJ. **World Alzheimer Report 2014: Dementia and risk reduction: An analysis of protective and modifiable factors.** Alzheimer's Disease International; 2014.
5. Magalingam KB, Radhakrishnan A, Ping NS, Haleagrahara N. **Current concepts of neurodegenerative mechanisms in Alzheimer's disease.** BioMed Research International. 2018; 2018(1):3740461.
6. Jellinger KA. **Basic mechanisms of neurodegeneration: A critical update.** Journal of Cellular and Molecular Medicine. 2010; 14(3):457-87.
7. Combs B, Hamel C, Kanaan NM. **Pathological conformations involving the amino terminus of tau occur early in Alzheimer's disease and are differentially detected by monoclonal antibodies.** Neurobiology of Disease. 2016; 94:18-31.
8. Apostolova LG. **Alzheimer disease.** Continuum: Lifelong Learning in Neurology. 2016; 22(2):419-34.
9. Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkmann J, et al. **Parkinson disease.** Nature reviews Disease Primers. 2017; 3(1):1-21.
10. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. **Oxidative stress, aging, and diseases.** Clin. Interv. Aging. 2018; 13:757-72.
11. Sienes Bailo P, Llorente Martín E, Calmarza P, Montolio Breva S, Bravo Gómez A, Pozo Giráldez A, et al. **The role of oxidative stress in neurodegenerative diseases and potential antioxidant therapies.** Advances in Laboratory Medicine/Avances en Medicina de Laboratorio. 2022; 3(4):342-50.
12. Carry E, Zhao D, Mogno I, Faith J, Ho L, Villani T, et al. **Targeted analysis of microbial-generated phenolic acid metabolites derived from grape flavanols by gas chromatography-triple quadrupole mass spectrometry.** JPBA. 2018; 159:374-83.
13. Pazos-Tomas CC, Cruz-Venegas A, Pérez-Santiago AD, Sánchez-Medina MA, Matías-Pérez D, García-Montalvo IA. **Vitis vinifera: An alternative for the prevention of neurodegenerative diseases.** Journal of Oleo Science. 2020; 69(10):1147-61.
14. Kamran H, Raza I, Saleem Y, Aslam M. **Health perspectives of grape seed extract (GSE).** Asian Journal of Allied Health Sciences (AJAHS). 2020; 5(1):88-98.
15. Natarajan SB, Hwang JW, Kim YS, Kim EK, Park PJ. **Ocular promoting activity of grape polyphenols-A review.** Environ. Toxicol. Pharmacol. 2017; 50:83-90.
16. Berahmand F, Anoush G, Hosseini MJ, Anoush M. **Grape seed oil as a natural therapy in male rats with Alzheimer's diseases.** Advanced Pharmaceutical Bulletin. 2020; 10(3):430.
17. Tikhonova MA, Tikhonova NG, Tenditnik MV, Ovsyukova MV, Akopyan AA, Dubrovina NI, et al. **Effects of grape polyphenols on the life span and neuroinflammatory alterations related to neurodegenerative Parkinson disease-like disturbances in mice.** Molecules. 2020; 25(22):5339.
18. Zhao D, Simon JE, Wu Q. **A critical review on grape polyphenols for neuroprotection: Strategies to enhance bioefficacy.** Critical Reviews in Food Science and Nutrition. 2020; 60(4):597-625.
19. Cheung Y, Meenu M, Yu X, Xu B. **Phenolic acids and flavonoids profiles of commercial honey from different floral sources and geographic sources.** Int. J. Food Prop. 2019; 22(1):290-308.
20. Sousa JM, De Souza EL, Marques G, Meireles B, de Magalhães Cordeiro ÂT, Gullón B, et al. **Polyphenolic profile and antioxidant and antibacterial activities of monofloral honeys produced by Meliponini in the Brazilian semiarid region.** Food Res. Int. 2016; 84:61-8.
21. Liu JR, Ye YL, Lin TY, Wang YW, Peng CC. **Effect of floral sources on the antioxidant, antimicrobial, and anti-inflammatory activities of honeys in Taiwan.** Food Chem. 2013; 139(1-4):938-43.
22. Rosli NH, Yahya HM, Ibrahim FW, Shahar S, Ismail IS, Azam AA, et al. **Serum metabolomics profiling of commercially mixed functional foods—effects in beta-amyloid induced rats measured using 1H NMR spectroscopy.** Nutrients. 2020; 12(12):3812.
23. Al-Abd NM, Kassim M, Zajmi A. **The inhibitory effect of galangin on cytokines and nitric oxide in microglia BV2 cell line.** Malaysian Journal of Science. 2017; 36(3):145-56.
24. Baranowska-Wójcik E, Szwajgier D, Winiarska-Mieczan A. **Honey as the potential natural source of cholineste rase inhibitors in Alzheimer's disease.** Plant Foods Hum. Nutr. 2020; 75:30-2.
25. Szwajgier D, Baranowska-Wójcik E, Winiarska-Mieczan A, Gajowniczek-Ałasa D. **Honeys as possible sources of cholinesterase inhibitors.** Nutrients. 2022; 14(14):2969.

26. Mohd Sairazi NS, Sirajudeen KN, Muzaimi M, Mummedy S, Asari MA, Sulaiman SA. **Tualang honey reduced neuroinflammation and caspase-3 activity in rat brain after Kainic acid-induced status epilepticus.** Evid. Based Complement. Alternat. Med 2018; 2018(1):7287820.
27. Campos HM, da Costa M, da Silva Moreira LK, da Silva Neri HF, da Silva CR, Pruccoli L, et al. **Protective effects of chrysin against the neurotoxicity induced by aluminium: In vitro and in vivo studies.** Toxicology. 2022; 465:153033.
28. Pluta R, Miziak B, Czuczwar SJ. **Apitherapy in post-ischemic brain neurodegeneration of alzheimer's disease proteinopathy: Focus on honey and its flavonoids and phenolic acids.** Molecules. 2023; 28(15):5624.
29. Baranowska-Wójcik E, Szwajgier D, Winiarska-Mieczan A. **Honey as the potential natural source of cholinesterase inhibitors in Alzheimer's disease.** Plant Foods for Human Nutrition. 2020; 75:30-2.
30. Szwajgier D, Baranowska-Wójcik E, Winiarska-Mieczan A, Gajowniczek-Ałasa D. **Honeys as possible sources of cholinesterase inhibitors.** Nutrients. 2022; 14(14):2969.
31. Harbane S, Escuredo O, Saker Y, Ghorab A, Nakib R, Rodríguez-Flores MS, et al. **The contribution of botanical origin to the physicochemical and antioxidant properties of Algerian honeys.** Foods. 2024; 13(4):573.
32. Zaidi H, Ouchemoukh S, Amessis-Ouchemoukh N, Debbache N, Pacheco R, Serralheiro ML, et al. **Biological properties of phenolic compound extracts in selected Algerian honeys—The inhibition of acetylcholinesterase and α-glucosidase activities.** European Journal of Integrative Medicine. 2019; 25:77-84.
33. Arshad NA, Lin TS, Yahaya MF. **Stingless bee honey reduces anxiety and improves memory of the metabolic disease-induced rats.** CNS & Neurological Disorders-Drug Targets-CNS & Neurological Disorders). 2020; 19(2):115-26.
34. Langley P. **Why a pomegranate?.** Bmj. 2000; 321(7269):1153-4.
35. Akaberi M, Boghrati Z, Sahebkar A, Emami SA. **Therapeutic potential of pomegranate in metabolic disorders.** Natural Products and Human Diseases: Pharmacology, Molecular Targets, and Therapeutic Benefits. 2021; 421-40.
36. Clementi ME, Pani G, Sampaolese B, Tringali G. **Punicalagin reduces H2O2-induced cytotoxicity and apoptosis in PC12 cells by modulating the levels of reactive oxygen species.** Nutritional Neuroscience. 2018; 21(6):447-54.
37. Clementi ME, Sampaolese B, Lazzarino G, Giardina B. **Effect of punicalagin and resveratrol on methionine sulfoxide reductase: A possible protective contribution against Alzheimer's disease.** J Prev Alzheimers Dis. 2015; 2(1):33-7.
38. Chu J, Han W. **Punicalagin exerts beneficial functions in 6-hydroxydopamine-treated SH-SY5Y cells by attenuating mitochondrial dysfunction and inflammatory responses.** Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2018; 24:5905.
39. Olajide OA, Kumar A, Velagapudi R, Okorji UP, Fiebich BL. **Punicalagin inhibits neuroinflammation in LPS-activated rat primary microglia.** Molecular Nutrition & Food Research. 2014; 58(9):1843-51.
40. Lo J, Liu CC, Li YS, Lee PY, Liu PL, Wu PC, et al. **Punicalagin attenuates LPS-induced inflammation and ROS production in microglia by inhibiting the MAPK/NF-κB signaling pathway and NLRP3 inflammasome activation.** Journal of Inflammation Research. 2022; 5347-59.
41. Scheltens P, De Strooper B, Kivipelto M, Holstege H, Chételat G, Teunissen CE, et al. **Alzheimer's disease.** The Lancet. 2021; 397(10284):1577-90.
42. Abu-Elfotuh K, Hamdan AM, Abbas AN, Alahmre AT, Elewa MA, Masoud RA, et al. **Evaluating the neuroprotective activities of vinpocetine, punicalagin, niacin and vitamin E against behavioural and motor disabilities of manganese-induced Parkinson's disease in Sprague Dawley rats.** Biomedicine & Pharmacotherapy. 2022; 153:113330.
43. Yaidikar L, Thakur S. **Punicalagin attenuated cerebral ischemia–reperfusion insult via inhibition of proinflammatory cytokines, up-regulation of Bcl-2, down-regulation of Bax, and caspase-3.** Molecular and Cellular Biochemistry. 2015; 402:141-8.
44. He X, Pei S, Meng X, Hua Q, Zhang T, Wang Y, et al. **Punicalagin attenuates neuronal apoptosis by upregulating 5-hydroxymethylcytosine in the diabetic mouse brain.** Journal of Agricultural and Food Chemistry. 2022; 70(16):4995-5004.
45. Zhong J, Reece EA, Yang P. **Punicalagin exerts protective effect against high glucose-induced cellular stress and neural tube defects.** Biochemical and Biophysical Research Communications. 2015; 467(2):179-84.
46. Mishra G, Singh P, Verma R, Kumar S, Srivastav S, Jha KK, et al. **Traditional uses, phytochemistry and pharmacological properties of Moringa oleifera plant: An overview.** Der Pharm Lett. 2011; 3:141-64.
47. Tao T, Liu M, Chen M, Luo Y, Wang C, Xu T, et al. **Natural medicine in neuroprotection for ischemic stroke: Challenges and prospective.** Pharmacology & Therapeutics. 2020; 216:107695.
48. Khalid S, Arshad M, Raza K, Mahmood S, Siddique F, Aziz N, et al. **Assessment of hepatoprotective, nephroprotective efficacy, and antioxidative potential of Moringa oleifera leaf powder and ethanolic extract against PCOS-induced female albino mice (Mus Musculus).** Food Science & Nutrition. 2023; 11 (11):7206-17.
49. Xu H, Wang E, Chen F, Xiao J, Wang M. **Neuroprotective phytochemicals in experimental ischemic stroke: mechanisms and potential clinical applications.** Oxidative Medicine and Cellular Longevity. 2021; 2021(1):6687386.
50. Amara I, Ontario ML, Scuto M, Lo Dico GM, Sciuto S, Greco V, et al. **Moringa oleifera protects SH-SY5YCells from DEHP-induced endoplasmic reticulum stress and apoptosis.** Antioxidants. 2021; 10(4):532.
51. Girnun GD, Domann FE, Moore SA, Robbins ME. **Identification of a functional peroxisome proliferator-activated receptor response element in the rat catalase promoter.** Molecular Endocrinology. 2002; 16(12):2793-801.

52. Arozal W, Purwoningsih E, Lee HJ, Barinda AJ, Munim A. **Effects of Moringa oleifera in two independents formulation and as neuroprotective agent against scopolamine-induced memory impairment in mice.** Frontiers in Nutrition. 2021; 9:799127.
53. Yadang FS, Nguezeye Y, Kom CW, Betote PH, Mamat A, Tchokouaha LR, et al. **Scopolamine-induced memory impairment in mice: Neuroprotective effects of Carissa edulis (Forssk.) Valh (Apocynaceae) aqueous extract.** International Journal of Alzheimer's Disease. 2020; (1):6372059.
54. Kumar Datusalia A, Sunder Sharma S. **NF-κB inhibition resolves cognitive deficits in experimental type 2 diabetes mellitus through CREB and glutamate/GABA neurotransmitters pathway.** Current Neurovascular Research. 2016; 13(1):22-32.
55. Végh MJ, Heldring CM, Kamphuis W, Hijazi S, Timmerman AJ, Li KW, et al. **Reducing hippocampal extracellular matrix reverses early memory deficits in a mouse model of Alzheimer's disease.** Acta Neuropathologica Communications. 2014; 2:1-1.
56. Omotoso GO, Gbadamosi IT, Olajide OJ, Dada-Habeeb SO, Arogundade TT, Yawson EO. **Moringa oleifera phytochemicals protect the brain against experimental nicotine-induced neurobehavioral disturbances and cerebellar degeneration.** Pathophysiology. 2018; 25(1):57-62.
57. Stanford SC. **The open field test: Reinventing the wheel.** Journal of Psychopharmacology. 2007; 21(2):134-5.

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1	**Surriyya Sarwat:** Concept and Final drafting.
2	**Kahkashan Parveen:** Literature search.
3	**Sonia Siddiqui:** Approval for publishing.
4	**Anam Pario:** Critical revisions.
5	**Tanzeela Kauser:** Critical revision.