Incorporation of adaptogens in functional products as a preventive sttrattegy for neurodegenerative diseases

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INTRODUCTION

CONTEXTUALIZATION

Neurodegenerative diseases (ND), such as Alzheimer and Parkinson, represent a growing challenge for public health worldwide (**Figure 1**).

Various studies warn that their incidence continues to rise and they are expected to become the second leading cause of death after cardiovascular diseases in the coming decades.

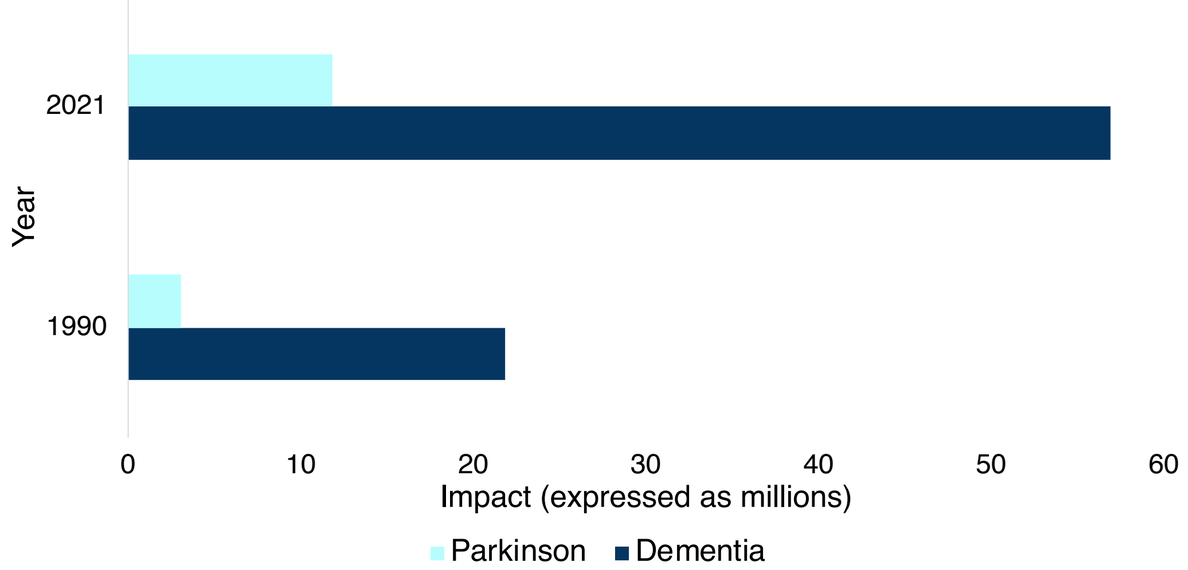

Figure 1. General vision on neurodegenerative diseases (ND) evolution globally. The two major ND, Dementia and Parkinson, are included. Dementia data includes Alzheimer disease (Shu Wang et al., **2024**).

There are several biomarkers that have been identified to be linked to neurodegeneration **(Figure 2)**. This biomarkers can be classified in:

- **sinaptic biomarkers**, which function is to which reflect neuronal function or plasticity, neuronal energy metabolism or mitochondrial biogenesis, which directly impact synaptic activity
- **apoptotic biomarkers**, which that are associated with neuronal cell death or cell survival mechanisms
- **neuroinflammatory biomarkers**, which reflect the activation of microglia and astrocytes, as well as the release of pro- and anti-inflammatory cytokines.

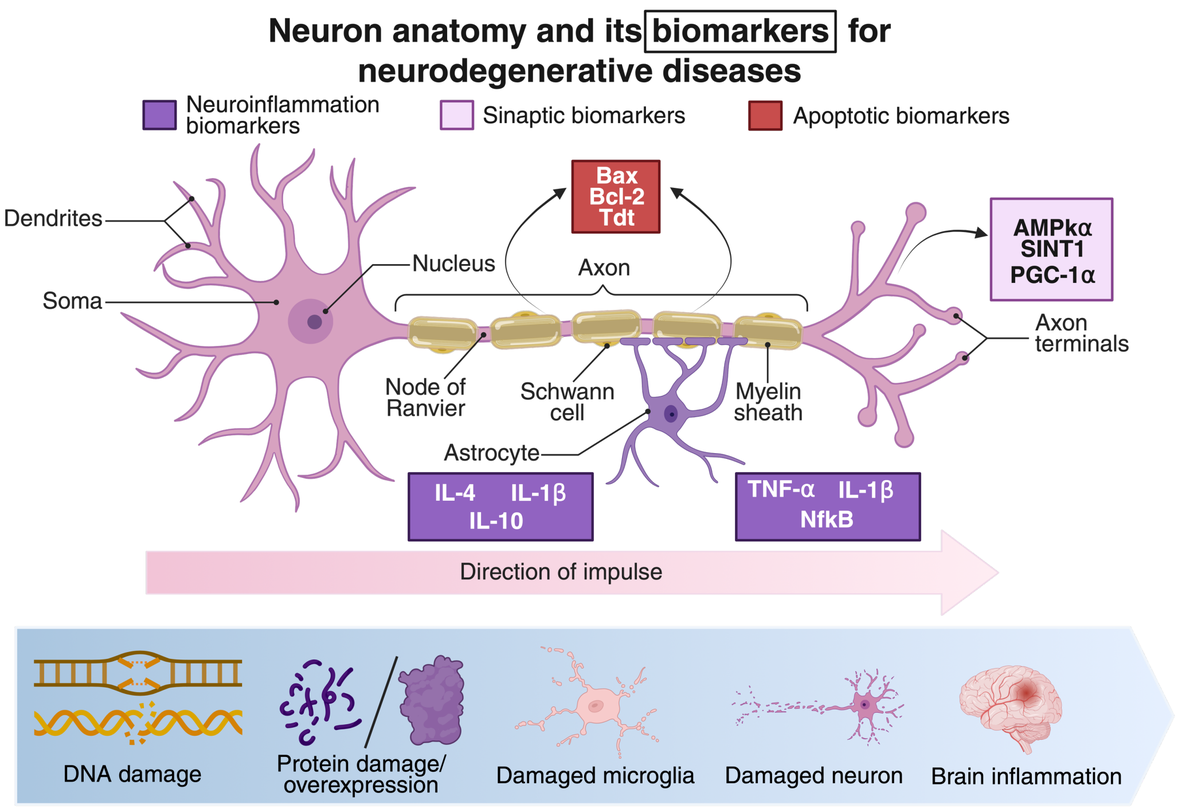

Figure 2. General vision of neuron anatomy with biomarkers to detect neurodegenerative diseases (up) and the neurodegenerative progression from DNA damage to brain inflammation (down). Abbreviations: AMPKα: protein kinase α; SIRT1: sirutin 1; PGC-1α: peroxisome proliferator-activated receptor γ coactivator-1α; TdT: terminal deoxunucleotidyl transferase; Bcl-2: B-cell limphoma 2; IL-1β: interleukin 1β; IL-6: interleukin 6; IL-4: interleukin 4; IL-10: interleukin 10; TNF-α: tumor necrosis factor α; NFkB: nuclear factor k B.

APPROACH

Current scientific evidence highlights the need for **effective preventive strategies**, with **dietary intervention emerging as a promising approach**.

RESULTS

Polyphenols, B vitamins, omega-3 fatty acids and certain dietary patterns have shown beneficial effects on key mechanisms involved in neurodegeneration, including inflammation, oxidative stress and mitochondrial dysfunction.

Particularly, resveratrol, hesperidin, theobromine, quercetin, and oleuropein, have demonstrated neuroprotective properties **(Table 1)**.

These compounds can also be considered adaptogens, defined as natural substances that enhance the body's resistance to physical, chemical, or biological stress while exerting a normalizing influence on physiological functions.

Table 1. Mechanisms linked to neurodegenerative disorders (ND) and the potential used of selected compounds as preventive strategies.

RF	Study	Treatment	Effect	Ref.
ND	*In vitro* (N2a cells)	**RT**, AP & **QT** 3.125-6.25 μM	↓Oxidative stress Prevention of mitochondrial dysfunction AMPKα, SIRT1 and PGC-1α activation	(Yammine et al., 2020)
Aging	*In vitro* (VSMC)	**QT** 50 μM, 6 hours	↓induced senescence Promotion of apoptosis through AMPK signalling pathway in senescent VSMC	(Kim et al., 2019)
DPN	*In vitro* (RSC96)	**QT** 5, 10, 20 μM	Activation of AMPK/PGC-1α	(Zhang et al., 2021)
	In vivo	**QT** 60 mg/Kg, 8 weeks		
SCI	*In vivo*	**OP** 20 mg/Kg, 8 weeks	↓malondialdehyde levels ↓Bax expression ↓TdT ↑glutathione levels ↑Bcl-2 expression	(Kalatbary & Ahmadvand, 2013)
AD	*In vivo*	**HP** 50-100 mg/Kg, 156 weeks	↑Bcl-2 expression ↓Bax expression	(Wang et al., 2014)
PD	*In vivo*	**HP** 50-100 mg/Kg, 14 days	↓IL-1β, TNF-α, IL- 6,4,10	(Tamilselvam, 2013)
tGCI	*In vivo*	**TB** 50-100 mg/Kg, 7 days	↑glutathione levels ↓TNF-α, NFkB	(Bhat et al., 2021)

General abbreviations: RF: Risk factor; ND: neurodegenerative diseases; DPN: diabetic peripheral neuropathy; SCI: spinal cord injury; AD: Alzheimer's disease; PD: Parkinson disease; tGCI: transient global cerebral ischemia; **Compounds:** RT: resveratrol; QT: quercetin; HP: heperidin; OP: oleuropeín; TB: theobromine; AP: apigenin; **Cell lines:** N2a: murine neuroblastoma 2a; VSMC: vascular smooth muscle cell line; RSC96: Rat schwann cell line; **Biomarker:** AMPKα: protein kinase α; SIRT1: sirutin 1; PGC-1α: peroxisome proliferator-activated receptor γ coactivator-1α; TdT: terminal deoxunucleotidyl transferase; Bcl-2: B-cell limphoma 2; IL-1β: interleukin 1β; IL-6: interleukin 6; IL-4: interleukin 4; IL-10: interleukin 10; TNF-α: tumor necrosis factor α; NFkB: nuclear factor k B.

These compounds can be sustainably sourced from agri-food by-products, such as grape skin, citrus peel, cocoa waste, apple peel, and olive leaves, and can be incorporated into functional food products as a preventive strategy for ND while promoting a circular economy.

CONCLUSIONS & FUTURE PERSPECTIVES

1. There is an urgent need to develop preventive strategies for the ND prevention.
2. There are compounds present in food matrices that have demonstrate neuroprotective effect through different pathways.
3. The use of these compound in the functional foods development present a suitable strategy for the prevention of neurodegenerative diseases, such as Parkinson and dementia related diseases.

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