

Review

Suitability of Banana and Plantain Fruits in Modulating Neurodegenerative Diseases: Implicating the In Vitro and In Vivo Evidence from Neuroactive Narratives of Constituent Biomolecules

Barnabas Oluwatomide Oyeyinka  and Anthony Jide Afolayan *

Medicinal Plants and Economic Development (MPED) Research Centre, Botany Department, University of Fort Hare, Alice 5700, South Africa; barnabastom@yahoo.com

* Correspondence: aafolayan@ufh.ac.za

Abstract: Active principles in plant-based foods, especially staple fruits, such as bananas and plantains, possess inter-related anti-inflammatory, anti-apoptotic, antioxidative, and neuromodulatory activities. Neurodegenerative diseases affect the functionality of the central and peripheral nervous system, with attendant cognitive deficits being hallmarks of these conditions. The dietary constitution of a wide range of bioactive compounds identified in this review further iterates the significance of the banana and plantain in compromising, halting, or preventing the pathological mechanisms of neurological disorders. The neuroprotective mechanisms of these biomolecules have been identified by using protein expression regulation and specific gene/pathway targeting, such as the nuclear and tumor necrosis factors, extracellular signal-regulated and mitogen-activated protein kinases, activator protein-1, and the glial fibrillary acidic protein. This review establishes the potential double-edged neuro-pharmacological fingerprints of banana and plantain fruits in their traditionally consumed pulp and less utilized peel component for human nutrition.

Keywords: anti-inflammation; biomechanism; biomolecules; fruits; *Musa* species; neurodegenerative diseases; neuroactivity



Citation: Oyeyinka, B.O.; Afolayan, A.J. Suitability of Banana and Plantain Fruits in Modulating Neurodegenerative Diseases: Implicating the In Vitro and In Vivo Evidence from Neuroactive Narratives of Constituent Biomolecules. *Foods* **2022**, *11*, 2263. <https://doi.org/10.3390/foods11152263>

Academic Editor: Amit K. Jaiswal

Received: 20 November 2021

Accepted: 14 December 2021

Published: 29 July 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Plant-based foods, such as fruits, contain natural active principles, ranging from primary metabolites (nutritive factors, vitamins, and minerals) to secondary metabolites (phytochemicals) [1]. These bioactive principles play significant roles in mitigating several chronic diseases [2–5]. Some epidemiological studies have identified antioxidant-rich secondary metabolites, such as flavonoids and anthocyanin, for their anti-inflammatory, antiproliferative, and ameliorative roles in neurological disorders [6,7]. Generally, natural polyphenols express their neuroprotective capacity by relying on their mechanism ability to cross the blood–brain barrier to scavenge the pathological concentrations of reactive oxygen and nitrogen species [8]. Equally, polyphenols modulate a series of mediating cell-signaling pathways of pathological diseases [9].

2. Overview and Prevalence of Neurodegenerative Diseases

Neurodegenerative diseases essentially relate to any pathological condition that primarily affects the neuron [10]. They affect the central nervous and are typified by the regression and progressive decline of neurological functioning and cognitive deficit [11], which results in major conditions, such as Alzheimer's, Parkinson's, and dementia [12,13]. This challenge is particularly devastating in aging populations, with Alzheimer's disease affecting about 40 million people globally [14,15]. Exposure to multiple factors (environmental and genetic) contributes to the onset of neurodegenerative diseases. Neurotoxic metal pollutants, such as mercury, lead, cadmium, and arsenic, have been identified with

Alzheimer's and Parkinson's disease, oxidative stress, neuronal death, mitochondrial dysfunction, modulation of metal homeostasis, and aggregation of α -synuclein proteins [16–18]. A schematic description of the aforementioned is depicted in Figure 1. It is even more concerning that these environmental factors can cause damage to the neurologic system via epigenetic mechanisms and then trigger neurodegenerative disease in later years [18,19]. Neurodegeneration consists of a series of pathways that have been closely linked to its inflammatory process and, in particular, the pro-inflammatory cytokines implicated in the pathogenesis of functional and neurologic impairment [20].

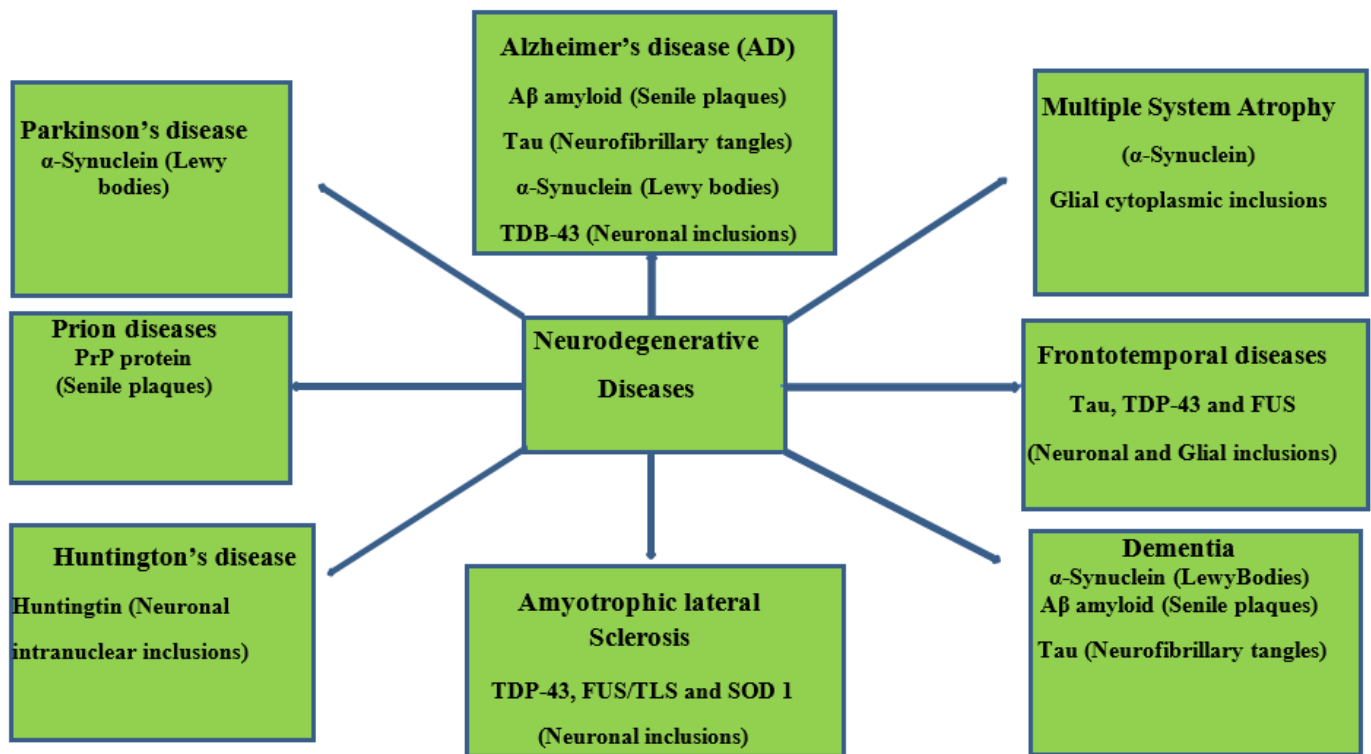


Figure 1. Schematic representation of neurodegenerative diseases, their pathology, and target proteins.

The burden of neurological disorders and conditions has necessitated reliable data to enhance effective health planning approaches. Epidemiological data for neuro conditions, particularly Parkinson's, dementia, and amyotrophic lateral sclerosis, have been reported in the last two decades [21–25]. Frontotemporal dementia is typically identified in middle age, with reports of about 13% occurrence in people below the age of 50 [26]. Furthermore, Ref. [26] a systematic analysis of a demographics-based study was carried out and estimated about 2–31 frontotemporal dementia incidences per 100,000 people in Europe and developed countries of Asia and North America [26]. An average occurrence of Multiple System Atrophy (MSA) (3 per 100,000 people), average onset age (54–61 years), and demographic prevalence in Europe and North America have been reported in various studies [27–29].

3. Fruits in Neurodegenerative Prevention/Management

The brain is especially a centrally significant organ of the nervous system which requires a healthy diet, with fruits potentially offering a wide range of rich nutrient supplies [30]. Fruits represent a major dietary component across Western and Asian demographics. They have been reported to have positive synergy with and relation to chronic disease management [31–34]. Examples of these common fruits include *Malus domestica*, *Persea americana*, *Musa sinensis*, *Citrus limon*, *Musa paradisiaca*, *Pyrus communis*, *Citrus sinensis*, *Fragaria ananassa*, and *Ananas comosus* (Figure 2).

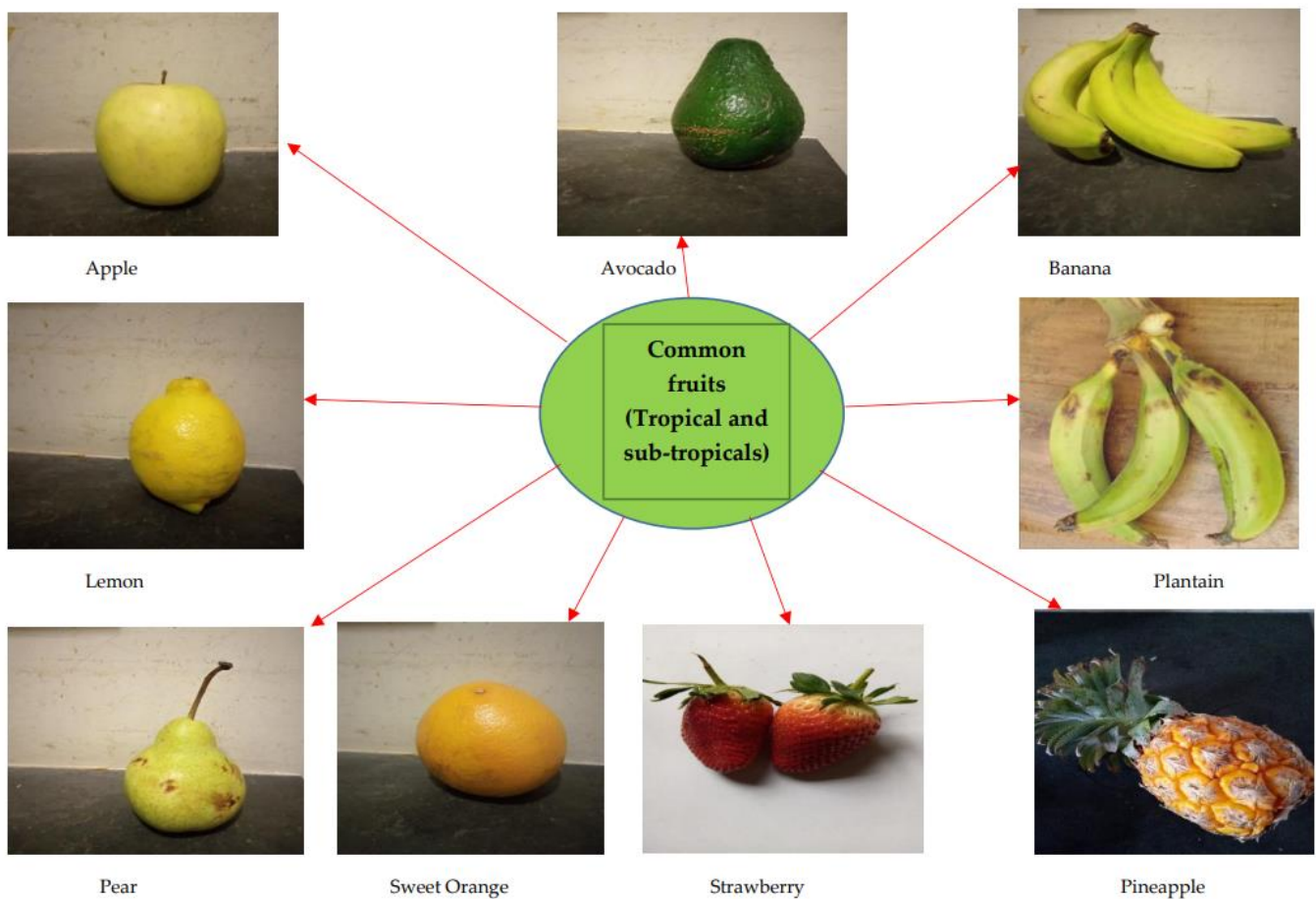


Figure 2. Commonly consumed fruits with bioactive capacities; including Banana and Plantain.

Date palm fruits (*Phoenix dactylifera*) have been reported in studies for their potential biological capacity in nephroprotective, hepatoprotective, and anticancer activity [35–37]. Recently, the inhibitory effect of avocado juice against trypsin aggregation has been reported: a formation process associated with several neurological diseases [38]. Similarly, other reports identified the beneficial role of berries (blackberry and blueberry) with regards to the obstruction of the central nervous system and cognitive deficit [39,40]. The cactus pear (*Opuntia ficus-indica*) fruit has also been reported to have the biological capacity to modulate neuron excitation in a distributive manner across sectors of the brain [41].

Over time, a host of bioactive molecules cutting across nutritive and antinutritive factors, vitamins, minerals, and secondary metabolites have been screened, evaluated, and elucidated in several species and varieties of banana and plantain fruits, as shown in Table 2.

Table 1. Compendium of active molecules in banana and plantain fruits.

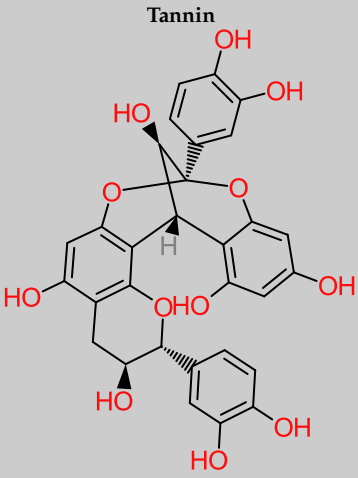
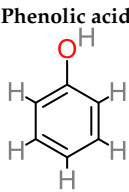
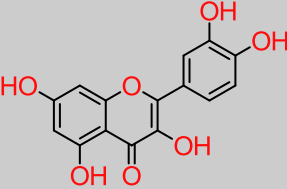
Active Molecules (Nutritive Factors and Secondary Metabolites)	Active Molecule Constituents in Banana and Plantain Fruit Components (Pulp and Peel)	Neuromechanism-Related Protein/Gene Targets
<p>Tannin</p> 	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> peel (unripe) (5.39 ± 0.02 mg/g) [42]; - <i>M. paradisiaca</i> peel (ripe) (4.24 ± 0.01 mg/g) [42]; - <i>M. paradisiaca</i> peel (over-ripe) (2.84 ± 0.03 mg/g) [42]; - <i>M. paradisiaca</i> fruit ($2.30 \pm 0.215\%$) [43]; - <i>M. paradisiaca</i> peel extract (aqueous) (14.69 ± 0.34 mg/g) [44]; - <i>M. paradisiaca</i> peel extract (80% ethanol) (17.66 ± 0.34 mg/g) [44]; - <i>M. paradisiaca</i> peel extract (80% methanol); (24.21 ± 0.17 mg/g) [44]; - <i>M. paradisiaca</i> peel extract (80% acetone) (15.90 ± 0.28 mg/g) [44]; - <i>M. paradisiaca</i> peel flour (30.98 ± 1.01 mgGAE/g) [45]; - Cavendish banana peel (5.60 ± 0.02 mg/g) [46]; - Red banana peel (5.75 ± 0.03 mg/g) [46]; - White banana peel (5.00 ± 0.37 mg/g) [46]; - <i>M. paradisiaca</i> raw pulp (7.05 ± 1.00 μgCE/mg) [47]. 	<ul style="list-style-type: none"> - GFAP [48]; - PGC-1α/Nrf-2/Ho-1 [49].
<p>Phenolic acid</p> 	<ul style="list-style-type: none"> - Banana pulp (76.3 mgGAE/g) [50]; - <i>M. acuminata</i> pulp (methanol extract) (778 mgQE/g) [51]; - <i>M. acuminata</i> peel (methanol extract) (1168 mgQE/g) [51]; - <i>M. acuminata</i> pulp (ethanol extract) (950 mgQE/g) [51]; - <i>M. acuminata</i> peel (ethanol extract) (897 mgQE/g) [51]; - <i>M. paradisiaca</i> pulp (methanol extract) (936 mgQE/g) [51]; - <i>M. paradisiaca</i> peel (methanol extract) (1346 mgQE/g) [51]; - <i>M. paradisiaca</i> pulp (ethanol extract) (950 mgQE/g) [51]; - <i>M. paradisiaca</i> peel (ethanol extract) (952 mgQE/g) [51]; - Banana pulp extracts (150.13 to 386.22 mgGAE/100 g) [52]; - <i>M. paradisiaca</i> pulp extract (166.90 ± 0.96 to 341.00 ± 34.6 mgGAE/g) [53]; - <i>M. acuminata</i> (75.01 to 685.57 mgGAE/g) [54]; - <i>M. sinensis</i> pulp (43.83 ± 1.13 to 119.05 ± 5.80 mgGAE/g) [55]; - <i>M. sinensis</i> peel (47.68 ± 2.14 to 157.19 ± 4.76 mgGAE/g) [55]; - <i>M. paradisiaca</i> pulp (17.41 ± 0.17 to 114.80 ± 1.49 mgGAE/g) [55]; - <i>M. paradisiaca</i> peel (75.14 ± 0.55 to 136.87 ± 5.69 mgGAE/g) [55]; - <i>M. acuminata</i> pulp (42.85 ± 0.80 to 523.60 ± 9.05 mgGAE/100 g) [56]; - <i>M. acuminata</i> peel (150.48 ± 16.17 to 199.61 ± 14.68 mgGAE/100 g) [56]. 	
<p>Quercetin</p> 	<ul style="list-style-type: none"> - Banana fruit (292 μg/100 g) [57]. 	<ul style="list-style-type: none"> - BDNF-TrkB-PI3K/Akt [58] - Bax/Bcl2 and caspase-3 [59].

Table 1. Cont.

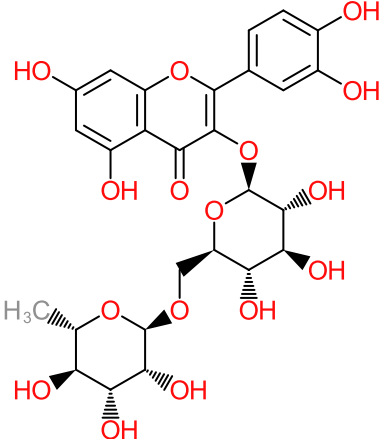
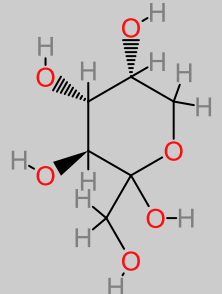
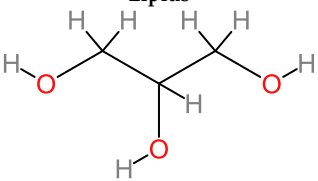
Active Molecules (Nutritive Factors and Secondary Metabolites)	Active Molecule Constituents in Banana and Plantain Fruit Components (Pulp and Peel)	Neuromechanism-Related Protein/Gene Targets
<p>Rutin</p> 	<ul style="list-style-type: none"> - Dessert banana (Gros Michel var.) (494.43 ± 153.71 µg/g) [60]. 	<ul style="list-style-type: none"> - Aβ, interleukin IL-1 [61,62]; - TNF-α and IL-1β [63]; - Poly ADP-ribosyl; - Polymerase and glutathione; - Reductase and glutathione; - Peroxidase [63]; - Caspase-3 and Prion protein peptide (Prp) [64]; - Interleukin-8; - Cyclooxygenase-2, NF-kB and GFAP [65,66]. - p38 MAPK [67].
<p>Carbohydrates</p> 	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> pulp (18.8 to 78.5 g/100 g) [68]; - <i>M. paradisiaca</i> peel (68.0 ± 0.3 g/100 g) [69]; - <i>Musa</i> spp. (16.72 to 35.24 g/100 g) [70]; - Banana fruit (21.70 to 41.33 g/100 g) [71]. 	<ul style="list-style-type: none"> - p-JNK and p-ERK [72]; - TrKA receptor and ERK1/2; - MPTP [73].
<p>Lipids</p> 	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> (0.9 ± 0.1 g/100 g) [69]; - <i>M. paradisiaca</i> (0.33 ± 0.34 g/100 g) [74]. 	
<p>Magnesium Mg</p>	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> peel (27.0 ± 0.08 to 76.0 ± 0.55 mg/g) [42]; - <i>M. paradisiaca</i> peel flour (14.5 ± 0.0 mg/100 g) [69]; - Banana peel (62.5 ± 0.01 mg/100 g) [75]; - Plantain peel (64.12 ± 0.04 mg/100 g) [75]; - <i>M. paradisiaca</i> pulp (29.00 ± 34.30 mg/kg) [76]; - <i>M. paradisiaca</i> peel (34.50 ± 34.80 mg/kg) [76]; - <i>M. paradisiaca</i> peel (324.50 ± 0.15 to 394.93 ± 0.11 mg/100 g) [77]. 	<ul style="list-style-type: none"> - N-methyl-D-aspartate [78].
<p>Zinc Zn</p>	<ul style="list-style-type: none"> - Plantain (<i>Musa</i> ABB) and cooking banana (<i>Musa</i> AAB); (0.2 ± 0.0 to 0.4 ± 0.0 mg/100 g) [79]; - <i>M. paradisiaca</i> pulp (1.00 to 13.35 mg/kg) [76]; - <i>M. paradisiaca</i> peel (3.10 to 3.70 mg/kg) [76]; - <i>M. paradisiaca</i> peel (26.96 ± 0.02 to 39.02 ± 0.01 mg/100 g) [77]. 	<ul style="list-style-type: none"> - Caspase [80]; - Maltose binding protein (MBP) [81].
<p>Copper Cu</p>	<ul style="list-style-type: none"> - Banana peel (2.55 ± 0.01 mg/100 g) [75]; - Plantain peel (5.82 ± 0.03 mg/100 g) [75]; - <i>M. paradisiaca</i> peel (3.29 ± 0.00 to 3.42 ± 0.01 mg/100 g) [77]. 	

Table 1. Cont.

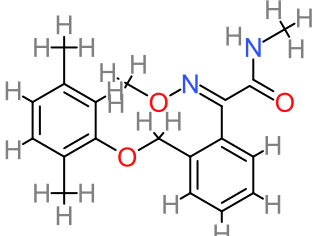
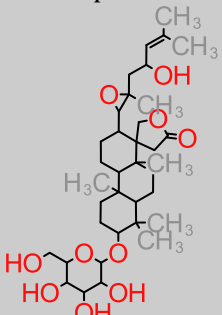
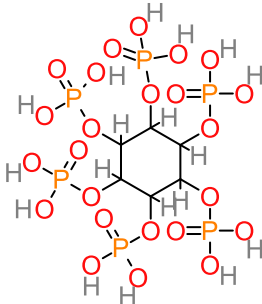
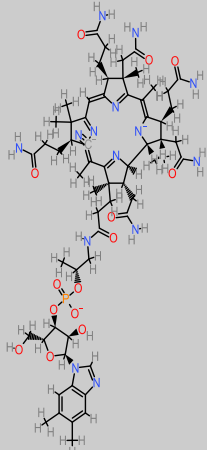
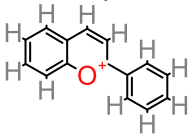
Active Molecules (Nutritive Factors and Secondary Metabolites)	Active Molecule Constituents in Banana and Plantain Fruit Components (Pulp and Peel)	Neuromechanism-Related Protein/Gene Targets
<p style="text-align: center;">Alkaloid</p> 	<ul style="list-style-type: none"> - <i>M. sapientum</i> fruit (0.251 ± 0.003 to $0.778 \pm 0.006\%$) [43]; - <i>M. paradisiaca</i> fruit (0.187 ± 0.001 to $1.027 \pm 0.003\%$) [43]; - <i>M. acuminata</i> fruit (0.083 ± 0.001 to $0.860 \pm 0.005\%$) [43]. 	<ul style="list-style-type: none"> - Aβ peptide [82]; - BDNF, MAP2, and GAP43; - PSD-95 and KLK 8 [83,84]
<p style="text-align: center;">Saponin</p> 	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> peel ($1.16 \pm 0.82\% \cong (1160 \text{ mg}/100 \text{ g})$) [85]; - Banana fruit ($11.6 \text{ mg}/100 \text{ g}$) [71]; - <i>M. sapientum</i> fruit (0.145 ± 0.005 to $2.268 \pm 0.003\%$) [43]; - <i>M. paradisiaca</i> fruit (0.773 ± 0.003 to $0.973 \pm 0.033\%$) [43]; - <i>M. sapientum</i> peel ($29.25 \pm 0.11 \text{ mg}/100 \text{ g}$) [86]. 	<ul style="list-style-type: none"> - p53 and p-p38 [87].
<p style="text-align: center;">Phytate (Phytic acid)</p> 	<ul style="list-style-type: none"> - <i>Musa</i> spp. (11.96 ± 1.05 to $24.15 \pm 0.95 \text{ mg}/100 \text{ g}$) [88]; - <i>M. paradisiaca</i> peel (9.064 ± 0.04 to $11.12 \pm 0.05 \text{ mg}/\text{g}$) [42]. 	<ul style="list-style-type: none"> - Aβ peptide [89].
<p style="text-align: center;">Vitamins B</p> 	<ul style="list-style-type: none"> - <i>Musa</i> ABB (0.002 to $0.032 \text{ mg}/100 \text{ g}$) [88]; - <i>M. sapientum</i> pulp (0.06 ± 0.002 to $0.08 \pm 0.001 \text{ mg}/100 \text{ g}$) [43]; - <i>M. paradisiaca</i> pulp (0.07 ± 0.000 to $0.08 \pm 0.001 \text{ mg}/100 \text{ g}$) [43]; - <i>M. acuminata</i> pulp (0.07 ± 0.001 to $0.08 \pm 0.002 \text{ mg}/100 \text{ g}$) [43]; - <i>M. sapientum</i> (0.29 ± 0.008 to $0.32 \pm 0.008 \text{ mg}/100 \text{ g}$) [43]; - <i>M. paradisiaca</i> (0.24 ± 0.008 to $0.28 \pm 0.118 \text{ mg}/100 \text{ g}$) [43]; - <i>M. acuminata</i> (0.30 ± 0.008 to $0.35 \pm 0.012 \text{ mg}/100 \text{ g}$) [43]; - <i>M. paradisiaca</i> fruit ($0.39 \pm 0.02 \text{ mg}/100 \text{ g}$) [90]. 	
<p style="text-align: center;">Anthocyanin</p> 	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> peel (aqueous extract) [91]. 	<ul style="list-style-type: none"> - ASK1-JNK/p38 [92]; - Interleukin-1β and TNF-α [93,94].

Table 1. Cont.

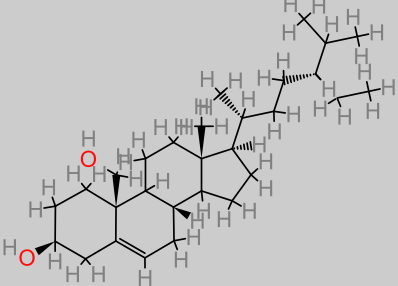
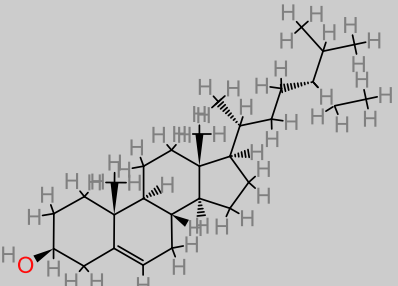
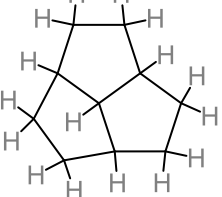
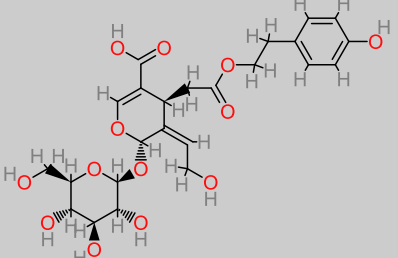
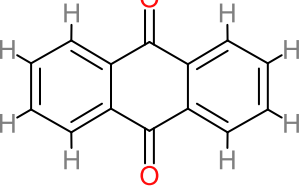
Active Molecules (Nutritive Factors and Secondary Metabolites)	Active Molecule Constituents in Banana and Plantain Fruit Components (Pulp and Peel)	Neuromechanism-Related Protein/Gene Targets
<p>Vitamin E (Tocopherol)</p> 	<ul style="list-style-type: none"> - <i>M. sapientum</i> pulp ($17.53 \pm 1.18 \mu\text{g/g}$) [95]; - <i>M. paradisiaca</i> pulp ($20.20 \pm 1.99 \mu\text{g/g}$) [95]. 	<ul style="list-style-type: none"> - ERβ-PI3K/Akt [96].
<p>Selenium SeH₄</p>	<ul style="list-style-type: none"> - Bananas ($0.024 \pm 0.0019 \mu\text{g/g}$) [97]; - Banana fruit ($< 0.001 \mu\text{g/g}$) [98]; - Bananas ($160 \pm 1.33 \mu\text{g/kg}$) [99]; - Bananas ($2.3 \pm 0.20 \mu\text{g/g}$) [100]. 	<ul style="list-style-type: none"> - Aβ peptide [101]; - N-acetylcysteine [102].
<p>Phytosterol</p> 	<ul style="list-style-type: none"> - Bananas ($7.8 \pm 6.9 \text{ mg/d}$) [103]. 	<ul style="list-style-type: none"> - Acetylcholinesterase [104]; - β-secretase [105].
<p>Terpenoids</p> 	<ul style="list-style-type: none"> - <i>M. acuminata</i> peel (0.21 ± 0.00 to $0.28 \pm 0.01 \text{ mg/g}$) [46]; - <i>M. paradisiaca</i> peel (1.83 ± 0.19 to $1.88 \pm 0.24 \text{ g/100 g}$) [106]. 	<ul style="list-style-type: none"> - Glutamate decarboxylase [107].
<p>Glycosides</p> 	<ul style="list-style-type: none"> - <i>M. sapientum</i> (0.261 ± 0.001 to $0.769 \pm 0.002 \text{ mg/100 g}$) [43]; - <i>M. paradisiaca</i> (0.35 ± 0.001 to $0.602 \pm 0.004 \text{ mg/100 g}$) [43]; - <i>M. acuminata</i> (0.498 ± 0.003 to $0.811 \pm 0.004 \text{ mg/100 g}$) [43]. 	<ul style="list-style-type: none"> - NF-kB and STAT 3 gene [108].
<p>Anthraquinone</p> 	<ul style="list-style-type: none"> - <i>M. paradisiaca</i> peel (aqueous extract) [91]. 	<ul style="list-style-type: none"> - NF-kB and TGF-β1 [109]; - ERK/MMP-9 and NOX2 (gp91phox) [110].

Table 1. Cont.

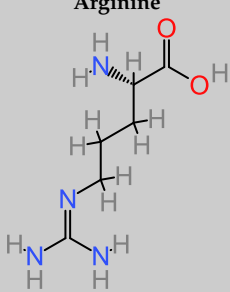
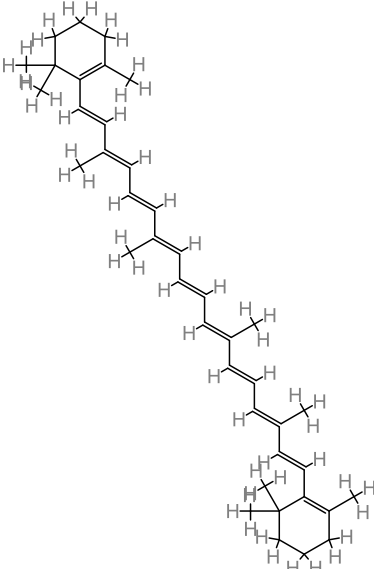
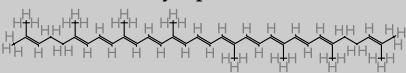
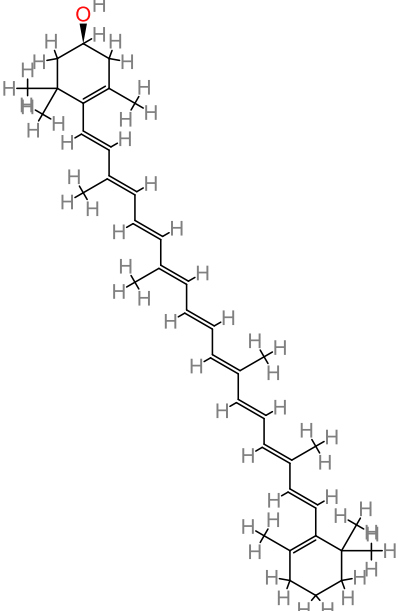
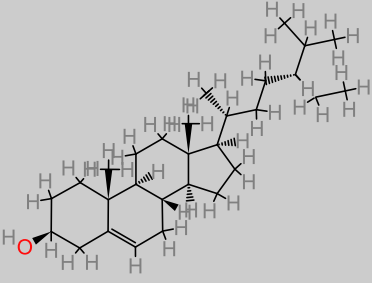
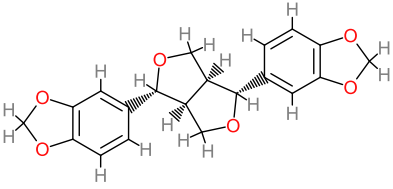
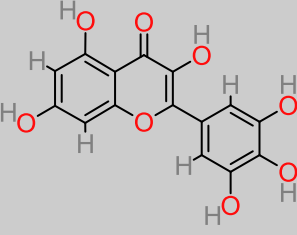
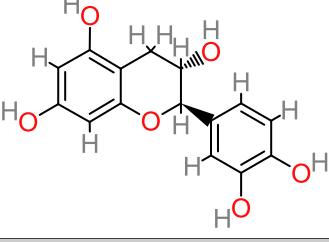
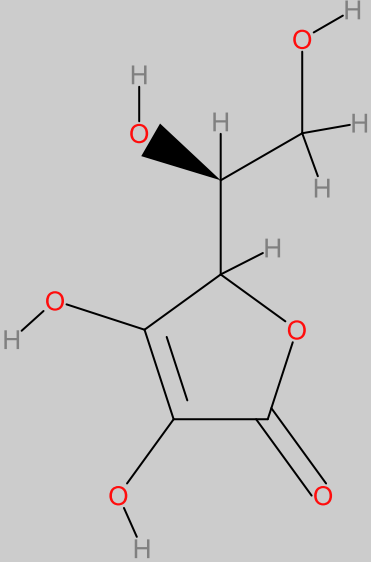
Active Molecules (Nutritive Factors and Secondary Metabolites)	Active Molecule Constituents in Banana and Plantain Fruit Components (Pulp and Peel)	Neuromechanism-Related Protein/Gene Targets
<p style="text-align: center;">Arginine</p>  <p>The chemical structure of Arginine shows a guanidino group (three nitrogen atoms in a triangular arrangement) attached to a side chain that includes a secondary amine and a terminal primary amine, all connected to a central carbon atom that is also bonded to a carboxylate group.</p>	<ul style="list-style-type: none"> - Sweet banana fruit pulp (57.0 mg/100 g) [111]. 	<ul style="list-style-type: none"> - HIF-1α/LDHA [112].
<p style="text-align: center;">β-carotene</p>  <p>The chemical structure of β-carotene is a long, linear polyene chain consisting of alternating single and double bonds, terminated at both ends by a cyclic end group containing a ring with a methyl group and a double bond.</p>	<ul style="list-style-type: none"> - Banana fruit (68.0 μg/100 g) [111]. - Plantain fruit (390–1035 μg/100 g) [111]. 	<ul style="list-style-type: none"> - Nrf2/Keap 1 [81].
<p style="text-align: center;">Lycopene</p>  <p>The chemical structure of Lycopene is a long, linear polyene chain with 11 conjugated double bonds and two non-conjugated double bonds, terminated by two methyl groups.</p>	<ul style="list-style-type: none"> - <i>M. sapientum</i> pulp (0.80 \pm 0.01 μg/g) [95]; - <i>M. paradisiaca</i> pulp (0.91 \pm 0.00 μg/g) [95]. 	<ul style="list-style-type: none"> - NF-kB [113]; - Tau protein and GSH-Px [114].
<p style="text-align: center;">β-cryptoxanthin</p>  <p>The chemical structure of β-cryptoxanthin is a long, linear polyene chain with 11 conjugated double bonds and two non-conjugated double bonds, terminated by a cyclic end group containing a ring with a methyl group and a hydroxyl group.</p>	<ul style="list-style-type: none"> - Banana (<i>Musa</i> sp.) peel (0.08 \pm 1.28 μg/g) [115]. 	

Table 1. Cont.

Active Molecules (Nutritive Factors and Secondary Metabolites)	Active Molecule Constituents in Banana and Plantain Fruit Components (Pulp and Peel)	Neuromechanism-Related Protein/Gene Targets
<p>β-sitosterol</p> 	<ul style="list-style-type: none"> - Bananas (7.8 ± 6.9 mg/d) [103]; - Banana (<i>Musa</i> sp.) peel extract (269–601 mg/kg) [116]. 	<ul style="list-style-type: none"> - $A\beta$, β-secretase, and γ-secretase [117,118].
<p>Sesamin</p> 	<ul style="list-style-type: none"> - <i>M. sapientum</i>/<i>M. acuminata</i> peel extracts (methanol) [119]. 	<ul style="list-style-type: none"> - MAPK and COX-2 [120]; - MMP-9 [121]; - ERK1/2 and SIRT1 [122].
<p>Myricetin</p> 	<ul style="list-style-type: none"> - Dessert banana peel (Grand Nain cultivar); (125.32 ± 17.18 to 172.28 ± 12.38 $\mu\text{g/g}$) [60]. - <i>Musa</i> sp. (banana fruit) (143 $\mu\text{g}/100$ g) [123]. 	<ul style="list-style-type: none"> - BDNF–Akt/GSK-3β/MTOR and P13K/Akt/MTORC1 [124].
<p>Catechin</p> 	<ul style="list-style-type: none"> - <i>M. Cavendish</i> peel ($1.34 \pm 0.27\%$ of 29.2 mgGAE/g); - Phenolic compounds [125]. 	
<p>Vitamin C (ascorbic)</p> 	<ul style="list-style-type: none"> - Dessert banana (<i>Musa</i> sp.) fruit pulp (4.5 to 12.7 mg/100 g) [126]. 	

4. Neuroprotective Mechanistic Narratives of Active Principles and Mineral Elements Listed in Banana and Plantain fruits

4.1. Tannins

Natural or dietary tannins are nutraceutical factors that have been reported in cognitive impairment amelioration [127,128]. Furthermore, dose-dependent cell-line neuroprotective activity has been reported in natural gallotannins and ellagitannins against H₂O₂-based oxidative damage, using the hybridoma cell line NG108–15 [129]. Similarly, gallotannin derivatives increased the cell viability of the hybrid neuroblastoma–glioma. Ellagitannin derivatives of *Phyllagathis rotundifolia* were identified for neuroprotective capacity by dose-dependent neuronal cell protection at concentration levels between 6.25 and 100 µM [129].

In other in vivo model studies, the neuromodulatory mechanisms of tannic acid supplementation were reported against brain injury [49,130]. This observation is a potential neurotherapeutic management avenue, with regards to issues such as neuron dysfunction and behavior alteration. Notably, tannic acid supplementation deploys the PGC-1α/Nrf-2/Ho-1 molecular activation mechanism that modulates neurological maladies and factors such as brain edema, pro-inflammatory cytokine expression, and the glial fibrillary protein immunoreactivity [49]. The neuroprotective activity of tannic acid has been elucidated in a study identifying its anti-inflammatory tendencies, with regards to the occlusion of the mid-cerebral artery in vivo [48]. The same study equally indicated tannic acid suppression of neuronal loss and downregulation of GFAP expression, leading to the protection against brain damage [48]. In vitro and in vivo studies have identified condensed tannin (proanthocyanidin) for its mechanisms of action, such as neuron loss attenuation and exhibition of anti-CHE activity, which offer neuroprotective roles against Parkinson's and Alzheimer's diseases, respectively [131,132].

4.2. Phenolic Acid

Phenol acid is a major polyphenolic member found in fruits and grains. A study has recently pointed out that a phenol-rich diet lowers the dispositional risk of depression [133].

4.3. Quercetin

Quercetin is another compound of flavonoid polyphenolic extraction, with fruits, vegetables, and herbs being the chief bio-stores. In vivo experiments have identified the role of quercetin in nerve regeneration and apoptotic index reduction, including axonal structure healing [134]. Another study has reported the neuroprotective properties of quercetin supplementation through the inhibition of aluminum-induced oxidative damage by halting aluminum buildup in the hippocampus and striatum sectors of the brain [135]. Furthermore, quercetin significantly improved muscle coordination and cognition in vivo [135]. Quercetin has a potential capacity to inhibit mitochondrial dysfunction/oxidative stress induced by oxaliplatin. Moreover, 10 and 20 mg/kg quercetin concentrations inhibited focal cerebral ischemic cell apoptosis by mechanistically activating the BDNF-TrkB-PI3K/Akt signal pathway [58,136]. Equally reported is the fact that quercetin shrunk the volume of infarct in the damaged contralateral hemispheric region of the brain in an in vivo model, from an initial $36.2 \pm 4.8\%$ to $24.8 \pm 2.7\%$ and $21.7 \pm 3.2\%$ upon 10 and 20 mg/kg daily treatments, respectively [58].

In a recent study, the modulatory effect of quercetin (30 mg/kg dosage) against lipopolysaccharide (neuroinflammatory trigger factor) was reported [137]. This was expressed by rescuing neuronal degeneration; mitochondrial apoptotic mechanisms, such as Bax/Bcl2, PARP-1 cleavage; and the stemming of caspase-3 activity in the cortico-hippocampal locations of the brain.

4.4. Rutin

Rutin is a typical flavonoid compound with abundance in plants. Studies have demonstrated a wide spectrum of rutin activities, such as antioxidant, cytoprotective, and neuroprotective capacities [63,138–141]. Another study identified rutin suppression of

proinflammatory cytokine activity through the mechanistic shrinkage of microglia-situated production of TNF- α and IL-1 β [62]. The ameliorator role of rutin against neurodegeneration was reported in neuroblastoma cell-based and in vivo models, where neurodetrimental factors such as apoptosis, episodic deficit in memory, and reactive oxygen species were attenuated [142]. Research findings have indicated that rutin pretreatment at 25 mg/kg daily dosage significantly ameliorated neuroinflammatory mechanisms by depleting the expressive activities of poly ADP-ribosyl polymerase, glutathione reductase, and glutathione peroxidase in the hippocampus [63].

In the same vein, recently, the neuroprotective capacity of rutin, expressed in its anti-inflammatory activity, has also been evaluated [67]. In this in vivo study, 30 mg/kg rutin was reported to have inhibited the p38 MAPK pathway that influences inflammation, thereby ameliorating injury to the spine. The PRP (106–126) model system was used to evaluate neurotoxicity in the hippocampus cell line (HT22), with the rutin treatment (5–50 $\mu\text{g}/\text{mL}$) identified in blocking the generation of reactive oxygen species and caspase-3 activity, a hallmark of the toxic effects of the PRP (106–126) [64].

Furthermore, the modulatory action of rutin treatment (40 to 80 mg/kg) over nitric oxide has been implicated as a possible link to its neuroprotective mechanisms, particularly in head-trauma-related cognitive dysfunction [143].

In vitro and in vivo neuroprotective evidential narratives show that rutin (100 mg/kg dosage) depleted the levels of neurotoxic A β oligomer and interleukin levels in the brain of Alzheimer-model mice [65]. More in vitro reports have put forward the putative roles of rutin in depleting the formation and accumulation of A β 25–35 fibril and modulating the aggregation of A β , TNF- α , and interleukin-1 [61,62].

4.5. Carbohydrates

These are major nutritive factors that are obtainable in fruit, vegetable, grain, and cereal diets. An in vitro cell line study has identified the protective mechanism of oligosaccharides (50 μM) in the cells of neuroblastoma [73]. These oligosaccharide-treated cells were identified with proteins involved in neuroprotective biochemical mechanisms (TrKA receptor interaction and ERK1/2 pathway activation), as well as the inhibition of the MPTP expression that stimulates Parkinson's disease [73]. Natural polysaccharides from *Lycium barbarum* fruits have also been reported to suppress p-JNK and p-ERK (a biomechanism that translates into neuromodulatory effects against neuron cell death upon hourly polysaccharide treatment at dosage 100–500 $\mu\text{g}/\text{mL}$) [72].

4.6. Lipids

Dietary lipids (fatty acids) are nutritive factors and are regulatory biomolecules for intracellular signaling, homeostasis, and functionality of the central nervous system [144].

In an in vitro neuronal stem cell study, it was also reported that the potential anti-stroke therapeutic option is the Omega-3 fatty acid (docosahexaenoic acid (DHA) [145]. The dietary fatty acid has been implicated in the preventive or attenuative roles in neuro disorder and degeneration [145]. Fatty acid (10^{-9} to 10^{-8} M) in this study significantly improved regenerative neurogenesis, partly due to its antioxidant properties. Even more pointedly, correlations have been drawn between increased fatty acid levels and improvement in brain structure markers, language, and proper cognitive levels [144,146]. Further in vitro evidence indicates the role of lipids in the increment of hippocampal neurite length at 1.5 μM supplemental dosage [146].

4.7. Magnesium

Magnesium is a nutritive mineral component of diets that has a wide range of significance to health. It is a key driver of nerve transmission in the nervous system and also inhibits hyper-excitatory-induced cell death and epileptogenesis [147,148]. Neuromechanistically, magnesium interacts with the N-methyl-D-aspartate receptor [78]. Furthermore, a couple of studies have implicated magnesium pretreatment in neuron protection [149,150].

4.8. Zinc

Zinc is an important mineral element that plays a significant role in nutrition and health, including regular brain function. An in vitro study has identified neurological mechanisms of zinc, such as MBP protein upregulation, cognitive impairment amelioration, and modulatory effect on the regenerative sprouting of the mossy fiber of the hippocampus [81]. Consequently, zinc supplementation (246 mg/kg) presents a therapeutic mechanism in compensating and repair of the damage to neuron membrane in developmental seizures [81]. Zinc deficiency has been examined and identified with impairment of the proliferation of neuron precursors, caspase, and apoptotic inducement [80,151].

4.9. Copper

Copper is a trace element of nutritive value and is an enzymatic structural component. It is involved in physiological processes, such as metabolic regulation and hormonal biosynthesis [152]. Deficiency in copper levels induces the depletion of several enzyme activities, with precursory implications in the Menkes neurological disorder [112]. For instance, dopamine- β -hydroxylase (DBH) enzyme is dependent on copper for its neurotransmission role in translating dopamine to norepinephrine [112]. Abnormal neurochemical trends in Menkes disease result when the copper-dependent DBH enzyme activity is altered [153,154]. In vitro copper-related therapeutic experimental propositions have been reported through the CuSO₄ pretreatment (10 μ mol/kg) modulation of Parkinson's-related protein nitration and depletion of dopamine [155].

4.10. Alkaloid

Alkaloids are non-nutritive phytochemical compounds with neuroactive potentials. Plant-derived alkaloid compounds (30-day 1 g/kg dosage) have been experimented with, in an in vivo model [156]. Resultantly, modulatory effects were observed against A β peptide accumulation and plaque buildup, as well as cognitive deficit reversal. In earlier work, p53-mediated alkaloid-based compounds have been reported for activity in vivo against neurotoxicity at 200 mg/kg [83]. Alkaloid-based compounds have the molecular capacity to upregulate the activation of synaptic plasticity genes, such as BDNF, MAP2, GAP43, PSD-95, and KLK8 [83,84]. Similarly, plant-based alkaloids from sources such as *Clausena lenis* and *Isatis indigota* have been reported for their in vitro neuroprotective activity against cell death in SH-SY5Y human neuroblastoma cells, at (0.68 to 18.76 μ M) and (25 to 100 μ M), respectively [157,158].

4.11. Saponin

Saponins are bioactive compounds found in plant-based foods. Preclinical studies have reportedly implicated saponins in neuromodulatory capacity and memory enhancement potential. The long-term effect of bacoside saponin (200 mg/kg) has been evaluated in vivo, with significant neuroprotection against aging-related cognitive decline [159]. Triterpenoid saponins of *Platycodi radix* have demonstrated inhibitory activity against neurotoxicity in cortical cells at 0.1 to 10 μ M [160]. The neuroprotective capacity of red-ginseng-derived saponins (50–150 mg/kg) has been demonstrated in terms of significantly lowering malondialdehyde levels, while increasing catalase, superoxide dismutase, and glutathione levels [81]. Saponin (2 mg/kg/d) from *Radix trichosanthis* exhibited neuroprotective activity, as evidenced by less damage to neuron cells, and inhibition of the expression of p53 and p38 in subarachnoid hemorrhage [87]. Furthermore, the saponin neuroactivity could be a result of the p38 and p53 signal pathway mediation [87]. Isolated saponin from *Astragalus glycyphylloides* showed the most significant neuroprotective capacity, at 60 μ g/mL, against oxidative stress in isolated brain synaptosomes [161].

4.12. Phytate

Phytic acid is a predominantly plant-based compound that tends to interact with the absorption or bioavailability of mineral nutrients. However, phytate possesses bioactive

properties that were identified in a study, with implicative roles in potentially intercepting the buildup of A β in the brain and neuroblastoma cells [162]. The inhibition of β -secretase 1 and γ -secretase enzymes offers a potential biomechanistic pathway or trajectory in the aversion of Alzheimer's disease. In an earlier finding, phytic acid was reported for inhibitory activity against amyloid- β -peptide pathogenesis in MC65 cell and in vivo model Tg2576 [89].

4.13. Vitamin B

Vitamin B is a water-soluble group of vitamins with subtypes [163]. They are essentially involved in red-blood-cell synthesis and metabolism and are sourced in foods such as fruits, vegetables, and grains. The B vitamins are co-factors of enzymes in a series of biochemical pathways [164].

Thiamine (vitamin B₁) is essential in glucose metabolism; nerve membrane functionality; and myelin synthesis, including neurotransmitters such as serotonin and acetylcholine [165].

Nicotinamide (Vitamin B₃), a precursor of NADH and NADPH coenzymes, has neuroprotective properties at low concentrations [166]. Similarly, a low dose of vitamin B₃ (10 mM) significantly induced embryonic-stem-cell differentiation into neurons [167]. In addition, another report has implicated nicotinamide (0.1/1.0 mM) in the increased survival rate of PC12 cells, using a simulated model of Parkinson's disease [168].

Pyridoxine (Vitamin B₆), at 600 mg/kg, improved locomotor behavioral performance and ameliorated a cortical injury model in vivo [169]. Pyridoxine has also been implicated in the regulation of GABA levels, an inhibitory neurotransmitter linked to excitatory epileptic seizures [170].

Cobalamin (Vitamin B₁₂) contributes to the protection of nerve fibers through myelin sheath synthesis [171]. In a recent study, vitamin B₁₂ was experimentally demonstrated to have modulatory neuroprotective and anti-inflammatory activities against pneumococcal meningitis and hippocampus damage [172]. In addition, hippocampus apoptosis, triggered by bacterial meningitis, was diminished by vitamin B₁₂ treatment (10 μ L intramuscular dosage) [172].

4.14. Vitamin C (Ascorbic Acid)

Vitamin C is a very prominent and essential water-soluble vitamin member that is a rich component of food, particularly citrus fruits, berries, and vegetables. Evidence exists on the neuroprotective potential of vitamin C through the mechanism of increased generation of DOPA upon neuroblastoma cell line incubation in ascorbic acid (dosage 100 mM to 500 mM) [173]. Furthermore, ascorbic acid has been identified as a potential early phase treatment of Parkinson's disease through the biomechanism of stimulating tyrosine gene expression at a specific dosage (200 μ M) [173]. It also inhibited beta-amyloid apoptosis in neuroblastoma cell SH-SY5Y at 50 μ M [174].

4.15. Vitamin E (Tocopherol)

These are fat-soluble compounds that are involved in key physiological frontiers, such as regulatory roles in gene expression and immune function. It has also been demonstrated that vitamin E exerted neuroprotective activity against MPP⁺-induced toxicity in SH-SY5Y cells and in vivo model of Parkinson's disease, by utilizing the signaling pathways ERB-PI3K/Akt therein [96]. In other Parkinson's studies, vitamin E (10⁻³ M) has been reported to block levodopa toxicity in neuroblastoma cell NB69, while in an in vivo BALB/c mice model, MPTP neurotoxicity was inhibited at 100 mg/kg ascorbic acid [175,176].

4.16. Selenium

Selenium is a trace mineral element that is usually required by the body in small quantities. It is a constituent of antioxidant-natured enzymes and selenoproteins. Selenium is found in plant foods, such as staples and cereals. The neuroprotective activity of selenium

(1.5 mg/kg), along with N-acetylcysteine (NAC) in brain trauma apoptosis and oxidative stress, in the hippocampus has been reported [162].

Furthermore, organo-selenium compounds had inhibitory activity against A β peptide-induced toxicity and equally enhanced the levels of the nerve terminal marker SNAP-25 [101]. More recently, the neuroprotective activity of selenium-rich polysaccharides from *Rosa laevigata* fruit has been demonstrated against oxidative stress in neuroblastoma cells, particularly at a concentration of 100 μ g/mL [157].

4.17. Phytosterol

Phytosterol has neuroactivity against cognitive deficits linked to high cholesterol levels. Phytosterol supplementation activity against neurological inflammation was evaluated in vivo [104]. Furthermore, phytosterol enhanced cholinergic function in the cerebral cortex through the restoration and depletion respectively [104]. Plant sterols have been hypothesized to possess the biomechanism of crossing the blood–brain barrier. They activate anti-inflammatory mechanisms that are involved in the buildup of amyloid- β clearance and depletion of β -secretase activity [105]. In another recent study, phytosterols were implicated neuroactive-wise in reducing A β plaque formation, as well as memory deficit amelioration [177].

4.18. Terpenoid

This is a large group of organic compounds (secondary metabolites) that are widely found in plants and have aromatic properties. Monoterpene (thymol) was identified for neuroprotective activity in an in vivo Parkinson's disease model against dopamine-related neurodegeneration [178]. In the investigation, thymol, at a dose of 2.5 mg/kg for four weeks, attenuated neuronal loss and inflammation and was related to the preservation of antioxidant networks of defense. Fractions of *Hygrophila auriculata*-derived terpenoids (100 and 200 mg/kg) reflected neuroprotective activity in CA1 neurons of the hippocampus, hand in hand with antioxidative restoration [179]. Similarly, terpenoids have been marked for potential mechanisms, such as boosting the activity of glutamate decarboxylase enzyme, as well as GABA in the brain [107,180].

4.19. Glycosides

Glycoside has been reported in the neuroprotective frontier, as evidenced in the evaluation study against neuroinflammation and brain injury [103]. It biomechanically inhibited nuclear factor (NF- κ B) and STAT3 activation in an experimental model of stroke.

In another narrative, phytoglycoside treatment (250 mg/kg) was identified to play recovery roles in the level of neurotransmitter hormones in the brain and serum in vivo [181].

4.20. Anthraquinones

Anthraquinone is the largest member of the quinones. It is a secondary metabolite with medicinal value. They are therapeutically relevant in central nervous system conditions, tumor and brain injury, cerebral hemorrhage, ischemic stroke, and Alzheimer's disease [182]. Anthraquinones reduce and inhibit inflammation and apoptosis respectively [183,184]. In addition, they have been identified in therapeutic roles targeted at glutamate-related excitatory toxicity in brain trauma [185,186]. Other neuroprotective mechanisms have been identified in the same regard, such as inhibition of the ERK/MMP-9 pathway and amelioration of brain edema through the combined biomechanism of ERK/MMP-9 inhibition, as well as the arrest of the activation of the NADPH oxidase subunit, gp91phox [110]. Emodin anthraquinone (20 to 40 μ M) has also been identified for its neuroprotective attenuation of TGF- β 1 by inhibiting the NF- κ B pathway [187].

4.21. Anthocyanins

Anthocyanins are important phytochemicals found in fruits, flowers, and vegetables, to which they confer purple to red pigmentation. An in vivo model reported anthocyanin's

capacity to stem memory-breach condition at 200 mg/kg weekly dosage [188]. Equally, anthocyanin extracted from *Glycine max* was involved in the inactivation mechanism of ASK1-JNK/p38, thus modulating oxidative stress. Similarly, anthocyanin inhibited cytotoxicity in the SK-N-SH cell at a concentration level of 25 µg/mL [92]. Notably, studies evidenced that anthocyanin-rich fraction or extract treatment significantly stems the tide against interleukin-1 β , tumor necrosis factor (TNF- α), and nitric oxide buildup [93,94].

4.22. Arginine

Arginine proffers therapeutic potentials in trauma-related brain injury [189]. It is, for instance, a precursor to the important brain and muscle tissue energy source, creatinine [189]. There have been reports of highly effective neuroprotective activity at 300 mg/kg L-arginine dosage in post-traumatic brain injury [190,191]. Furthermore, the focal arginase inhibitor (NW-hydroxy-nor-arginine) is also implicated in the in vivo amelioration of post-traumatic brain injury contusion [192,193]. Polyarginine peptide complexes have also been identified to be stroke neuroprotective in both in vitro and in vivo investigations [194–196]. In ischemic cerebral injury, arginine suppressed the HIF-1 α /LDHA biomechanism that usually mediates inflammation in the microglia [112].

4.23. β -Carotene

This molecule is sourced from a wide range of fruits, such as bananas, mango, and apricots; and vegetables, such as spinach, pumpkin, and tomato. β -carotene treatment (10 to 50 mg/kg) improved cognitive output and neural functionality [81]. Further neuroprotective activity was reported in form of brain edema reduction in trauma. Then modulation of the Nrf2/Keap1 pathway was implicated in β -carotene's alleviation of oxidative stress [81].

4.24. Lycopene

Dietary lycopene is widely found in vegetables and fruits. Lycopene, in an Alzheimer's disease model, attenuated oxidative damage of the mitochondria and inhibited the activity of NF-kB, while equally regulating the proinflammatory cytokine expression [113,197]. This triggered suppression of A β buildup. Lycopene supplements have been reported in an in vivo Alzheimer's disease study to improve cognitive factors via the mechanisms of lowering malondialdehyde level, marked attenuation of tau hyperphosphorylation, and enhanced activity of glutathione peroxidase (GSH-Px) [114].

4.25. β -Cryptoxanthin

Human cell line studies have reported beta-cryptoxanthin neuroactivity against hydrogen peroxide-induced oxidative damage, consequently acting as an antioxidant [198].

4.26. β -Sitosterol

β -sitosterol, relative to the central nervous system, can cross the blood–brain barrier. Hippocampus cell-line studies have reported the role of β -sitosterol derived from *Rhinacanthus nasutus* in shielding cells from neurotoxicity and oxidative damage [199]. Furthermore, the prevention of neuron damage has also been identified in a couple of studies, including inhibitory roles against the release of A β , β -secretase, and γ -secretase [117,118]. Stem-cell multiplication in neurons has been credited to the extract form or, otherwise, of β -sitosterol, based on in vitro and in vivo investigations. A typical finding was, for instance, identified in seeds of *Alyssum homolocarpum* [200,201].

4.27. Sesamin

Neuroprotectively, sesamin attenuated excess buildup of detrimental nitric oxide in the primary cells of the microglia [202]. In addition, in vivo investigation revealed neuroprotective action of sesamin in a cerebral ischemic experimental model. Furthermore, consequently, sesamin treatment, along with sesamol, shrank the infarction region by up to 56% [202]. Sesamin pretreatment (50 µM) inhibited ROS generation intracellularly and

vastly lowered proapoptotic protein expression, cellular apoptosis, and MMP-9 overexpression in SH-SY5Y cells [121].

The ameliorative effects of sesamin extract (30 mg/kg) against epileptics’ oxidative stress via the biomechanistic inhibition of MAPK and COX-2 have been reported [120]. More recently, neurite growth of PC12 cells was reportedly promoted by sesamin (10 mM), at a rate of 61.65% to 82% [122]. In this process, sesamin modulated the ERK1/2 passage, as well as the protein SIRT1 [122].

4.28. Myricetin

Myricetin regulates the signaling pathway BDNF–Akt/GSK-3β/mTOR, thereby enabling the regeneration of the peripheral nerve in a simulated sciatic nerve injury [124]. Notably, the nerve-regeneration-signal-related factor PI3K/Akt/mTORC1 is upregulated by myricetin (25 to 100 mg/kg). Another experimental outcome indicated that the myricetin compound, at 300 mM, reduced beta-amyloid-related cellular injury in cortical neurons [203]. Furthermore, the anti-tau effect of myricetin (50 μM) in the HeLa-C₃ cells was elucidated [204].

4.29. Catechin

The anti-inflammatory and antioxidant properties contribute to the neuroprotective features of *Camellia sinensis* catechin extracts against the Parkinson’s disease model 6-OHDA [205]. Furthermore, the catechin extracts (10 mg/kg) have been reported to increase locomotor activity, reverse behavioral irregularity, and improve cognitive functionality improvement in the hippocampus [205].

Active principles and natural products can exhibit biomechanistic actions that contribute to several bioactivities related to the neuroprotective mechanism [206,207]. In this regard, Table 2 depicts some important active principles identified, along with their series of bioactive mechanisms.

Table 2. Other neuroprotective-related bioactivity mechanisms of key bioactive compounds.

Bioactive Compounds	Biological Mechanisms of Action Related to Neuroactivity	Bioactive Compounds	Biological Mechanisms of Action Related to Neuroactivity
TANNINS	- Condensed tannins and hydrolysable tannins Antioxidant (free-radical scavenging) (metal chelation) (pro-oxidative enzyme inhibition) (endogenous antioxidant system interaction) (inhibition of xanthine oxidase-induced Lipid peroxidation) [208,209].	ANTHOCYANIN	Delphinidin Cyanidin Anti-inflammatory, anti-Alzheimer, antitumor, and antioxidative properties by depleting the expression of cytokine markers [211].
	- Procyanidins Antioxidant enzyme gene expression in cells [210]. - Ellagitannins (geranin, corilagin, and furosin) Anti-inflammatory mechanisms, such as depletion of apoptotic cells [208].		

Table 2. Cont.

Bioactive Compounds	Biological Mechanisms of Action Related to Neuroactivity	Bioactive Compounds	Biological Mechanisms of Action Related to Neuroactivity
QUERCETIN	<ul style="list-style-type: none"> - Oxygen radical scavenging, metal chelation, and attenuation of nitric oxide synthase [212]. - Expressive mechanism of paraoxonase 2 for neuroprotection in neurons and brain cells [213–215]. - Anti-inflammatory mechanism via inflammatory gene repression (blocking) [216]. - Regulation of apoptosis and inhibition of cleaving enzyme (BACE 1) [217,218]. - Impairment of chemokines and cytokines [219]. <hr/> <ul style="list-style-type: none"> - Quercetin-3-O-diglucoside-7-O-glucoside Anti-inflammatory, antioxidant effects, and lipoxygenase inhibitory effects [220]. 	MYRICETIN	<p style="text-align: center;">Kaempferol</p> Antitumor, anti-inflammation, and antioxidant properties are exercised via an antiproliferative mechanism in cells, attenuation mechanism against inflammation, and tumor growth factors [124,221].
ALKALOIDS	<p style="text-align: center;">Vincristine</p> Antineuroblastoma property exerted via the mechanisms truncating the glutathione metabolism [222]. <p style="text-align: center;">Tetrandrine</p> Anti-inflammatory and antitumor activities are linked to the calcium-channel blocking mechanism [223]. <p style="text-align: center;">Skimmianine</p> Anti-inflammatory property via the inhibition of nitric oxide production [224].	CATECHIN	<ul style="list-style-type: none"> - Anti-inflammation and antioxidative stress mechanism via modulation of tyrosine kinase receptor [225]. - Modulation of signal transduction pathways to protect cell proliferation, inflammation, and metastasis [226].
TERPENOIDS Paeoniflorin, Triptolidenol, Tripterine, Triptonide, Gindenoside, Oleanoic Acid	Anti-inflammatory activity via interleukin-6 inhibition [227]. Anti-nociceptive, antioxidant and anti-inflammatory properties [228].	RUTIN	<ul style="list-style-type: none"> - Anti-apoptotic mechanism against cell death [112]. - Depletion of pro-inflammatory cytokine expression [229].
LIPID Omega-3 DHA	Anti-inflammatory properties, Cell survival promoters [230].	Neuroprotectin D1 Lipid	Inhibition of apoptosis-related damage to DNA [230].

5. Concluding Remarks

The advent of ultra-cutting edge spectroscopy in the form of the HPLC, NMR, HNMR, and FTIR will continue to remain at the heart of bioactive natural product testing. The optimization of measurability methods for natural product bioactivity, such as the *in silico*, *in vitro*, and *in vivo* models, as well as the cell-based and cell-line assays, will be key in driving the replicability of data neuroprotective-related research frontiers.

Furthermore, the *in silico* computational model will help to potentially generate the biomechanistic and chemical information of natural products. In addition, the *in silico* and *in vitro* to *in vivo* frontiers offer more possibilities in bioactivity response simulation.

Substantial *in vitro*, *in vivo*, and *ex vivo* evidence has been drawn about the capacity of naturally sourced bioactive principles (nutritive factors and secondary metabolites) to hijack or, even better, prevent the degenerative mechanisms that result in the widely known neurological diseases. Key neurologically relevant biochemical mechanisms, such as protein expression, up/downregulation, and gene targeting, provide insight into the modulatory fingerprints of these active molecules against neuropathogenesis.

In this review, several active molecules of banana and plantain fruits were identified in the peel compartment, thus offering the peel as a complementary functional food option alongside the traditionally and commonly eaten fruit pulp. Furthermore, the natural

synergistic combinations among various molecules in fruits offer a bioactivity-initiation tendency. These fiber-rich peels, upon boiling, have potential dietary incorporation similar to a “vegetable”, as well as in combination with cooked vegetable, tomato, and pepper diets.

With several yet-to-be neuroprotectively implicated bioactive compounds, such as manool, palustrol, piperitenone, β -phellandrene, and cyclododecane, still in the offing, banana and plantain fruits, being biological stores of these molecules, consequently offer more potential significance in a broader pharmacological sense. Thus, the peel compartment of these fruits presents an interesting functional food option in human nutrition, as well as in further explorable neuropharmacological frontiers.

Author Contributions: Conceptualization, B.O.O. and A.J.A.; methodology, B.O.O.; software, B.O.O.; formal analysis, B.O.O.; writing—original draft preparation, B.O.O.; supervision, A.J.A.; project administration, A.J.A.; funds acquisition, A.J.A. All authors have read and agreed to the published version of the manuscript.

Funding: We appreciate the Govan Mbeki Research and Development Centre (GMRDC), University of Fort Hare for their research support.

Data Availability Statement: Data are available in the open-access article.

Conflicts of Interest: The authors declare that there is no conflict of interest.

Abbreviations

NG108–15	glioblastoma
PGC-1/Nrf-2/HO-1	peroxisome proliferator-activated receptor coactivator /Nuclear factor2/Heme oxygenase
GFAP	glial fibrillary acidic protein
BDNF–TrkB–PI3K/Akt	brain-derived neurotrophic factor–tropomyosin-related kinase B/phosphatidylinositol
Bax/Bcl2	Bcl2 associated x/apoptosis regulator
TNF- α	tumor necrosis factor-alpha
IL-1 β	interleukin-1 β
COX-2	cyclooxygenase-2
P38MAPK	p38 mitogen-activated protein kinase
PRP	Prion Protein Peptide
HT22	hippocampus cell line
A β	Amyloid Beta Peptide
TrKA	tropomyosin receptor kinase A
ERK1/2	extracellular signal-related kinases ^{1/2}
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
p-JNK	p-Jun N-terminal kinase
p-ERK	p-extracellular signal-regulated kinase protein
MBP	maltose binding protein
DBH	dopamine- β -hydroxylase
MAP2	microtubule-associated protein 2
GAP 43	growth-associated protein 43
PSD-95	postsynaptic density protein
KLK8	Kallikrein 8 gene
SH-SY5Y	human neuroblastoma cell line
P53	tumor protein
β -secretase 1	Beta secretase 1
γ -secretase	gamma secretase protein
NADH	nicotinamide adenine dinucleotide hydrogen
NADPH	nicotinamide adenine dinucleotide phosphate
PC12	pheochromocytoma cell line
GABA	gamma-aminobutyric acid
ER β	estrogen receptor beta gene
NB69	Cellosaurus cell line

NAC	N-acetylcysteine
SNAP-25	synaptosomal-associated protein 25
CA1	Cortical Area 1
NF-kB	nuclear factor-kappa B cells
STAT3	signal transducer and activator of transcription 3
ERK/MMP-9	extracellular signal-related kinases/matrix metalloproteinase-9
gp91phox	91-KD glycoprotein
TGF- β 1	transforming growth factor
SK-N-SH	neuroblastoma cell line
HIF-1 α /LDHA	hypoxia-inducible factor-1 alpha/Lactate dehydrogenase A gene
Nrf-2/Keap1	nuclear factor 2/Kelch-like ECH-associated protein 1
GSK-3 β	glycogen synthase kinase-3 beta
mTOR	mammalian target of rapamycin
6-OHDA	6-hydroxydopamine
SOD-1	superoxide dismutase 1
TDP-43	TAR-DNA-binding protein 43
FUS/TLS	fused in sarcoma/translocated in liposarcoma
anti-CHE	anti-cholinesterase activity
ROS	reactive oxygen species
HPLC	High-Performance Liquid Chromatography
NMR	Nuclear Magnetic Resonance
HNMR	Proton Nuclear Magnetic Resonance
FTIR	Fourier-Transform Infrared Spectroscopy
GAE	gallic acid equivalent
QE	quercetin equivalent
CE	catechin equivalent

References

- González-Aguilar, G.; Robles-Sánchez, R.M.; Martínez-Téllez, M.A.; Olivas, G.I.; Alvarez-Parrilla, E.; de la Rosa, L.A. Bioactive compounds in fruits: Health benefits and effect of storage conditions. *Stewart Postharvest Rev.* **2008**, *4*, 1–10.
- Dragović-Uzelac, V.; Levaj, B.; Bursać, D.; Pedisić, S.; Radojčić, I.; Biško, A. Total Phenolics and Antioxidant Capacity Assays of Selected Fruits. *Agric. Consp. Sci.* **2007**, *72*, 279–284.
- Coats, R.; Martirosyan, D. The effects of bioactive compounds on biomarkers of obesity. *Funct. Foods Health Dis.* **2015**, *5*, 365–380. [[CrossRef](#)]
- Calixto, N.O.; Pinto, M.E.F.; Ramalho, S.D.; Burger, M.C.M.; Bobey, A.F.; Young, M.C.M.; Bolzani, V.S.; Pinto, A.C. The Genus *Psychotria*: Phytochemistry, Chemotaxonomy, Ethnopharmacology, and Biological Properties. *J. Braz. Chem. Soc.* **2016**, *27*, 1355–1378.
- Karasawa, M.M.G.; Mohan, C. Fruits as Prospective Reserves of Bioactive Compounds: A Review. *Nat. Prod. Bioprospect.* **2018**, *8*, 335–346. [[CrossRef](#)] [[PubMed](#)]
- Rendeiro, C.; Guerreiro, J.D.T.; Williams, C.M.; Spencer, J.P.E. Flavonoids as modulators of memory and learning: Molecular interactions resulting in behavioral effects. *Proc. Nutr. Soc.* **2012**, *71*, 246–262. [[CrossRef](#)]
- Solanki, I.; Parihar, P.; Mansuri, M.L.; Parihar, M.S. Flavonoid-Based Therapies in the Early Management of Neurodegenerative Diseases. *Adv. Nutr.* **2015**, *6*, 64–72. [[CrossRef](#)] [[PubMed](#)]
- Aquilano, K.; Baldelli, S.; Rotilio, G.; Ciriolo, M.R. Role of nitric oxide synthases in Parkinson's disease: A review on the antioxidant and anti-inflammatory activity of polyphenols. *Neurochem. Res.* **2008**, *33*, 2416–2426. [[CrossRef](#)] [[PubMed](#)]
- Patel, S.S.; Acharya, A.; Ray, R.S.; Agrawal, R.; Raghuvanshi, R.; Jain, P. Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. *Crit. Rev. Food Sci. Nutr.* **2019**, *60*, 887–939. [[CrossRef](#)]
- Przedborski, S.; Vila, M.; Jackson-Lewis, V. Neurodegeneration: What is it and where are we? *J. Clin. Investig.* **2003**, *111*, 3–10. [[CrossRef](#)] [[PubMed](#)]
- Johnston, M. Neurodegenerative disorders of childhood. In *Nelson Textbook of Pediatrics*, 20th ed.; Behrman, R.E., Kliegman, R.M., Jenson, H.B., Eds.; Elsevier: Philadelphia, PA, USA, 2016; p. 4264.
- Hardy, J. Pathways to Primary Neurodegenerative Disease. *Mayo Clin. Proc.* **1999**, *74*, 835–837. [[CrossRef](#)] [[PubMed](#)]
- Chen, W.W.; Zhang, X.; Huang, W.J. Role of neuroinflammation in neurodegenerative diseases (Review). *Mol. Med. Rep.* **2016**, *13*, 3391–3396. [[CrossRef](#)] [[PubMed](#)]
- Mobbs, C.V.; Hof, P.R. *Body Composition and Aging; Interdisciplinary Top Gerontology*; Karger: Basel, Switzerland, 2010; Volume 37, pp. 175–192.
- Lasonde, M.; Candel, S.; Hacker, J.; Quadrio-Curzio, A.; Onishi, T.; Ramakrishnan, V.; McNutt, M. *The Challenge of Neurodegenerative Diseases in an Aging Population; G7 Academies' Joint Statement; The Royal Society*: London, UK, 2017; pp. 1–2.

16. Taylor, J.P.; Hardy, J.; Fischbeck, K.H. Toxic proteins in neurodegenerative disease. *Science* **2002**, *296*, 1991–1995. [[CrossRef](#)] [[PubMed](#)]
17. Chen, H.; Chan, D.C. Mitochondrial dynamics- fusion, fission, movement, and mitophagy in neurodegenerative diseases. *Hum. Mol. Genet.* **2009**, *18*, R169–R176. [[CrossRef](#)] [[PubMed](#)]
18. Chin-Chan, M.; Navarro-Yepes, J.; Quintanilla-Vega, B. Environmental pollutants as risk factors for neurodegenerative disorders: Alzheimer and Parkinson diseases. *Front. Cell. Neurosci.* **2015**, *124*, 1–21. [[CrossRef](#)] [[PubMed](#)]
19. Dorsey, E.R.; Holloway, R.G.; Ravina, B.M. Biomarkers in Parkinson’s disease. *Expert Rev. Neurother.* **2006**, *6*, 823–831. [[CrossRef](#)]
20. Campbell, I.L.; Krucker, T.; Steffensen, S.; Akwa, Y.; Powell, H.C.; Lane, T.; Carr, D.J.; Gold, L.H.; Henriksen, S.J.; Siggins, G.R. Structural and functional neuropathology in transgenic mice with CNS expression of IFN- α . *Brain Res.* **1999**, *835*, 46–61. [[CrossRef](#)]
21. Ineichen, B. The epidemiology of dementia in Africa: A review. *Soc. Sci. Med.* **2000**, *50*, 1673–1677. [[CrossRef](#)]
22. Okubadejo, N.U.; Bower, J.H.; Rocca, W.A.; Maraganore, D.M. Parkinson’s disease in Africa. A systematic review of epidemiologic and genetic studies. *Mov. Disord.* **2006**, *21*, 2150–2156. [[CrossRef](#)] [[PubMed](#)]
23. Cilia, R.; Akpalu, A.; Cham, M.; Bonetti, A.; Amboni, M.; Faceli, E.; Pezzoli, G. Parkinson’s disease in sub-Saharan Africa: Step-by-step into the challenge. *Neurodegener. Dis. Manag.* **2011**, *1*, 193–202. [[CrossRef](#)]
24. George-Carey, R.; Adeloje, D.; Chan, K.Y.; Paul, A.; Kolčić, I.; Campbell, H.; Rudan, I. An estimate of the prevalence of dementia in Africa: A systematic analysis. *J. Glob. Health* **2012**, *2*, 1–13. [[CrossRef](#)] [[PubMed](#)]
25. Marin, B.; Kacem, I.; Diagana, M.; Boulesteix, M.; Gouider, R.; Preux, P.M.; Couratier, P. Juvenile, and adult-onset ALS/MND among Africans: Incidence, phenotype, survival: A review. *ALS* **2012**, *13*, 276–283.
26. Onyike, C.U.; Diehl-Schmid, J. The epidemiology of frontotemporal dementia. *Int. Rev. Psychiatry* **2013**, *25*, 130–137. [[CrossRef](#)] [[PubMed](#)]
27. Bower, J.H.; Maraganore, D.M.; McDonnell, S.K.; Rocca, W.A. Incidence of progressive supranuclear palsy and multiple system atrophy in Olmsted County, Minnesota, 1976 to 1990. *Neurology* **1997**, *49*, 1284–1288. [[CrossRef](#)]
28. Coon, E.A.; Sletten, D.M.; Suarez, M.D.; Mandrekar, J.N.; Ahlskog, J.E.; Bower, J.H.; Matsumoto, J.Y.; Silber, M.H.; Benarroch, E.E.; Fealey, R.D.; et al. Clinical features and autonomic testing predict survival in multiple system atrophy. *Brain* **2015**, *138*, 3623–3631. [[CrossRef](#)] [[PubMed](#)]
29. Köllensperger, M.; Geser, F.; Ndayisaba, J.; Boesch, S.; Seppi, K.; Ostergaard, K.; Dupont, E.; Cardozo, A.; Tolosa, E.; Abele, M.; et al. Presentation, diagnosis, and management of multiple system atrophy in Europe: Final analysis of the European multiple system atrophy registry. *Mov. Disord.* **2010**, *25*, 2604–2612. [[CrossRef](#)] [[PubMed](#)]
30. Tan, S.J.; Ismail, I.S. Potency of Selected Berries, Grapes, and Citrus Fruit as Neuroprotective Agents. *Evid. Based Complement. Alternat. Med.* **2020**, *2020*, 1–12. [[CrossRef](#)]
31. Xia, E.Q.; Deng, G.F.; Guo, Y.J.; Li, H.B. Biological activities of polyphenols from grapes. *Int. J. Mol. Sci.* **2010**, *11*, 622–646. [[CrossRef](#)]
32. Fu, L.; Xu, B.T.; Xu, X.R.; Gan, R.Y.; Zhang, Y.; Xia, E.Q.; Li, H.B. Antioxidant capacities and total phenolic contents of 62 fruits. *Food Chem.* **2011**, *129*, 345–350. [[CrossRef](#)] [[PubMed](#)]
33. Deng, G.F.; Shen, C.; Xu, X.R.; Kuang, R.D.; Guo, Y.J.; Zeng, L.S.; Gao, L.L.; Lin, X.; Xie, J.F.; Xia, E.Q.; et al. Potential of Fruit Wastes as Natural Resources of Bioactive Compounds. *Int. J. Mol. Sci.* **2012**, *13*, 8308–8323. [[CrossRef](#)] [[PubMed](#)]
34. Li, F.; Li, S.; Li, H.B.; Deng, G.F.; Ling, W.H.; Wu, S.; Xu, X.R.; Chen, F. Antiproliferative activity of peels, pulps, and seeds of 61 fruits. *J. Funct. Foods* **2013**, *5*, 1298–1309. [[CrossRef](#)]
35. Ishurda, O.; John, F.K. The anti-cancer activity of polysaccharides prepared from Libyan dates (*Phoenix dactylifera* L.). *Carbohydr. Polym.* **2005**, *59*, 531–535. [[CrossRef](#)]
36. Al-Qarawi, A.A.; Abdel-Rahman, H.; Mousa, H.M.; Ali, B.H.; El-Mougy, S.A. Nephroprotective action of *Phoenix dactylifera* in Gentamicin-Induced Nephrotoxicity. *Pharm. Biol.* **2008**, *46*, 227–230. [[CrossRef](#)]
37. Saafi, E.B.; Louedi, M.; Elfeki, A.; Zakhama, A.; Najjar, M.F.; Hammami, M.; Achour, L. Protective effect of date palm fruit extract (*Phoenix dactylifera* L.) on dimethoate induced oxidative stress in rat liver. *Exp. Toxicol. Pathol.* **2011**, *63*, 433–441. [[CrossRef](#)] [[PubMed](#)]
38. Kasi, P.B.; Kotormán, M. Avocado juice prevents the formation of Trypsin amyloid-like fibrils in aqueous ethanol. *Nat. Prod. Commun.* **2019**, *14*, 1–5. [[CrossRef](#)]
39. Joseph, J.A.; Shukitt-Hale, B.; Denisova, N.A.; Prior, R.L.; Cao, G.; Martin, A.; Taghialatela, G.; Bickford, P.C. Long-term dietary strawberry, spinach, or vitamin E supplementation retards the onset of age-related neuronal signal-transduction and cognitive behavioral deficits. *J. Neurosci.* **1998**, *18*, 8047–8055. [[CrossRef](#)]
40. Joseph, J.A.; Shukitt-Hale, B.; Denisova, N.A.; Bielinski, D.; Martin, A.; McEwen, J.J.; Bickford, J.J. Reversals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spinach, or strawberry dietary supplementation. *J. Neurosci.* **1999**, *19*, 8114–8121. [[CrossRef](#)] [[PubMed](#)]
41. Gambino, G.; Allegra, M.; Sardo, P.; Attanzio, A.; Tesoriere, L.; Livrea, M.A.; Ferraro, G.; Carletti, F. Brain distribution and modulation of neuronal excitability by indicaxanthin from *Opuntia ficus indica* administered at nutritionally relevant amounts. *Front. Aging Neurosci.* **2018**, *10*, 1–11. [[CrossRef](#)] [[PubMed](#)]
42. Oduje, A.A.; Oboh, G.; Ayodele, A.J.; Stephen, A.A. Assessment of the nutritional, antinutritional, and antioxidant capacity of unripe, ripe, and overripe plantain (*Musa paradisiaca*) peel. *Int. J. Curr. Adv. Res.* **2015**, *3*, 63–72.

43. Ogbonna, O.A.; Izundu, A.I.; Okoye, N.H.; Ikeyi, A.P. Phytochemical compositions of fruits of three *Musa* species at three stages of development. *IOSR J. Pharm.* **2016**, *11*, 48–59.
44. Aboul-Enein, A.M.; Salama, Z.A.; Gaafar, A.A.; Aly, H.F.; Abou-Ellella, F.; Ahmed, H.A. Identification of phenolic compounds from the banana peel (*Musa paradisiaca* L.) as antioxidant and antimicrobial agents. *J. Chem. Pharm.* **2016**, *8*, 46–55.
45. Agama-Acevedo, E.; Sañudo-Barajas, J.A.; Vélez De La Rocha, R.; González-Aguilar, G.A.; Bello-Peréz, L.A. Potential of plantain peels flour (*Musa paradisiaca* L.) as a source of dietary fiber and antioxidant compound. *CYTA J. Food* **2016**, *14*, 117–123. [[CrossRef](#)]
46. Aina, O.O.; Oyediji, M.B.; Adegboyega, D.A.; Owolaja, A.O. Phytochemical screening of some selected banana peels of *Musa acuminata* species. *Int. J. Agric.* **2019**, *4*, 68–78.
47. Boua, B.B.; Ouattara, D.; Traoré, L.; Mamyrbekova-Békro, J.A.; Békro, Y.A. Effect of domestic cooking on the total phenolic, flavonoid and condensed tannin content from plantain of Côte d'Ivoire. *J. Mater. Environ. Sci.* **2020**, *11*, 396–403.
48. Ashafaq, M.; Tabassum, H.; Vishnoi, S.; Salman, M.; Raisuddin, S.; Parvez, S. Tannic acid alleviates lead acetate-induced neurochemical perturbations in rat brain. *Neurosci. Lett.* **2016**, *617*, 94–100. [[CrossRef](#)] [[PubMed](#)]
49. Salman, M.; Tabassum, H.; Parvez, S. Nrf2/HO-1 mediates the neuroprotective effects of pramipexole by attenuating oxidative damage and mitochondrial perturbation after traumatic brain injury in rats. *Dis. Model Mech.* **2020**, *13*, 1–11. [[CrossRef](#)]
50. Sulaiman, S.F.; Yusoff, N.A.M.; Eldeen, I.M.; Seow, E.M.; Sajak, A.A.; Supriatno; Ooi, K.L. Correlation between total phenolic and mineral contents with antioxidant activity of eight Malaysian bananas (*Musa* sp.). *J. Food Compos. Anal.* **2011**, *24*, 1–10. [[CrossRef](#)]
51. Chauhan, A.; Nagar, A.; Bala, K.; Sharma, Y. Comparative study of different parts of fruits of *Musa* Sp. on the basis of their antioxidant activity. *Der Pharm. Lett.* **2016**, *8*, 88–100.
52. Al Amri, F.S.; Hossain, M.A. Comparison of total phenols, flavonoids, and antioxidant potential of local and imported ripe bananas. *Egypt. J. Basic Appl. Sci.* **2018**, *5*, 245–251. [[CrossRef](#)]
53. Kamaayi, F.; Baah, F.A.; Ansah, F.O. Phenolic content, polyphenol oxidase activity, and antioxidant scavenging activity in three species of plantain in Ghana. *Int. J. Sci. Res.* **2020**, *10*, 551–557. [[CrossRef](#)]
54. Fatemeh, S.R.; Saifullah, R.; Abbas, F.M.A.; Azhar, M.E. Total phenolics, flavonoids, and antioxidant activity of banana pulp and peel flours: Influence of variety and stage of ripeness. *Int. Food Res. J.* **2012**, *19*, 1041–1046.
55. Oyeyinka, B.O.; Afolayan, A.J. Comparative and Correlational evaluation of the phytochemical constituents and antioxidant activity of *Musa sinensis* L. and *Musa paradisiaca* L. fruit compartments (Musaceae). *Sci. World J.* **2020**, *2020*, 1–12. [[CrossRef](#)] [[PubMed](#)]
56. Ssonko, U.L.; Muranga, F.I. Phenolic compounds identification and antioxidant activity in bananas of AAB and ABB genomes grown in Uganda. *J. Health Popul. Nutr.* **2020**, *4*, 1–8.
57. Kevers, C.; Falkowski, M.; Tabart, J.; Defraigne, J.O.; Dommes, J.; Pincemail, J. Evolution of antioxidant capacity during storage of selected fruits and vegetables. *J. Agric. Food Chem.* **2007**, *55*, 8596–8603. [[CrossRef](#)] [[PubMed](#)]
58. Yao, J.; Irwin, R.; Chen, S.; Hamilton, R.; Cadenas, E.; Brinton, R.D. Ovarian hormone loss induces bioenergetic deficits and mitochondrial β -amyloid. *Neurobiol. Aging* **2012**, *33*, 1507–1521. [[CrossRef](#)] [[PubMed](#)]
59. Khan, I.; Bahuguna, A.; Bhardwaj, M.; Khaket, T.P.; Kang, S.C. Carvacrol nano-emulsion evokes cell cycle arrest, apoptosis induction, and autophagy inhibition in a doxorubicin-resistant A549 cell line. *Artif. Cells Nanomed. Biotechnol.* **2018**, *46*, S664–S675. [[CrossRef](#)] [[PubMed](#)]
60. Tsamo, C.V.P.; Herent, M.F.; Tomekpe, K.; Emaga, T.H.; Quetin-Leclercq, J.; Rogez, H.; Larondelle, Y.; Andre, C. Phenolic profiling in the pulp and peel of nine plantain cultivars (*Musa* sp.). *Food Chem.* **2015**, *167*, 197–204. [[CrossRef](#)]
61. Jiménez-Aliaga, K.; Bermejo-Bescós, P.; Benedí, J.; Martín-Aragón, S. Quercetin and rutin exhibit antiamyloidogenic and fibril-disaggregating effects in vitro and potent antioxidant activity in APPswe cells. *Life Sci.* **2011**, *89*, 939–945. [[CrossRef](#)] [[PubMed](#)]
62. Wang, Y.; Szretter, K.J.; Vermi, W.; Gilfillan, S.; Rossini, C.; Cella, M.; Barrow, A.D.; Diamond, M.S.; Colonna, M. IL-34 is a tissue-restricted ligand of CSF1R required for the development of Langerhans cells and microglia. *Nat. Immunol.* **2012**, *13*, 753–760. [[CrossRef](#)] [[PubMed](#)]
63. Javed, H.; Khan, M.M.; Ahmad, A.; Vaibhav, K.; Ahmad, M.E.; Khan, A.; Ashafaq, M.; Islam, F.; Siddiqui, M.S.; Safhi, M.M.; et al. Rutin prevents cognitive impairments by ameliorating oxidative stress and neuroinflammation in the rat model of sporadic dementia of Alzheimer's type. *Neuroscience* **2012**, *210*, 340–352. [[CrossRef](#)]
64. Na, J.Y.; Kim, S.; Song, K.; Kwon, J. Rutin alleviates Prion peptide-induced cell death through inhibiting apoptotic pathway activation in dopaminergic neuronal cells. *Cell. Mol. Neurobiol.* **2014**, *34*, 1071–1079. [[CrossRef](#)] [[PubMed](#)]
65. Xu, Y.; Zhang, M.; Ramos, C.A.; Durett, A.; Liu, E.; Dakhova, O.; Liu, H.; Creighton, C.J.; Gee, A.P.; Heslop, H.E.; et al. Closely related T-memory stem cells correlate with *in vivo* expansion of CAR.CD19-T cells and are preserved by IL-7 and IL-15. *Blood* **2014**, *123*, 3750–3759. [[CrossRef](#)] [[PubMed](#)]
66. Ganeshpurkar, A.; Saluja, A.K. The pharmacological potential of Rutin. *Saudi Pharm. J.* **2017**, *25*, 149–164. [[CrossRef](#)] [[PubMed](#)]
67. Song, H.; Zhang, X.; Wang, W.; Liu, R.; Zhao, K.; Liu, M.; Gong, W.; Ning, B. Neuroprotective mechanisms of rutin for spinal cord injury through anti-oxidation and anti-inflammation and inhibition of the p38 mitogen-activated protein kinase pathway. *Neural Regen. Res.* **2018**, *13*, 128–134.
68. Adepoju, O.T.; Sunday, B.E.; Folaranmi, O.A. Nutrient composition and contribution of plantain (*Musa paradisiaca*) products to dietary diversity of Nigerian consumers. *Afr. J. Biotechnol.* **2012**, *11*, 13601–13605. [[CrossRef](#)]
69. Okareh, O.T.; Adeolu, A.T.; Adepoju, O.T. Proximate and mineral composition of plantain (*Musa paradisiaca*) wastes flour; a potential nutrients source in the formulation of animal feeds. *Afr. J. Food Sci.* **2015**, *6*, 53–57. [[CrossRef](#)]

70. Hapsari, L.; Lestari, D.A. Fruit characteristics and nutrient values of four Indonesian banana cultivars (*Musa* spp.) at different genomic groups. *AGRAVITA J. Agric. Sci.* **2016**, *38*, 303–311. [[CrossRef](#)]
71. Siji, S.; Nandini, P.V. Chemical and nutrient composition of selected banana varieties of Kerala. *Int. J. Adv. Eng. Manag. Sci.* **2017**, *3*, 401–404.
72. Ho, Y.S.; Yu, M.S.; Yang, X.F.; So, K.F.; Yuen, W.H.; Chang, R.C.C. Neuroprotective effects of polysaccharides from wolfberry, the fruits of *Lycium barbarum*, against homocysteine-induced toxicity in rat cortical neurons. *J. Alzheimer's Dis.* **2010**, *19*, 813–827. [[CrossRef](#)]
73. Chiricozzi, A.; De Simone, C.; Fossati, B.; Peris, K. Emerging treatment options for the treatment of moderate to severe plaque psoriasis and psoriatic arthritis: Evaluating bimekizumab and its therapeutic potential. *Psoriasis Targets Ther.* **2019**, *9*, 29–35. [[CrossRef](#)] [[PubMed](#)]
74. Hasanah, R.; Daningsih, E.; Titin, T. The analysis of nutrient and fiber content of banana (*Musa paradisiaca*) sold in Pontianak, Indonesia. *Biofarmasi J. Nat. Prod. Biochem.* **2017**, *15*, 21–25. [[CrossRef](#)]
75. Abubakar, U.S.; Yusuf, K.M.; Safiyanu, I.; Abdullahi, S.; Saidu, S.R.; Abdu, G.T.; Indee, A.M. Proximate and mineral composition of corn cob, banana, and plantain peels. *Int. J. Food Sci.* **2016**, *1*, 25–27.
76. Adamu, A.S.; Ojo, I.O.; Oyetunde, J.G. Evaluation of nutritional values in ripe, unripe, boiled, and roasted plantain (*Musa paradisiaca* L.) pulp and peel. *Eur. J. Basic Appl. Sci.* **2017**, *4*, 9–12.
77. Shadrach, I.; Banji, A.; Adebayo, O. Nutraceutical potential of ripe and unripe plantain peels: A comparative study. *Chem. Int.* **2020**, *6*, 83–90.
78. Kirkland, A.E.; Sarlo, G.L.; Holton, K.F. The role of magnesium in neurological disorders. *Nutrients* **2018**, *10*, 730. [[CrossRef](#)] [[PubMed](#)]
79. Annor, G.A.; Asamoah-Bonti, P.; Sakyi-Dawson, E. Fruit physical characteristics, proximate, mineral and starch characterization of FHIA 19 and FHIA 20 plantain and FHIA 03 cooking banana hybrids. *SpringerPlus* **2016**, *5*, 796. [[CrossRef](#)] [[PubMed](#)]
80. Seth, R.; Corniola, R.S.; Gower-Winter, S.D.; Morgan, T.J., Jr.; Bishop, B.; Levenson, C.W. Zinc deficiency induces apoptosis via mitochondrial p53- and caspase-dependent pathways in human neuronal precursor cells. *J. Trace Elem. Med. Biol.* **2015**, *30*, 59–65. [[CrossRef](#)]
81. Chen, N.N.; Zhao, D.J.; Sun, Y.X.; Wang, D.D.; Ni, H. Long-Term Effects of Zinc Deficiency and Zinc Supplementation on Developmental Seizure-Induced Brain Damage and the Underlying GPR39/ZnT-3 and MBP Expression in the Hippocampus. *Front. Neurosci.* **2019**, *13*, 1–10. [[CrossRef](#)]
82. Marasco, D.; Vicidomini, C.; Krupa, P.; Cioffi, F.; Huy, P.D.Q.; Li, M.S.; Florio, D.; Broersen, K.; Francesca De Pandis, M.; Roviello, G.N. Plant isoquinoline alkaloids as potential neuro drugs: A comparative study of the effects of benzo[c]phenanthridine and berberine-based compounds on β -amyloid aggregation. *Chem. Biol. Interact.* **2021**, *334*, 109300. [[CrossRef](#)]
83. Konar, A.; Shah, N.; Singh, R.; Saxena, N.; Kaul, S.C.; Wadhwa, R.; Thakur, M.K. Protective Role of *Ashwagandha* leaf extract and its component Withanone on scopolamine-induced changes in the brain and brain-derived cells. *PLoS ONE* **2011**, *6*, e27265. [[CrossRef](#)]
84. Konar, A.; Gupta, R.; Shukla, R.K.; Maloney, B.; Khanna, V.K.; Wadhwa, R.; Lahiri, D.K.; Thakur, M.K. M1 muscarinic receptor is a key target of neuroprotection, neuroregeneration, and memory recovery by i-Extract from *Withania somnifera*. *Sci. Rep.* **2019**, *9*, 13990. [[CrossRef](#)]
85. Oyeyinka, B.O.; Afolayan, A.J. Comparative Evaluation of the Nutritive, Mineral, and Antinutritive Composition of *Musa sinensis* L. (Banana) and *Musa paradisiaca* L. (Plantain). *Plants* **2019**, *8*, 598. [[CrossRef](#)] [[PubMed](#)]
86. Oyeyemi, S.D.; Otoide, J.E.; Obembe, M.O.; Ogunleye, B.J. Nutritional and phytochemical assessment of *Musa sapientum* var. velutina. *The Pharm. Chem. J.* **2019**, *6*, 56–64.
87. Chen, Y.; Sun, H.; Huang, L.; Li, J.; Zhou, W.; Chang, J. Neuroprotective effect of *Radix trichosanthis* saponins on subarachnoid hemorrhage. *Evid. Based Complement. Alternat. Med.* **2015**, *2015*, 1–10. [[CrossRef](#)] [[PubMed](#)]
88. Khawas, P.; Das, A.J.; Sit, N.; Badwaik, L.S.; Deka, S.C. Nutritional composition of culinary *Musa* ABB at Different Stages of Development. *Am. J. Food Technol.* **2014**, *2*, 80–87. [[CrossRef](#)]
89. Anekonda, T.S.; Quinn, J.F.; Harris, C.; Frahler, K.; Wadsworth, T.L.; Woltjer, R.L. L-type voltage-gated calcium channel blockade with isradipine as a therapeutic strategy for Alzheimer's disease. *Neurobiol. Dis.* **2011**, *41*, 61–70. [[CrossRef](#)]
90. Thinh, B.B.; Trong, L.V.; Lam, L.T.; Hien, V.T.T. Nutritional value of persimmon, banana, lemon, and longan cultivated in Northern Vietnam. *IOP Conf. Ser. Earth Environ. Sci.* **2021**, *640*, 022030. [[CrossRef](#)]
91. Velumani, S. Phytochemical screening and antioxidant activity of banana peel. *Int. J. Adv. Res. Innov. Ideas Educ.* **2016**, *2*, 91–102.
92. Kim, S.M.; Chung, M.J.; Ha, T.J.; Choi, H.N.; Jang, S.J.; Kim, S.O.; Chun, M.H.; Do, S.I.; Choo, Y.K.; Park, Y.I. Neuroprotective effects of black soybean anthocyanins via inactivation of ASK1-JNK/p38 pathways and mobilization of cellular sialic acids. *Life Sci.* **2012**, *90*, 874–882. [[CrossRef](#)]
93. Lau, F.C.; Joseph, J.A.; McDonald, J.E.; Kalt, W. Attenuation of iNOS and COX2 by blueberry polyphenols is mediated through the suppression of NF- κ B activation. *J. Funct. Foods* **2009**, *1*, 274–283. [[CrossRef](#)]
94. Ma, C.; Zhao, L.L.; Zhao, H.J.; Cui, J.W.; Li, W.; Wang, N.Y. Lentivirus-mediated MDA7/IL24 expression inhibits the proliferation of hepatocellular carcinoma cells. *Mol. Med. Rep.* **2018**, *17*, 5764–5773. [[CrossRef](#)]
95. Agoreyo, B.O.; Agoreyo, F.O.; Omigie, M.I. Antioxidant activity, phytochemical and antioxidant levels of *Musa paradisiaca* L. and *Musa sapientum* L. at various ripening stages. *Eur. Food Res. Technol.* **2017**, *5*, 41–59.

96. Nakaso, K.; Tajima, N.; Horikoshi, Y.; Nakasone, M.; Hanaki, T.; Kamizaki, K.; Matura, T. The estrogen receptor β -PI3K/Akt pathway mediates the cytoprotective effects of tocotrienol in a cellular Parkinson's disease model. *Biochim. Biophys. Acta BBA Mol. Basis Dis.* **2014**, *1842*, 1303–1312. [[CrossRef](#)] [[PubMed](#)]
97. Al-Ahmary, K.M. Selenium content in selected foods from the Saudi Arabia market and estimation of the daily intake. *Arab. J. Chem.* **2009**, *2*, 95–99. [[CrossRef](#)]
98. Choi, Y.; Kim, J.; Lee, H.S.; Kim, C.; Hwang, I.K.; Park, H.K.; Oh, C.H. Selenium content in representative Korean foods. *J. Food Compos. Anal.* **2009**, *22*, 117–122. [[CrossRef](#)]
99. Al-Othman, A.M.; Al-Othman, Z.A.; El-Desoky, G.E.; Aboul-Soud, M.A.M.; Habila, M.A.; Giesy, J.P. Daily intake of selenium and concentrations in blood of residents of Riyadh City, Saudi Arabia. *Environ. Geochem. Health* **2012**, *34*, 417–431. [[CrossRef](#)]
100. Moatkhef, F.; Ismail, H.; Agamy, N.; Aborhyem, S. Quantitative determination of selenium in the most common food items sold in Egypt. *J. Egypt. Public Health Assoc.* **2020**, *95*, 1–9. [[CrossRef](#)]
101. Naziroğlu, M.; Kutluhan, S.; Yilmaz, M. Selenium and topiramate modulate brain microsomal oxidative stress values, Ca²⁺-ATPase activity, and EEG records in pentylenetetrazol-induced seizures in rats. *J. Membr. Biol.* **2008**, *225*, 39–49. [[CrossRef](#)]
102. Naziroğlu, M.; Şenol, N.; Ghazizadeh, V.; Yyürüker, V. Neuroprotection induced by N-acetylcysteine and selenium against traumatic brain injury-induced apoptosis and calcium entry in the hippocampus of the rat. *Cell. Mol. Neurobiol.* **2014**, *34*, 895–903. [[CrossRef](#)]
103. Klingberg, S.; Andersson, H.; Mulligan, A.; Bhaniani, A.; Welch, A.; Bingham, S.; Khaw, K.T.; Andersson, S.; Ellegard, L. Food sources of plant sterols in the EPIC Norfolk population. *Eur. J. Clin. Nutr.* **2008**, *62*, 695–703. [[CrossRef](#)]
104. Rui, X.; Wenfang, L.; Jing, C.; Meng, C.; Chengcheng, D.; Jiqu, X.; Shuang, R. Neuroprotective effects of phytosterol esters against high cholesterol-induced cognitive deficits in the aged rat. *Food Funct.* **2017**, *8*, 1323–1332. [[CrossRef](#)]
105. Kopylov, A.T.; Malsagova, K.A.; Stepanov, A.A.; Kaysheva, A.L. Diversity of Plant Sterols Metabolism: The impact on human health, sport, and accumulation of contaminating sterols. *Nutrients* **2021**, *13*, 1623. [[CrossRef](#)] [[PubMed](#)]
106. Uzairu, S.M.; Kano, M.A. Assessment of phytochemical and mineral composition of unripe and ripe plantain (*Musa paradisiaca*) peels. *Afr. J. Food Sci.* **2021**, *15*, 107–112.
107. Kasture, V.S.; Deshmukh, V.K.; Chopde, C.T. Anticonvulsant and behavioral actions of triterpene isolated from *Rubia cordifolia* Linn. *Indian J. Exp. Biol.* **2000**, *38*, 675–680.
108. Yu, L.; Chen, C.; Wang, L.F.; Kuang, X.; Liu, K.; Zhang, H.; Du, J.R. Neuroprotective effect of Kaempferol glycosides against brain injury and neuroinflammation by inhibiting the activation of NF- κ B and STAT3 in transient focal stroke. *PLoS ONE* **2013**, *8*, e55839. [[CrossRef](#)]
109. Yang, J.; Zeng, Z.; Wu, T.; Yang, Z.; Liu, B.; Lan, T. Emodin attenuates high glucose-induced TGF- β 1 and fibronectin expression in mesangial cells through inhibition of the NF- κ B pathway. *Exp. Cell Res.* **2013**, *319*, 3182–3189. [[CrossRef](#)]
110. Wang, T.; Fan, X.; Tang, T.; Fan, R.; Zhang, C.; Huang, Z.; Peng, W.; Gan, P.; Xiong, X.; Huang, W.; et al. Rhein, and rhubarb similarly protect the blood-brain barrier after experimental traumatic brain injury via gp91phox subunit of NADPH oxidase/ROS/ERK/MMP-9 signaling pathway. *Sci. Rep.* **2016**, *6*, 37098. [[CrossRef](#)] [[PubMed](#)]
111. Aurore, G.; Parfait, B.; Fährasmane, L. Bananas, raw materials for making processed food products. *Trends Food Sci. Technol.* **2009**, *20*, 78–91. [[CrossRef](#)]
112. Chen, Y.M.; Li, H.; Chiu, Y.S.; Huang, C.C.; Chen, W.C. Supplementation of L-arginine, L- glutamine, Vitamin C, Vitamin E, folic acid, and green tea extract enhances serum nitric oxide content and anti-fatigue activity in mice. *Evid. Based Complement. Alternat. Med.* **2020**, *2020*, 1–10. [[CrossRef](#)]
113. Prakash, A.; Kumar, A. Implicating the role of lycopene in the restoration of mitochondrial enzymes and BDNF levels in β -amyloid induced Alzheimer's disease. *Eur. J. Pharmacol.* **2014**, *741*, 104–111. [[CrossRef](#)]
114. Hong, Y.G.; Roh, S.; Paik, D.; Jeong, S. Development of a reporter system for *in vivo* monitoring of γ -secretase activity in *Drosophila*. *Mol. Cells* **2017**, *40*, 73–81. [[CrossRef](#)] [[PubMed](#)]
115. Heng, Z.; Sheng, O.; Yan, S.; Lu, H.; Motorykin, I.; Gao, H.; Li, C.; Yang, Q.; Hu, C.; Kuang, R.; et al. Carotenoid profiling in the peel and pulp of 36 selected *Musa* varieties. *Food Sci. Technol. Res.* **2017**, *23*, 603–611. [[CrossRef](#)]
116. Villaverde, J.J.; Oliveira, L.; Vilela, C.; Domingues, R.M.; Freitas, N.; Cordeiro, N.; Freire, C.S.R.; Silvestre, A.J.D. High valuable compounds from the unripe peel of several *Musa* species cultivated in Madeira Island (Portugal). *Ind. Crops Prod.* **2013**, *42*, 507–512. [[CrossRef](#)]
117. Shi, C.; Liu, J.; Wu, F.; Zhu, X.; Yew, D.T.; Xu, J. β -sitosterol inhibits high cholesterol-induced platelet β -amyloid release. *J. Bioenerg. Biomembr.* **2011**, *43*, 691–697. [[CrossRef](#)]
118. Shi, C.; Wu, F.; Zhu, X.C.; Xu, J. Incorporation of beta-sitosterol into the membrane increases resistance to oxidative stress and lipid peroxidation via estrogen receptor-mediated PI3K/GSK3 β signaling. *Biochim. Biophys. Acta* **2013**, *1830*, 2538–2544. [[CrossRef](#)] [[PubMed](#)]
119. Mordi, R.C.; Fadiaro, A.E.; Owoeye, T.F.; Olanrewaju, I.O.; Uzoamaka, G.C.; Olorunshola, S.J. Identification by GC-MS of the components of oils of banana peels extract, phytochemical and antimicrobial analyses. *Res. J. Phytochem.* **2016**, *10*, 39–44. [[CrossRef](#)]
120. Hsieh, P.F.; Hou, C.W.; Yao, P.W.; Wu, S.P.; Peng, Y.F.; Shen, M.L.; Lin, C.H.; Chao, Y.Y.; Chang, M.H.; Jeng, K.C. Sesamin ameliorates oxidative stress and mortality in kainic acid-induced status epilepticus by inhibition of MAPK and COX-2 activation. *J. Neuroinflamm.* **2011**, *8*, 57. [[CrossRef](#)]

121. Xu, Z.; Liu, Y.; Yang, D.; Yuan, F.; Ding, J.; Chen, H.; Tian, H. Sesamin protects SH-SY5Y cells against mechanical stretch injury and promoting cell survival. *BMC Neurosci.* **2017**, *18*, 57. [[CrossRef](#)]
122. Udomruk, S.; Kaewmool, C.; Phitak, T.; Pothacharoen, P.; Kongtawelert, P. Sesamin promotes neurite outgrowth under insufficient nerve growth factor condition in PC12 cells through the ERK1/2 pathway and SIRT1 modulation. *Evid. Based Complement. Alternat. Med.* **2020**, *2020*, 1–12. [[CrossRef](#)]
123. Singh, B.; Singh, J.P.; Kaur, A.; Singh, N. Bioactive compounds in banana and their associated health benefits—A review. *Food Chem.* **2016**, *206*, 1–11. [[CrossRef](#)]
124. Zhang, N.; Feng, H.; Liao, H.H.; Chen, S.; Yang, Z.; Deng, W.; Tang, Q.Z. Myricetin attenuated LPS induced cardiac injury in vivo and in vitro. *Phytother. Res.* **2018**, *32*, 459–470. [[CrossRef](#)] [[PubMed](#)]
125. Rebello, L.P.G.; Ramos, A.M.; Pertuzatti, P.B.; Barcia, M.T.; Muñoz, N.C.; Hermosín-Gutiérrez, I. Flour of banana (*Musa AAA*) peel as a source of antioxidant phenolic compounds. *Food Res. Int.* **2014**, *55*, 397–403. [[CrossRef](#)]
126. Rinaldo, D. Carbohydrate and bioactive compounds composition of starchy tropical fruits and tubers, in relation to pre and postharvest conditions: A review. *J. Food Sci.* **2020**, *85*, 249–259. [[CrossRef](#)]
127. Vlachos, G.S.; Scarmeas, N. Dietary interventions in mild cognitive impairment and dementia. *Dialogues Clin. Neurosci.* **2019**, *21*, 69–82. [[PubMed](#)]
128. Singh, P.; Sivanandama, T.M.; Konar, A.; Thakur, M.K. Role of nutraceuticals in cognition during aging and related disorders. *Neurochem. Int.* **2021**, *143*, 104928. [[CrossRef](#)]
129. Tan, H.P.; Wong, D.Z.H.; Ling, S.K.; Chuah, C.H.; AbdulKadir, H. Neuroprotective activity of galloylated cyanogenic glucosides and hydrolyzable tannins isolated from leaves of *Phyllagathis rotundifolia*. *Fitoterapia* **2012**, *83*, 223–229. [[CrossRef](#)]
130. Winiarska-Mieczan, A. Protective effect of tannic acid on the brain of adult rats exposed to cadmium and lead. *Environ. Toxicol. Pharmacol.* **2013**, *36*, 9–18. [[CrossRef](#)] [[PubMed](#)]
131. Calou, I.; Bandeira, M.A.; Aguiar-Galvão, W.; Cerqueira, G.; Siqueira, R.; Neves, K.R.; Brito, G.A.; Viana, G. Neuroprotective properties of a standardized extract from *Myracrodruon urundeuwa* Fr. All. (Aroeira-Do-Sertão), as evaluated by a Parkinson's disease model in rats. *Parkinsons Dis.* **2014**, *2014*, 1–12. [[CrossRef](#)]
132. Zengin, G.; Locatelli, M.; Carradori, S.; Mocan, A.M.; Aktumsek, A. Total phenolics, flavonoids, condensed tannins content of eight *Centaurea* species and their broad inhibitory activities against cholinesterase, tyrosinase, α -amylase, and α -glucosidase. *Not. Bot. Horti Agrobot.* **2016**, *44*, 195–200. [[CrossRef](#)]
133. Liu, X.; Yan, Y.; Li, F.; Zhang, D. Fruit and vegetable consumption and the risk of depression: A meta-analysis. *Nutrition* **2016**, *32*, 296–302. [[CrossRef](#)] [[PubMed](#)]
134. Türedi, S.; Yuluğ, E.; Alver, A.; Bodur, A.; İnce, I. A morphological and biochemical evaluation of the effects of quercetin on experimental sciatic nerve damage in rats. *Exp. Ther. Med.* **2018**, *15*, 3215–3224.
135. Sharma, D.R.; Wani, W.Y.; Sunkaria, A.; Kandimalla, R.J.L.; Verma, D.; Cameotra, S.S.; Gill, K.D. Quercetin protects against chronic aluminum-induced oxidative stress and ensuing biochemical, cholinergic, and neurobehavioral impairments in rats. *Neurotox. Res.* **2013**, *23*, 336–357. [[CrossRef](#)] [[PubMed](#)]
136. Wassem, M.; Parvez, S. Neuroprotective activities of curcumin and quercetin with potential relevance to mitochondrial dysfunction induced by oxaliplatin. *Protoplasma* **2015**, *253*, 417–430. [[CrossRef](#)]
137. Khan, A.; Ali, T.; Ur Rehman, S.; Khan, M.S.; Alam, S.I.; Ikram, M.; Muhammad, T.; Saeed, K.; Badshah, H.; Kim, K.O. Neuroprotective effect of quercetin against the detrimental effects of LPS in the adult Mouse brain. *Front. Pharmacol.* **2018**, *9*, 1–16. [[CrossRef](#)] [[PubMed](#)]
138. La Casa, C.; Villegas, I.; Alarcón de la Lastra, C.; Motilva, V.; Martín Calero, M.J. Evidence for protective and antioxidant properties of rutin, a natural flavone, against ethanol-induced gastric lesions. *J. Ethnopharmacol.* **2000**, *71*, 45–53. [[CrossRef](#)]
139. Schwedhelm, E.; Maas, R.; Troost, R.; Boger, R.H. Clinical pharmacokinetics of antioxidants and their impact on systemic oxidative stress. *Clin. Pharmacokinet.* **2003**, *42*, 437–459. [[CrossRef](#)] [[PubMed](#)]
140. Nassiri-Asl, M.; Mortazavi, S.R.; Samiee-Rad, F.; Zangivand, A.A.; Safdari, F.; Saroukhani, S.; Abbasi, E. The effects of rutin on the development of pentylentetrazole kindling and memory retrieval in rats. *Epilepsy Behav.* **2010**, *18*, 50–53. [[CrossRef](#)]
141. Richetti, S.K.; Blank, M.; Capiotti, K.M.; Piato, A.L.; Bogo, M.R.; Vianna, M.R.; Bonan, C.D. Quercetin and rutin prevent scopolamine-induced memory impairment in zebrafish. *Behav. Brain Res.* **2011**, *217*, 10–15. [[CrossRef](#)]
142. Ramalingayya, G.V.; Cheruku, S.P.; Nayak, P.G.; Kishore, A.; Shenoy, R.; Rao, C.M.; Krishnadas, N. Rutin protects against neuronal damage in vitro and ameliorates doxorubicin-induced memory deficits in vivo in Wistar rats. *Drug Des. Devel. Ther.* **2017**, *11*, 1011–1026. [[CrossRef](#)]
143. Kumar, A.; Rinwa, P.; Dhar, H. Possible nitric oxide modulation in the protective effects of rutin against experimental head trauma-induced cognitive deficits: Behavioral, biochemical, and molecular correlates. *J. Surg. Res.* **2014**, *188*, 268–279. [[CrossRef](#)]
144. Robinson, D.T.; Martin, C.R. Fatty acid requirements for the preterm infant. *Semin. Fetal Neonatal Med.* **2017**, *22*, 8–14. [[CrossRef](#)] [[PubMed](#)]
145. Lo Van, A.; Sakayori, N.; Hachem, M.; Belkouch, M.; Picq, M.; Fourmaux, B.; Lagarde, M.; Osumi, N.; Bernoud-Hubac, N. Targeting the brain with a neuroprotective Omega-3 fatty acid to enhance neurogenesis in the hypoxic condition in culture. *Mol. Neurobiol.* **2018**, *56*, 986–999. [[CrossRef](#)]
146. Calderon, F.; Kim, H.Y. Docosahexaenoic acid promotes neurite growth in hippocampal neurons. *J. Neurochem.* **2004**, *90*, 979–988. [[CrossRef](#)] [[PubMed](#)]

147. Barker-Haliski, M.L.; Dahle, E.J.; Heck, T.D.; Pruess, T.H.; Vanegas, F.; Wilcox, K.S.; White, H.S. Evaluating an etiologically relevant platform for therapy development for temporal lobe epilepsy: Effects of carbamazepine and valproic acid on acute seizures and chronic behavioral comorbidities in the Theiler's murine encephalomyelitis virus mouse model. *J. Pharmacol. Exp. Ther.* **2015**, *353*, 318–329. [[CrossRef](#)]
148. Gröber, U.; Schmidt, J.; Kisters, K. Magnesium in Prevention and Therapy. *Nutrients* **2015**, *7*, 8199–8226. [[CrossRef](#)] [[PubMed](#)]
149. Clerc, P.; Young, C.A.; Bordt, E.A.; Grigore, A.M.; Fiskum, G.; Polster, B.M. Magnesium sulfate protects against the bioenergetic consequences of chronic glutamate receptor stimulation. *PLoS ONE* **2013**, *8*, e79982. [[CrossRef](#)]
150. Lambuk, L.; Jafri, A.J.A.; Arfuzir, N.N.N.; Iezhitsa, I.; Agarwal, R.; Rozali, K.N.B.; Agarwal, P.; Bakar, N.S.; Kutty, M.K.; Yusof, A.P.; et al. Neuroprotective effect of Magnesium acetyltaurate against NMDA-induced excitotoxicity in rat retina. *Neurotox. Res.* **2017**, *31*, 31–45. [[CrossRef](#)]
151. Adamo, A.M.; Zago, M.P.; Mackenzie, G.G.; Aimo, L.; Keen, C.L.; Keenan, A.; Oteiza, P.I. The role of zinc in the modulation of neuronal proliferation and apoptosis. *Neurotox. Res.* **2010**, *17*, 1–14. [[CrossRef](#)]
152. Osredkar, J.; Sustar, N. Copper and Zinc, Biological Role and Significance of Copper/Zinc Imbalance. *J. Clin. Toxicol. S* **2011**, *3*, 1–18. [[CrossRef](#)]
153. Kaler, S.G.; Holmes, C.S.; Goldstein, D.S.; Tang, J.; Godwin, S.C.; Donsante, A.; Liew, C.J.; Sato, S.; Patronas, N. Neonatal diagnosis, and treatment of Menkes disease. *N. Engl. J. Med.* **2008**, *358*, 605–614. [[CrossRef](#)]
154. Kaler, S.G. ATP7A-related copper transport diseases-emerging concepts and future trends. *Nat. Rev. Neurol.* **2011**, *7*, 15–29. [[CrossRef](#)] [[PubMed](#)]
155. Rubio-Osornio, M.; Montes, S.; Perez-Severiano, F.; Aguilera, P.; Floriano-Sanchez, E.; Monroy-Noyola, A.; Rubio, C.; Rios, C. Copper reduces striatal protein nitration and tyrosine hydroxylase inactivation induced by MPP+ in rats. *Neurochem. Int.* **2009**, *54*, 447–451. [[CrossRef](#)]
156. Sehgal, N.; Gupta, A.; Valli, R.K.; Joshi, S.D.; Mills, J.T.; Hamel, E.; Khanna, P.; Jain, S.C.; Thakur, S.S.; Ravindranath, V. *Withania somnifera* reverses Alzheimer's disease pathology by enhancing low-density lipoprotein receptor-related protein in the liver. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 3510–3515. [[CrossRef](#)] [[PubMed](#)]
157. Liu, Y.; Liu, X.; Hua, W.; Wei, Q.; Fang, X.; Zhao, Z.; Chun, G.; Chao, L.; Chen, C.; Yifu, T.; et al. Berberine inhibits macrophage M1 polarization via AKT1/SOCS1/NF- κ B signaling pathway to protect against DSS-induced colitis. *Int. Immunopharmacol.* **2018**, *57*, 121–131. [[CrossRef](#)]
158. Yan, G.; Li, Y.J.; Zhao, Y.Y.; Guo, J.M.; Zhang, W.H.; Zhang, M.M.; Fua, Y.H.; Liu, Y.P. Neuroprotective Carbazole alkaloids from the stems and leaves of *Clausena lenis*. *Nat. Prod. Res.* **2021**, *35*, 2002–2009. [[CrossRef](#)]
159. Rastogi, M.; Ojha, R.P.; Prabu, P.C.; Parimala Devi, B.; Agrawal, A.; Dubey, G.P. Prevention of age-associated neurodegeneration and promotion of healthy brain aging in female Wistar rats by long-term use of bacosides. *Biogerontology* **2012**, *13*, 183–195. [[CrossRef](#)]
160. Son, I.S.; Kim, J.H.; Sohn, H.Y.; Son, K.H.; Kim, J.S.; Kwon, C.S. Antioxidative and hypolipidemic effects of diosgenin, a steroidal saponin of Yam (*Dioscorea* spp.), on high cholesterol-fed rats. *Biosci. Biotechnol. Biochem.* **2007**, *71*, 70471–70479. [[CrossRef](#)]
161. Kondeva-Burdina, M.; Krasteva, I.; Popov, G.; Manov, V. Neuroprotective and antioxidant activities of saponins' mixture from *Astragalus glycyphylloides* in a model of 6-hydroxy- dopamine-induced oxidative stress on isolated rat brain synaptosomes. *Pharmacia* **2019**, *66*, 233–236. [[CrossRef](#)]
162. Abe, T.K.; Taniguchi, M. Identification of Myo-inositol hexakisphosphate (IP6) as a β -secretase 1 (BACE1) inhibitory molecule in rice grain extract and digest. *FEBS Open Bio.* **2014**, *4*, 162–167. [[CrossRef](#)] [[PubMed](#)]
163. Sánchez-Hernández, D.; Anderson, G.H.; Poon, A.N.; Pannia, E.; Cho, C.E.; Huot, P.S.P.; Kubant, R. Maternal fat-soluble vitamins, brain development, and regulation of feeding behavior: An overview of research. *Nutr. Res. Rev.* **2016**, *36*, 1045–1054. [[CrossRef](#)]
164. Mikkelsen, K.; Stojanovska, L.; Tangalakis, K.; Bosevski, M.; Apostolopoulos, V. Cognitive decline: A vitamin B perspective. *Maturitas* **2016**, *93*, 108–113. [[CrossRef](#)]
165. Martin, P.R.; Singleton, C.K.; Hiller-Sturmhöfel, S. The role of thiamine deficiency in alcoholic brain disease. *Alcohol Res. Health* **2003**, *27*, 134–142.
166. Williams, A.; Ramsden, D. Nicotinamide: A double-edged sword. *Parkinsonism Relat. Disord.* **2005**, *11*, 413–420. [[CrossRef](#)]
167. Griffin, S.M.; Pickard, M.R.; Orme, R.P.; Hawkins, C.P.; Fricker, R.A. Nicotinamide promotes neuronal differentiation of mouse embryonic stem cells in vitro. *Neuroreport* **2013**, *24*, 1041–1046. [[CrossRef](#)] [[PubMed](#)]
168. Lu, L.; Tang, L.; Wei, W.; Hong, Y.; Chen, H.; Ying, W.; Chen, S. Nicotinamide mononucleotide improves energy activity and survival rate in an in vitro model of Parkinson's disease. *Exp. Ther. Med.* **2014**, *8*, 943–950. [[CrossRef](#)]
169. Kuypers, N.J.; Hoane, M.R. Pyridoxine administration improves behavioral and anatomical outcomes after unilateral contusion injury in the rat. *J. Neurotrauma* **2010**, *27*, 1275–1282. [[CrossRef](#)]
170. Calderón-Ospina, C.A.; Nava-Mesa, M.O. B Vitamins in the nervous system: Current knowledge of the biochemical modes of action and synergies of thiamine, pyridoxine, and cobalamin. *CNS Neurosci. Ther.* **2020**, *26*, 5–13. [[CrossRef](#)]
171. Volkov, I. The master key effect of vitamin B12 in the treatment of malignancy- A potential therapy? *Med. Hypotheses* **2008**, *70*, 324–328. [[CrossRef](#)] [[PubMed](#)]
172. De Queiroz, K.B.; Cavalcante-Silva, V.; Lopes, F.L.; Rocha, G.A.; D'Almeida, V.; Coimbra, R.S. Vitamin B12 is neuroprotective in experimental pneumococcal meningitis through modulation of hippocampal DNA methylation. *J. Neuroinflamm.* **2020**, *17*, 1–12. [[CrossRef](#)]

173. Seitz, G.; Gerbhardt, S.; Beck, J.F.; Bohm, W.; Lode, H.N.; Niethammer, D.; Bruchelt, G. Ascorbic acid stimulates DOPA synthesis and tyrosine hydroxylase gene expression in the human neuroblastoma cell line SK-N-SH. *Neurosci. Lett.* **1998**, *244*, 33–36. [[CrossRef](#)]
174. Huang, H.O.; Caballero, B.; Chang, S.; Alberg, A.; Semba, R.; Schneyer, C.; Wilson, R.F.; Cheng, T.Y.; Prokopowicz, G.; Barnes, G.J.; et al. Multivitamin/mineral supplements and prevention of chronic disease. *Evid. Rep. Technol. Assess.* **2006**, *139*, 1–117.
175. Sershen, H.; Mason, M.F.; Reith, M.E.A.; Hashim, A.; Lajtha, A. Effect of nicotine and amphetamine on the neurotoxicity of N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in mice. *Neuropharmacology* **1985**, *25*, 1231–1234. [[CrossRef](#)]
176. Pardo, J.V.; Pardo, P.J.; Raichle, M.E. Neural correlates of self-induced dysphoria. *Am. J. Psychiatry* **1993**, *150*, 713–719.
177. Schepers, M.; Martens, N.; Tiane, A.; Vanbrabant, K.; Liu, H.B.; Lütjohann, D.; Mulder, M.; Vanmierlo, T. Edible seaweed-derived constituents: An undisclosed source of neuroprotective compounds. *Neural Regen. Res.* **2020**, *15*, 790–795. [[PubMed](#)]
178. Javed, H.; Meeran, M.F.N.; Azimullah, S.; Adem, A.; Sadek, B.; Ojha, S.K. Plant extracts and phytochemicals targeting α -synuclein aggregation in Parkinson's disease models. *Front. Pharmacol.* **2019**, *9*, 1–27. [[CrossRef](#)]
179. Kanhere, R.; Anjana, A.; Anbu, J.; Sumithra, M.; Ahamed, N. Neuroprotective and antioxidant potential of terpenoid fraction from *Hygrophila auriculata* against transient global cerebral ischemia in rats. *Pharm. Biol.* **2013**, *51*, 181–189. [[CrossRef](#)]
180. Choi, S.U.; Park, S.H.; Kim, K.H.; Choi, E.J.; Kim, S.; Park, W.K.; Zhang, Y.H.; Kim, H.S.; Jung, N.P.; Lee, C.O. The bisbenzylisoquinoline alkaloids, tetrandrine, and fangchinoline enhance the cytotoxicity of multidrug resistance-related drugs via modulation of P-glycoprotein. *Anticancer Drugs* **1998**, *9*, 255–261. [[CrossRef](#)]
181. Sun, J.; Li, M.; Zou, F.; Bai, S.; Jiang, X.; Tian, L.; Ou, S.; Jiao, R.; Bai, W. Protection of cyanidin-3-O-glucoside against acrylamide and glycidamide-induced reproductive toxicity in Leydig cells. *Food Chem. Toxicol.* **2018**, *119*, 268–274. [[CrossRef](#)] [[PubMed](#)]
182. Li, X.; Chu, S.; Liu, Y.; Chen, N. Neuroprotective effects of anthraquinones from *Rhubarb* in central nervous system diseases. *Evid. Based Complement. Alternat. Med.* **2019**, *2019*, 1–12. [[CrossRef](#)]
183. Bo, S.; Lai, J.; Lin, H.; Luo, X.; Zeng, Y.; Du, T. Purpurin, an anthraquinone that induces ROS-mediated A549 lung cancer cell apoptosis via inhibition of PI3K/AKT and proliferation. *J. Pharm. Pharmacol.* **2021**, *73*, 1101–1108. [[CrossRef](#)] [[PubMed](#)]
184. Liu, B.; Xie, J.; Ge, X.; Xu, P.; Wang, A.; Heb, Y.; Zhoub, Q.; Pan, L.; Chen, R. Effects of anthraquinone extract from *Rheum officinale* Bail on the growth performance and physiological responses of *Macrobrachium rosenbergii* under high-temperature stress. *Fish Shellfish Immunol.* **2010**, *29*, 49–57. [[CrossRef](#)] [[PubMed](#)]
185. Ma, L.; Zhao, L.; Hu, H.; Qin, Y.; Bian, Y.; Jiang, H.; Zhou, H.; Yu, L.; Zeng, S. Interaction of five anthraquinones from rhubarb with human organic anion transporter 1 (SLC22A6) and 3 (SLC22A8) and drug-drug interaction in rats. *J. Ethnopharmacol.* **2014**, *153*, 864–871. [[CrossRef](#)] [[PubMed](#)]
186. Aldbass, A.; Amina, M.; Al Musayeib, N.M.; Bhat, R.S.; Al-Rashed, S.; Marraiki, N.; Fahmy, R.; El-Ansary, A. Cytotoxic and anti-excitotoxic effects of selected plant and algal extracts using COMET and cell viability assays. *Sci. Rep.* **2021**, *11*, 8512. [[CrossRef](#)] [[PubMed](#)]
187. Yang, N.; Xiang, L.; Cao, F.; Li, H.; Wang, X. Research progress on the effects and mechanisms of emodin in Tumor Metastasis. *Zhong Liu Yao Xue* **2016**, *6*, 173–177.
188. Gutierrez, J.M.; Carvalho, F.B.; Schetinger, M.R.C.; Rodrigues, M.V.; Schmatz, R.; Pimentel, V.C.; Vieira, J.M.; Rosa, M.M.; Marisco, P.; Ribeiro, D.A.; et al. Protective effects of anthocyanins on the ectionucleotidase activity in the impairment of memory induced by scopolamine in adult rats. *Life Sci.* **2012**, *91*, 1221–1228. [[CrossRef](#)]
189. Jeter, C.B.; Hergenroeder, G.W.; Ward, N.H., III; Moore, A.N.; Dash, P.K. L-arginine, and its metabolite levels: A possible link to cerebral blood flow, extracellular matrix remodeling, and energy status. *J. Neurotrauma* **2012**, *29*, 119–127. [[CrossRef](#)]
190. Liu, H.; Goodman, J.C.; Robertson, C.S. The effects of L-arginine on cerebral hemodynamics after controlled cortical impact injury in the mouse. *J. Neurotrauma* **2004**, *19*, 327–334. [[CrossRef](#)]
191. Cherian, L.; Chacko, G.; Goodman, C.; Robertson, C.S. Neuroprotective effects of L-arginine administration after cortical impact injury in rats: Dose-response and time window. *J. Pharmacol. Exp. Ther.* **2003**, *304*, 617–623. [[CrossRef](#)] [[PubMed](#)]
192. Bitner, B.R.; Brink, D.C.; Mathew, L.C.; Pautler, R.G.; Robertson, C.S. Impact of arginase II on CBF in experimental cortical impact injury in mice using MRI. *J. Cereb. Blood Flow Metab.* **2010**, *30*, 1105–1109. [[CrossRef](#)]
193. De George, M.L.; Marlowe, D.; Werner, E.; Soderstrom, K.E.; Stock, M.; Mueller, A.; Bohn, M.C.; Kozlowski, D.A. Combining glial cell line-derived neurotrophic factor gene delivery (AdGDNF) with L-arginine decreases contusion size but not behavioral deficits after traumatic brain injury. *Brain Res.* **2011**, *1403*, 45–56. [[CrossRef](#)] [[PubMed](#)]
194. Meloni, B.P.; Craig, A.J.; Milech, N.; Hopkins, R.M.; Watt, P.M.; Knuckey, N.W. The neuroprotective efficacy of cell-penetrating peptides TAT, penetratin, Arg-9, and Pep-1 in glutamic acid, kainic acid, and in vitro ischemia injury models using primary cortical neuronal cultures. *Cell. Mol. Neurobiol.* **2014**, *34*, 173–181. [[CrossRef](#)] [[PubMed](#)]
195. Meloni, B.P.; Milani, D.; Cross, J.L.; Clark, V.W.; Edwards, A.B.; Anderton, R.S.; Blacker, D.J.; Knuckey, N.W. Assessment of the neuroprotective effects of arginine-rich protamine peptides, poly-arginine peptides (R12-Cyclic, R22), and arginine-tryptophan-containing peptides following *in vitro* excitotoxicity and/or permanent middle cerebral artery occlusion in rats. *Neuromolecular Med.* **2017**, *19*, 271–285. [[CrossRef](#)]
196. Edwards, A.B.; Cross, J.L.; Anderton, R.S.; Knuckey, N.W.; Meloni, B.P. Poly-arginine R18 and R18D (D-enantiomer) peptides reduce infarct volume and improve behavioral outcomes following perinatal hypoxic-ischaemic encephalopathy in the P7 rat. *Mol. Brain* **2018**, *11*, 1–12. [[CrossRef](#)] [[PubMed](#)]

197. Sachdeva, A.K.; Chopra, K. Lycopene abrogates A β (1-42)-mediated neuroinflammatory cascade in an experimental model of Alzheimer's disease. *J. Nutr. Biochem.* **2015**, *26*, 736–744. [[CrossRef](#)] [[PubMed](#)]
198. Lorenzo, Y.; Azqueta, A.; Luna, L.; Bonilla, F.; Domínguez, G.; Collins, A.R. The carotenoid β -cryptoxanthin stimulates the repair of DNA oxidation damage in addition to acting as an antioxidant in human cells. *Carcinogenesis* **2008**, *30*, 308–314. [[CrossRef](#)]
199. Brimson, J.M.; Brimson, S.J.; Brimson, C.A.; Rakkhitawatthana, V.; Tencomnao, T. *Rhinacanthus nasutus* extracts prevent glutamate and amyloid- β neurotoxicity in HT-22 mouse hippocampal cells: Possible active compounds include lupeol, stigmasterol, and β -sitosterol. *Int. J. Mol. Sci.* **2012**, *13*, 5074–5097. [[CrossRef](#)] [[PubMed](#)]
200. Hamedi, A.; Ghanbari, A.; Saeidi, V.; Razavipour, R.; Azari, H. Effects of β -sitosterol oral administration on the proliferation and differentiation of neural stem cells. *J. Funct. Foods* **2014**, *8*, 252–258. [[CrossRef](#)]
201. Hamedi, A.; Ghanbari, A.; Razavipour, R.; Saeidi, V.; Zarshenas, M.M.; Sohrabpour, M.; Azari, H. *Alyssum homolocarpum* seeds: Phytochemical analysis and effects of the seed oil on neural stem cell proliferation and differentiation. *J. Nat. Med.* **2015**, *69*, 387–396. [[CrossRef](#)]
202. Cheng, F.C.; Jinn, T.R.; Hou, R.C.W.; Tzen, J.T.C. Neuroprotective effects of sesamin and sesamol on Gerbil brain in cerebral ischemia. *Int. J. Biomed.* **2006**, *2*, 284–288.
203. Shimmyo, Y.; Kihara, T.; Akaike, A.; Niidome, T.; Sugimoto, H. Multifunction of myricetin on A beta: Neuroprotection via a conformational change of A-beta and reduction of A beta via the interference of secretases. *J. Neurosci. Res.* **2008**, *86*, 368–377. [[CrossRef](#)]
204. Jones, J.R.; Lebar, M.D.; Jinwal, U.K.; Abisambra, J.K.; Koren, J., III; Blair, L.; O'Leary, J.C.; Davey, Z.; Trotter, J.; Johnson, A.G.; et al. The diarylheptanoid (+)-aR, 11S-myricanol, and two flavones from bayberry (*Myrica cerifera*) destabilize the microtubule-associated protein Tau. *J. Nat. Prod.* **2011**, *74*, 38–44. [[CrossRef](#)] [[PubMed](#)]
205. Pinto, N.B.; Alexandre, B.; Neves, K.R.T.; Silva, A.H.; Leal, L.K.A.M.; Viana, G.S.B. Neuroprotective properties of the standardized extract from *Camellia sinensis* (Green Tea) and its main bioactive components, epicatechin and epigallocatechin gallate, in the 6-OHDA model of Parkinson's disease. *Evid. Based Complement. Alternat. Med.* **2015**, *2015*, 161092.
206. Cifuentes, J.; Salazar, V.A.; Cuellar, M.; Castellanos, M.C.; Rodríguez, J.; Cruz, J.C.; Muñoz-Camargo, C. Antioxidant and Neuroprotective Properties of Non-Centrifugal Cane Sugar and Other Sugarcane Derivatives in an In Vitro Induced Parkinson's Model. *Antioxidants* **2021**, *10*, 1040. [[CrossRef](#)]
207. Mendonça-Junior, F.J.B.; Scotti, M.T.; Muratov, E.N.; Scotti, L.; Nayarissari, A. Natural Bioactive Products with Antioxidant Properties Useful in Neurodegenerative Diseases 2020. *Oxid. Med. Cell. Longev.* **2021**, *2021*, 1–2. [[CrossRef](#)]
208. Hossain, M.T.; Furhatun-Noor; Asadujjaman; Matin, A.; Tabassum, F.; Ar Rashid, H. A Review study on the pharmacological effects and mechanism of action of Tannins. *Eur. J. Pharm. Med. Res.* **2021**, *8*, 5–10.
209. Soldado, D.; Bessa, R.J.B.; Jeronimo, E. Condensed Tannins as Antioxidants in Ruminants—Effectiveness and Action Mechanisms to Improve Animal Antioxidant Status and Oxidative Stability of Products. *Animals* **2021**, *11*, 3243. [[CrossRef](#)]
210. Puiggròs, F.; Llópiz, N.; Ardévol, A.; Bladé, C.; Arola, L.; Salvadó, M.J. Grape Seed Procyanidins Prevent Oxidative Injury by Modulating the Expression of Antioxidant Enzyme Systems. *J. Agric. Food Chem.* **2005**, *53*, 6080–6086. [[CrossRef](#)] [[PubMed](#)]
211. Ali, T.; Kim, T.; Rehman, S.U.; Khan, M.S.; Amin, F.U.; Khan, M.; Ikram, M.; Kim, M.O. Natural Dietary Supplementation of Anthocyanins via PI3K/Akt/Nrf2/HO-1 Pathways Mitigate Oxidative Stress, Neurodegeneration, and Memory Impairment in a Mouse Model of Alzheimer's Disease. *Mol. Neurobiol.* **2018**, *55*, 6076–6093. [[CrossRef](#)]
212. Echeverry, C.; Arredondo, F.; Abin-Carriquiry, J.A.; Midiwo, J.O.; Ochieng, C.; Kerubo, L.; Dajas, F. Pretreatment with Natural Flavones and Neuronal Cell Survival after Oxidative Stress: A Structure-Activity Relationship Study. *J. Agric. Food Chem.* **2010**, *58*, 2111–2115. [[CrossRef](#)]
213. Boesch-Saadatmandi, C.; Pospissil, R.T.; Graeser, A.; Canali, R.; Boomgaarden, I.; Doering, F.; Wolffram, S.; Egert, S.; Mueller, M.J.; Rimbach, G. Effect of Quercetin on Paraoxonase 2 Levels in RAW264.7 Macrophages and in Human Monocytes- Role of Quercetin Metabolism. *Int. J. Mol. Sci.* **2009**, *10*, 4168–4177. [[CrossRef](#)] [[PubMed](#)]
214. Costa, L.G.; Tait, L.; de Laat, R.; Dao, K.; Giordano, G.; Pellacani, C.; Cole, T.B.; Furlong, C.E. Modulation of paraoxonase 2 (PON2) in mouse brain by the polyphenol quercetin: A mechanism of neuroprotection? *Neurochem. Res.* **2014**, *38*, 1809–1818. [[CrossRef](#)] [[PubMed](#)]
215. Grewal, A.K.; Singha, T.G.; Sharma, D.; Sharma, V.; Singh, M.; Rahman, H.; Najda, A.; Walasek-Janusz, M.; Kamel, M.; Albadrani, G.M.; et al. Mechanistic insights and perspectives involved in neuroprotective action of quercetin. *Biomed. Pharmacother.* **2021**, *140*, 111729. [[CrossRef](#)] [[PubMed](#)]
216. Zhang, Z.J.; Cheang, L.C.V.; Wang, M.W.; Lee, S.M. Quercetin exerts a neuroprotective effect through inhibition of the iNOS/NO system and pro-inflammation gene expression in PC12 cells and in zebrafish. *Int. J. Mol. Med.* **2011**, *27*, 195–203.
217. Ansari, M.A.; Abdul, H.M.; Joshi, G.; Opii, W.O.; Butterfield, D.A. Protective effect of quercetin in primary neurons against Abeta(1-42): Relevance to Alzheimer's disease. *J. Nutr. Biochem.* **2009**, *20*, 269–275. [[CrossRef](#)] [[PubMed](#)]
218. Salehi, B.; Machin, L.; Monzote, L.; Sharifi-Rad, J.; Ezzat, S.M.; Salem, M.A.; Merghany, R.M.; El Mahdy, N.M.; Kılıç, C.S.; Sytar, O.; et al. Therapeutic Potential of Quercetin: New Insights and Perspectives for Human Health. *ACS Omega* **2020**, *5*, 11849–11872. [[CrossRef](#)] [[PubMed](#)]
219. Khazdair, M.R.; Ghafari, S.; Sadeghi, M. Possible therapeutic effects of *Nigella sativa* and its thymoquinone on COVID-19. *Pharm. Biol.* **2021**, *59*, 696–703. [[CrossRef](#)]

220. Kavya Bhatt, S.; Manjunatha Javagal, R.; Shashirekha Nanjarajurs, M.; Eligar, S.M. In vitro anti-inflammatory property of a Quercetin-3-O-diglucoside-7-O-glucoside characterized from fresh leaves of *Trigonella foenum-graecum* L. *Int. J. Food Prop.* **2021**, *24*, 1438–1452. [[CrossRef](#)]
221. Wang, J.; Fang, X.; Ge, L.; Cao, F.; Zhao, L.; Wang, Z.; Xiao, W. Antitumor, antioxidant and anti-inflammatory activities of kaempferol and its corresponding glycosides and the enzymatic preparation of kaempferol. *PLoS ONE* **2018**, *13*, e0197563. [[CrossRef](#)]
222. Isah, T. Anticancer Alkaloids from Trees: Development into Drugs. Pharmacognosy Reviews. *Pharmacogn. Rev.* **2016**, *10*, 90–99. [[CrossRef](#)]
223. Huang, Y.; Cui, S.; Cui, X.; Cao, Q.; Ding, H.; Song, J.; Hu, X.; Ye, H.; Yu, B.; Sheng, Z.; et al. Tetrandrine, an alkaloid from *S. tetrandra* exhibits anti-hypertensive and sleep-enhancing effects in SHR via different mechanisms. *Phytomedicine* **2016**, *23*, 1821–1829. [[CrossRef](#)]
224. Yang, Z.; Zhang, D.; Ren, J.; Yang, M. Skimmianine, a furoquinoline alkaloid from *Zanthoxylum nitidum* as a potential acetylcholinesterase inhibitor. *Med. Chem. Res.* **2012**, *2*, 722–725. [[CrossRef](#)]
225. Shimizu, M.; Shirakami, Y.; Moriwaki, H. Targeting Receptor Tyrosine Kinases for Chemoprevention by Green Tea Catechin, EGCG. *Int. J. Mol. Sci.* **2008**, *9*, 1034–1049. [[CrossRef](#)] [[PubMed](#)]
226. Coșarcă, S.; Tanase, C.; Muntean, D.L. Therapeutic aspects of Catechin and its derivatives—An Update. *Acta Biol. Marisiensis* **2019**, *2*, 21–29. [[CrossRef](#)]
227. Yang, W.; Chen, X.; Li, Y.; Guo, S.; Wang, Z.; Yu, X. Advances in Pharmacological Activities of Terpenoids. *Nat. Prod. Commun.* **2020**, *15*, 1–13. [[CrossRef](#)]
228. Yoo, K.; Park, S. Terpenoids as potential anti-Alzheimer’s disease therapeutics. *Molecules* **2012**, *17*, 3524–3538. [[CrossRef](#)] [[PubMed](#)]
229. Kwon, K.H.; Murakami, A.; Tanaka, T.; Ohigashi, H. Dietary rutin, but not its aglycone quercetin, ameliorates dextran sulfate sodium-induced experimental colitis in mice: Attenuation of pro-inflammatory gene expression. *Biochem. Pharmacol.* **2005**, *69*, 395–406. [[CrossRef](#)] [[PubMed](#)]
230. Shamim, A.; Mahmood, T.; Ahsan, F.; Kumar, A.; Bagga, P. Lipids: An insight into the neurodegenerative disorders. *Clin. Nutr. Exp.* **2018**, *20*, 1–19. [[CrossRef](#)]