A healthy diet shapes a healthy mind. Diet quality has a strong association with brain health. Diet influences the onset and consequences of neurological diseases, and dietary factors may influence mental health at individual and population level. The link between unhealthy diet, impaired cognitive function and neurodegenerative diseases indicates that adopting a healthy diet would ultimately afford prevention and management of neurological diseases and brain aging. Neurodegenerative diseases are of multifactorial origin and result in progressive loss of neuronal function in the brain, leading to cognitive impairment and motor neuron disorders. The so-called Mediterranean diet (MedDiet) with its healthy ingredients rich in antioxidant, anti-inflammatory, immune, neuroprotective, antidepressant, antistress and senolytic activity plays an essential role in the prevention and management of neurological diseases and inhibits cognitive decline in neurodegenerative diseases such as Alzheimer’s, Parkinson’s and Huntington’s diseases. The MedDiet also modulates the gut-brain axis by promoting a diversity of gut microbiota. In view of the importance of diet in neurological diseases management, this review focuses on the dietary components, natural compounds and medicinal plants that have proven beneficial in neurological diseases and for brain health. Among them, polyphenols, omega-3 fatty acids, B vitamins and several ayurvedic herbs have promising beneficial effects.

**Introduction**

Neurodegenerative diseases (NDs) involve a progressive loss of neuronal activity, resulting in impairment of cognitive function. They have genetic and epigenetic etiology and are increasing at an alarming rate. For instance, 17.2 million people worldwide are suffering from NDs such as Alzheimer’s disease (AD), Parkinson’s disease (PD), amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Huntington’s disease (HD) and dementia [1, 2]. As the symptoms appear only when neurological degeneration has reached an advanced stage, the prevention of NDs and the search for new therapeutic agents is a challenge. Although the mechanisms of NDs are multifactorial and complex, they share common pathways, such as oxidative stress, inflammation, mitochondrial dysfunction and intracellular Ca$^{2+}$ overload. In addition, cross talk between these multiple pathways often makes therapeutic intervention less effective. The brain is highly sensitive to oxidative stress and increased reactive oxygen species produced during neuroinflammatory processes. As the antioxidant defence system has low activity in the brain, increased oxidative stress results in NDs and aging [3]. Genetic and epigenetic factors greatly influence the onset and development of these disorders, while nutrition and metabolism play a key role in the manifestation of epigenetic modifications of DNA in the central nervous system [4-5]. Bioactive ingredients in food and gut microbiota can greatly influence DNA methylation in the adult central nervous system, indicating a role of diet and dietary components in NDs [6]. The so-called Mediterranean diet (MedDiet) is currently regarded as the healthiest diet in the world. It includes daily intake of whole grains, vegetables, fruit, legumes, white meats, fish, nuts, olives and olive oil. Rich in antioxidants, fibre, vitamins, minerals, phytosterols, probiotics, omega-3 and omega-6 fatty acids, B vitamins and several ayurvedic herbs have promising beneficial effects.

**Clinical studies on efficacy of MedDiet in major neurodegenerative disorders**

Several studies have evaluated the efficacy of the MedDiet in prevention and management of neurodegenerative disorders (Tab. I). These studies inferred that following the MedDiet not only decreases the incidence of NDs but also improves overall cognitive function and hampers the onset and progress of decline caused by NDs and cerebral aging.
Animal studies and clinical trials have shown that the MedDiet has anti-inflammatory, antioxidant and free radical-scavenging properties that alleviate or mitigate neurotoxicity and neurodegeneration (Tab. II).

**MedDiet and depression**

Increasing evidence suggests that depression, the foremost global cause of disability, is a subtle neurological disorder [22, 23]. Besides other therapies, diet may be useful for improving overall mental health and relieving stress and anxiety. The MedDiet, rich in vitamins, minerals, antioxidants, healthy fats and proteins, reduces the risk of depression [24]. Research-based evidence suggests that dietary measures can be an adjunctive treatment for mental disorders. For instance, a healthy diet has been tested clinically in two different trials for its effects on symptoms and remission rates of depression, showing promising results [25, 26]. As many as 37 studies have reported a reduction in symptoms of depression in groups of persons on diets rich in polyphenols [27]. An observational study also revealed that following the MedDiet was crucial for reducing depressive outcomes in overweight patients with metabolic syndrome [28]. Vicinanza et al. (2020) reported a positive impact of the MedDiet on mental health in elderly patients with multimorbidity [29]. They also observed that the diet prevented symptoms of depression in these patients, promoting healthy aging. Yet another promising clinical study named PREDI-DEP is underway to assess the MedDiet supplemented with extra virgin olive oil or nuts for precluding relapse of unipolar depression [30]. Diet plays an important role in shaping behaviour and modulating mood (Tab. III). For instance, omega-3 essential fatty acid supplements alleviated symptoms of bipolar disorder in 30 patients [31].

**Effect of natural compounds and medicinal plants on neurological disorders**

Several medicinal plants and natural compounds have been deployed to prevent or alleviate neurological diseases and symptoms in vivo and in clinical trials. Here we discuss important natural compounds that can be obtained from dietary sources or nutritional supplements and that mediate various aspects of practical utility in the management of neurodegenerative disorders.

**N-acetylcysteine (NAC) in neurological disorders**

N-acetylcysteine (NAC) is a mucolytic thiol known for its ability to alleviate stress and mediate the impacts of toxicity, infections and inflammatory conditions by supporting the body’s antioxidant and nitric oxide systems [37]. It crosses blood brain barrier (BBB) and is a precursor of l-cysteine and reduced glutathione GSH, as well as a source of sulfhydryl groups in cells. It scavenges free radicals and interacts with reactive oxygen species (ROS) [38]. It has a multifaceted mode of action, acting as a drug, a xenobiotic and a cytoprotectant. The effects of NAC on various neurological and neurodegenerative diseases are summarized in Table IV.

**Effects of phospholipids on neurological conditions**

The brain and nervous system have a more diverse lipid composition than the rest of the body, showing a pre-
dominance of phospholipids [45]. Phospholipids occur in varying concentrations in the brain, e.g. 31 nmol/mg phosphatidylcholine, 54 nmol/mg phosphatidylethanolamine, 8 nmol/mg phosphatidylserine and 5 nmol/mg of phosphatidylinositol [46]. Sphingomyelin levels in the hippocampus and prefrontal cortex are similar to those of phosphatidylethanolamine in adult male rats [47]. Phospholipids also occur in the membranes of organelles such as mitochondria, endoplasmic reticulum, Golgi apparatus, peroxisomes and lysosomes, which illustrates their importance in cells. Studies have revealed that phospholipid-enriched diets can modulate cognitive processes [48] and phospholipid supplementation has been shown to increase cognitive function in a polyunsaturated fatty acid-deficient mice model and to improve memory in piglets on permanent supplements [49].

Phosphatidylserine

Phosphatidylserine (PS) is an acidic phospholipid and a natural component of brain neuronal membranes and other biological membranes. It plays a pivotal role in normal neuronal function by determining neuronal membrane surface potential and the local ionic environment [50]. Phosphatidylserine is a brain-specific nutrient [51] and activates protein kinase C (PKC) in neural membranes. It is thought to decrease in the brain with aging, leading to cognitive decline and impairment as well as lower PKC

| Neurological conditions | Description | Study type | Participants | Duration | Findings | Reference |
|-------------------------|-------------|------------|--------------|----------|----------|-----------|
| Alzheimer’s disease     | Formation of widespread extracellular amyloid plaques and intraneuronal neurofibrillary tangles in the brain (Reitz and Mayeux, 2014), a major cause of dementia | Follow-up study | 70 subjects with normal cognitive function, age 50-60 years | 3 | Not following MedDiet was correlated with progressive AD abnormalities | [7] |
| Dementia                | Loss of cognitive function due to brain aging or neurodegenerative diseases | Longitudinal | 1865 (41%M) patients with dementia, mean age 75 years | 1.4 | 10% decrease in dementia on MedDiet. Cereals shown to have positive impact on mental performance | [9] |
| Huntington’s disease    | a rare, hereditary condition that causes progressive neurodegeneration | Prospective | 211 patients with expanded CAG repeats | 3.4 | Diet and high energy intake may delay onset | [11] |
| Parkinson’s disease (PD)| Neuronal degeneration, dopaminergic loss. PD symptoms include tremors, motoneuron changes, cognitive decline, dementia and loss of muscle strength (Gratwicke et al., 2015) | Population-based cohort | 1731 (41% male) PD-free individuals, age 65 and over | - | MedDiet lowered probability of prodromal PD in elderly people | [12] |
| Amyotrophic lateral sclerosis (ALS) | Degeneration of brainstem and spinal cord motoneurons resulting in progressive muscle atrophy, paralysis and respiratory failure (Oh et al., 2015) | Cross sectional baseline analysis | 302 patients with a history of ALS symptoms of 18 months or less | - | Better function associated with antioxidants and with carotenoids in fruit and vegetables | [13] |
| Multiple sclerosis      | Demyelination of nerve fibres and myelin sheaths, affecting the optic nerves, brain and spinal cord | Survey | 396 | - | MedDiet reduces risk of relapses | [14] |
**Tab. III.** Effect of dietary components and regimes on mood and psychological disorders.

| Dietary components/ regimes | Effect on mood | Study type | Participants | Reference |
|-----------------------------|----------------|------------|--------------|-----------|
| Vitamin D                   | Improved mood  | Double-blind placebo-controlled | 44 healthy volunteers | [22]      |
| Vitamins, minerals, and essential fatty acids | Reduction in antisocial behaviour | Double-blind, placebo-controlled | 231 young adult prisoners | [32]      |
| Tryptophan depletion         | Worsening of mood in seasonal affective disorder/winter type (SAD) | Randomized, balanced, double-blind crossover | 11 SAD patients with recurrent episodes of winter depression | [33]      |
| Folic acid therapy          | Improved intellectual function | - | 16 patients with impaired intellectual function | [34, 35] |
| Folic acid deficiency        | Increased depression, impaired cognitive function, impaired abstract thinking | - | 260 healthy subjects 60 to 94 years old | [36]      |
| Omega 3 fatty acids          | Improved short-term course of illness in bipolar disorder | Placebo controlled | 30 patients with bipolar disorder | [23]      |
| Traditional vs western diet  | Traditional diet reduced odds in bipolar disorder | Epidemiological cohort study | 25 women with bipolar disorder and 691 normal subjects | [31]      |

**Tab. II.** Antioxidant and anti-inflammatory nutrients of the Mediterranean diet used in animal and human studies.

| MedDiet component | Nutrient | Study design | Study population | Proposed antioxidant activity | References |
|-------------------|----------|--------------|------------------|------------------------------|------------|
| Extra virgin olive oil | Total polyphenol fraction of olive oil and hydroxytyrosol. | In vitro | Endothelial cells and murine myoblasts | Redox potential enhanced by increasing glutathione levels and free radical scavenging | [15,16] |
|                    | Hydroxytyrosol and tyrosol | Randomized | Male Wistar rats | Hydroxytyrosol and tyrosol activate GSH, reduce lipid peroxidation, restore glutathione balance in liver | [17] |
|                    | Extra virgin olive oil, oleuropein aglycone | Randomized | TgCRND8 mice | Inflammation and neurotoxicity reduced by induction of autophagy and recovery of lysosome system | [18] |
| Fish and dairy     | B-vitamin folate (vitamin B9) and vitamin B12 | Transverse | ALS patients | Less inflammatory damage and oxidation, improvement in myocytic atrophy | [19] |
| Citrus and green tea | Phytochemicals, triterpenoids, resveratrol | Randomized clinical | SOD1 (G93A) mice | Increased SIRT and AMPK resulting in enhanced survival of motor neurons. Resveratrol treatment reduces activation of NF-kB pathway in LPS-activated microglia and stabilizes autophagic flux | [20] |
| Diet enriched with oily fish, seafood, dairy, nuts, vegetables, fruit and eggs | Docosahexaenoic acid (DHA) | Transverse | BV-2 murine microglial cells | Unsaturated fatty acid-based decrease in toxic effects of 7-ketocholesterol | [21] |
Phosphatidylserine functions equally well in adults, children and the elderly. For instance, in young healthy males it mitigates stress-induced activation of the hypothalamus-pituitary-adrenal axis [53]. Phosphatidylserine-omega 3 supplementation reduces attention deficit hyperactivity disorder (ADHD) symptoms in children [54]. This indicates that PS may prove beneficial in correcting disrupted neural function under various conditions. It also modulates several important enzymes and proteins, such as synapsin I, that maintain neural function [55]. Table V lists some of the studies depicting the role of PS in neurological conditions.

Phosphatidylcholine

Phosphatidylcholine (PC) is the major phospholipid component of cell membranes, lecithin, organ meats, nuts and spinach. Phosphatidylcholine supplements derived from egg yolk are well-absorbed in the gut and their levels can vary in different regions of the brain under different circumstances. For instance, PC and phosphatidylethanolamine levels increase in the whole brain of a stress-induced mouse model [56], while phosphatidylethanolamine and sphingomyelin levels decrease in the prefrontal cortex, and sphingomyelin in the hippocampus [47]. Likewise, an age-induced reduction in PC and phosphatidylethanolamine levels was detected by HPLC in the hippocampus and frontal cortex of elderly persons (89-92 years) [57].

### Effects of Gamma-aminobutyric acid on brain and behaviour

Gamma-aminobutyric acid (GABA) is a non-protein amino acid found in high concentrations in different...
parts of the brain [67]. Foods such as germinated brown rice, soybean, green tea, cabbage, yogurt, kimchi and pickles are excellent sources of GABA. GABA is the main inhibitory neurotransmitter in the human cerebral cortex [68]. As a food supplement it is used to alleviate anxiety and improve sleep quality. Several studies have reported that GABA crosses the blood-brain barrier, albeit in small amounts [69]. GABA is a known antihypertensive, anti-inflammatory, antidiabetic, antimicrobial, antiallergic, hepatoprotective, renal protective and intestine protective agent [70], and it demonstrated effects on several neurological disorders (Tab. VI).

**Melatonin in neurodegeneration**

Melatonin, a neurohormone secreted by the epiphysis cerebri and extra pineal structures, has several important functions (chronobiotic, normothermal, immune-modulating, antioxidant, oncostatic, cryoprotective and anxiolytic) in the body [79]. Melatonin affects the gastrointestinal tract, cardiovascular system, reproductive system and metabolism, and regulates body weight. Acting as a chronobiotic, melatonin modifies the phase and amplitude of biological rhythms. It acts as a cytoprotective molecule in neurodegenerative disorders and aging by reversing inflammatory damage. It also prevents neurodegeneration in experimental models of Alzheimer’s and Parkinson’s disease. Melatonin supplementation has been recommended for the treatment of insomnia [80].

Table VII lists the effects of melatonin supplementation on various neurological conditions.

**Omega-3 fatty acids**

Omega-3 fatty acids are essential for a variety of physiological functions involved in neuroinflammation, neurotransmission and neurogenesis and therefore play a major role in brain development, performance and aging. The importance of omega-3 fatty acids is indicated by the fact that a deficiency leads to many neurological conditions such as depression, ADHD, schizophrenia, bipolar disorder, dementia and autism (Tab. VIII). Eicosapentaenoic (EA) and docosahexaenoic (DA) acid modulate inflammatory processes and maintain mental health, while a deficiency results in mental disorders (Tab. VIII). They also directly affect neuronal membrane fluidity and receptor function. Although omega-3 supplementation and enriched foods have long been studied for their vital role in neurological homeostasis, randomized clinical trials investigating their therapeutic potential have yielded inconclusive results, limiting their use in psychiatry. High-quality clinical trials are urgently needed to evaluate the effectiveness of omega-3 fatty acids in inhibiting and treating NDs.

**Neurotropic B vitamins**

Neurotropic B vitamins have crucial roles in the nervous system, not only as coenzymes. Their importance is in-

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**Tab. VI. GABA and prevention of neurological disorders.**

| Neurological conditions                  | Sources of GABA | Subjects                                                                 | Effect on neurological conditions                                                                 | Reference |
|-----------------------------------------|-----------------|--------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|-----------|
| Alzheimer’s disease                     | Naturally produced by cerebral cortex | Thirty-eight AD risk participants, 14 with normal cognitive function, 11 with cognitive decline, 13 with impaired cognitive function | In high-AD risk participants GABA levels were associated with the dorsomedial-dorsolateral frontal cortex | [71]      |
| Menopausal depression, insomnia and autonomic disorder | GABA-enriched rice germ | Twenty menopausal patients | Improvement in sleep, somnipathy and depression | [72]      |
| Depression                              | GABA-rich Monascus-fermented product | Depression animal model | Prevented depression | [73]      |
| Sleep quality                           | GABA powder from lactic acid bacteria fermentation | 32 Japanese volunteers | Prevented sleep disorders | [74]      |
| Sleep latency and non-REM sleep         | GABA (90.8%) and l-theanine (99.3%) | Pentobarbital-induced sleep in ICR mice | Decreased sleep latency and enhanced sleep duration | [75]      |
| Stress                                  | GABA from natural fermentation with lactic acid bacteria | 8 stressed volunteers | Increased relaxation, reduced anxiety and raised immunity | [76]      |
| Cognitive function                      | GABA-enriched product fermented with kimchi-derived lactic acid bacteria | 50 mice | Improved long-term memory loss and increased neuronal proliferation | [77]      |
|                                         | GABA-enriched fermented Laminaria japonica product | 40 elderly persons | Prevented cognitive impairment in the elderly | [78]      |
Specified by the fact that their deficiency leads to various NDs such as depression, beriberi, Wernicke’s encephalopathy, seizures, subacute combined degeneration of the spinal cord and peripheral neuropathy [92, 93]. Synergistic interaction of vitamins B1, B6 and B12 has been reported to improve neuropathic pain, motor control and nociception (Tab. IX) [94].

**S-adenosyl methionine (SAMe)**

S-adenosyl methionine (SAMe) is a major methyl donor that influences central nervous system function via cell transmethylation pathways, including but not limited to DNA methylation. It is a strong antidepressant with impacts in mouse models of amyotrophic lateral sclerosis, epilepsy and Alzheimer’s disease [100]. SAMe supplementation alters brain bioenergetics and is an effective treatment for depression (Tab. X) [101, 102].

**Tryptophan**

Essential amino acid tryptophan (TRP) is involved in various physiological processes including immunity, neuronal function and gut homeostasis. Its metabolism in humans takes place via the kynurenine and serotonin pathways and produces niacin, serotonin and melatonin. In addition, to endogenous TRP, the gut microbiota also produces specific TRP metabolites that indirectly influence host physiology. An alteration in TRP metabolites results in neurological and psychiatric disorders. Tryptophan supplementation has been used to treat a number of neuropsychological disorders in various clinical trials (Tab. XI) and has been found to improve serotonin and tryptophan deficiency, thus alleviating the severity of symptoms in depression, schizophrenia and bipolar disorder.

**Magnesium**

Magnesium is an important mineral for homeostasis in the human body. It plays an essential role in neuroprotection, neuromuscular conduction and nerve transmission. It is a mineral of intense interest due to its capacity to protect the nervous system against ecotoxicity, thus im-

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### Tab. VII. Effects of melatonin supplementation on various neurological conditions.

| Clinical condition                        | Melatonin dose                          | Findings                                           | References |
|------------------------------------------|-----------------------------------------|----------------------------------------------------|------------|
| Parkinson’s disease                      | 0.25 and 1.25 mg/kg i.v.                | Striking improvement in symptoms                  | [81]       |
| Amyotrophic lateral sclerosis            | 60 mg/day oral for 13 months            | Neuroprotective effects                            | [82]       |
|                                          | 500 mg/day rectal for 2 years in 31 sporadic patients | Reduced oxidative damage                          | [83]       |
| Muscular dystrophy                       | 70 mg/day for 9 months                 | Mitigated hyperoxidative state of erythrocytes    | [84]       |
| Multiple sclerosis                       | 50-300 mg/day oral for 4 years         | Improved overall symptoms of progressive MS with long-term use | [85]       |
| Migraine                                 | 3 mg/day for 4 months                  | Lower duration, frequency, and intensity of pain   | [86]       |

### Tab. VIII. Neurological implications of omega-3 fatty acids.

| Neurological condition/function | Subjects | Study type | Supplements/ doses | Findings | Reference |
|--------------------------------|----------|------------|--------------------|----------|-----------|
| Anxiety and inflammation       | 68 medical students under low-stress such as exams | Placebo-controlled, double-blind 12-week RCT | n-3 (2.5 g/day, 2085 mg eicosapentaenoic acid and 348 mg docosahexaenoic acid) or placebo | 14% decrease in lipopolysaccharide-stimulated interleukin 6 production and 20% reduction in anxiety symptoms; lowered n-6:n-3 ratio and anxiety | [87] |
| Dementia                       | 5386 patients without dementia           | Prospective evaluation of incidence of dementia  | Fatty-acid-rich fish | Fish intake decreased dementia | [88] |
| Cognitive function             | 867 elderly persons                     | Observational epidemiological                  | Oily fish containing long-chain PUFA | Fish consumption was positively associated with delayed unadjusted recall in CVLT | [89] |
| Parkinson’s disease            | 31 patients with major depression      | Double-blind, placebo-controlled              | Fish oil (containing omega-3 fatty acids) or mineral oil capsules for 3 months | Omega-3 enriched fish oil improved depression | [90] |
| Alzheimer’s disease and vascular dementia | 49 controls, 25 AD and 15 VD | Cross-sectional | Excess intake of n-6 polyunsaturated fatty acids | AD and VD associated with higher intake of n-6 animal fats | [91] |
proving many neurological disorders. Table XII shows some selective studies of magnesium in NDs.

**POLYPHENOLS**

Polyphenols are important nutrients abundant in spices and foods. They have antioxidant, anti-inflammatory and senolytic activities; they inhibit oxtosis, modulate the gut microbiome and promote protein aggregation and stability. They also maintain GSH levels and neurotrophic signalling pathways [113]. They show promise for preventing neurodegenerative diseases such as dementia, PD, HD, ALS, stroke, TBI, diabetes, cardiovascular diseases, liver disease and cancers. In addition, polyphenols control symptoms of depression. For instance, the antioxidant potential of polyphenols could possibly improve depression symptoms in women [114]. However, the effect of polyphenols in disease prevention and treatment depends on adequate dietary consumption. Fresh fruit and vegetables contain plenty of polyphenols that offer a variety of neurological benefits (Tab. XII).

Polyphenol supplements, such as Pycnogenol® (a proanthocyanidin) obtained from French maritime pine bark by Horphag Research (Geneva, Switzerland), have shown promising antioxidant and anti-inflammatory properties in various in vitro, animal and/or human models [115], besides improving endothelial function and showing beneficial effects in ADHD [116]. Another important commercially available polyphenol is silymarin, extract-
It is commonly known as flavonolignans and is a mixture of eight stereoisomers: taxofolin, silybin A and B, isosilybin A and B, silychristin, isosilychristin and silydianin [117].

Silymarin shows neuroprotective mechanisms in AD, PD and cerebral ischemia including mediation of antioxidant mechanisms, regulation of kinases in cell-signalling pathways, anti-inflammatory properties, neurotrophic effects, modulation of neurotransmitters and inhibition of apoptosis [118, 119]. Silymarin also controls production of amyloid-β by inhibiting β-amyloid precursor protein and cholinesterase activity, thus inhibiting the onset of AD [120]. Its low cost, bioavailability and safety make silymarin a natural drug of choice for neuroprotection and hepatoprotection [119, 120].

**Ayurvedic herbs in the treatment of neurodegenerative diseases**

Ayurvedic medicine has been practised in the Asian subcontinent since ancient times. Many herbs and medicinal plants have been explored for their antioxidant, anti-inflammatory, anti-diabetic, anticancer and cytoprotective properties. Medicinal plants such as *Withania somnifera* (ashwagandha), *Bacopa monnieri*, *Acorus calamus* and *Hypericum perforatum* have been shown to prevent or alleviate neurological diseases and symptoms (Tab. XIV).

**Bacopa monnieri**

*Bacopa monnieri* is a traditional Indian ayurvedic medicinal plant belonging to the family *Scrophulariaceae*. This memory enhancer, known as Brahmi, has been used
traditionally for more than 3000 years to treat various neurological disorders, to enhance digestion and to improve learning, cognitive function and concentration. It helps restore cognitive deficit and enhances mental and brain function. This nootropic plant promotes repair of damaged neurons, neuronal synthesis and synaptic activity. Recent studies show that it contains surplus bioactive phytochemical compounds with synergistic properties that are useful in the management of ND [130].

**Withania somnifera**

*Withania somnifera* or ashwagandha is another traditional Indian medicinal plant that promotes long life, youthful vigour and good intellectual powers. It is used traditionally in the treatment of neurodegenerative diseases, general frailty, nervous exhaustion and insomnia. It has anti-inflammatory, anti-tumour, antioxidant, immunomodulatory and anti-neuropsychiatric effects [131].

**Acorus calamus**

*Acorus calamus* or vacha is a traditional Indian ayurvedic medicinal plant. Its rhizomes are used to treat insomnia, melancholy, memory loss, hysteria, depression and mental disorders. Almost all parts of the plant have proven beneficial in the treatment of neurological, gastrointestinal, kidney, respiratory, liver, and metabolic disorders. Its action is anticonvulsant, anti-depressant, anti-hypersensitive, anti-inflammatory, cardioprotective, immunomodulatory and anti-obesity [132].

**Hypericum perforatum**

*Hypericum perforatum* or St. John’s wort is a perennial plant. It is used in traditional medicine to treat external and internal disorders such as minor burns, anxiety and mild to moderate depression. It is also a herbal remedy for neurological disorders such as mental ailments, hypersensitivity, neuralgia, spinal convulsion, hydrophobia, spastic paralysis, cerebral irritation, coxalgia and menopausal neurosis [47].

**Conclusion**

Oxidative stress and neuroinflammation are key factors in the onset and progression of neurodegenerative diseases. A diet rich in biologically active compounds with antioxidative and anti-inflammatory properties affords significant neuroprotection. Many recent studies have attempted to evaluate and recommend the Mediterranean diet and its ingredients with neuroprotective, oxidative stress mitigating and anti-inflammatory properties that impede the progression, delay the onset and reduce the severity of neurodegeneration in neurological disorders such as AD, PD, HD, MS, ALS and natural age-related brain aging. Several natural compounds, minerals and medicinal plants have been tested in clinical trials and animal studies and some, such as PLs, GABA, NAC, omega-3 fatty acids, magnesium, curcumin, resveratrol, *Hypericum perforatum, Acorus calamus* and *Bacopa monnieri*, have proven beneficial, safe and economical in the treatment of NDs. However, their effects are dose-dependent and must be administered in a precise manner. These potentially beneficial dietary components need to be evaluated in large clinical trials to assess their wider application across patients of different ethnic origin.

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**Tab. XIV. Neuroprotective properties and therapeutic potential of selected medicinal plants.**

| Medicinal plants | Active ingredients | Neuroprotective properties | Therapeutic potential | Reference |
|------------------|--------------------|---------------------------|-----------------------|-----------|
| *Bacopa monnieri* (L.) Dunal (*folk name: brahmi*) | Bacopasides III-V, bacosomes A and B, bacosaponins A, B and C | Antioxidant, antistress, anti-inflammatory, antimicrobial and smooth muscle relaxant. Improves memory | Neuroprotection in AD and bipolar disorder, improves intelligence and memory | [130, 133, 134] |
| *Withania somnifera* (L.) Dunal (*folk name: ashwaganda*) | Ashwagandhine, withanolides, withanospermin, withanosperminol and withanine | Memory enhancer and anti-stress agent with effects on locomotor function and neural growth | Inhibits oxidative stress, improves cholinergic function and mitochondrial respiration in rotenone-induced Parkinsonism in *Drosophila melanogaster* | [131] |
| *Acorus calamus* (*folk name: sweet flag, sway or muskrat root*) | 145 compounds α-asarone, β-asarone, eugenol, isoeugenol, 44 sesquiterpenes including lactones, monoterpenes (C-10), triterpenoid saponins | Antioxidant, anti-depressant, anti-inflammatory, anticonvulsant, neuroprotective, antianxiety, cytoprotective, immunomodulatory | Neuroprotection and anti-inflammatory agent in AD and PD | [132, 135] |
| *Hypericum perforatum* (*folk name: St. John’s wort*) | Quercetin, hyperoside, quercuritin, rutin, hypercin, kaempferol, hyperforin | Antidepressive, antioxidant, neuroprotective | Restoration and improvement of microglial viability, inhibits amyloid-β toxicity in AD and brain malondialdehyde in PD | [47] |
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Conflicts of interest statement

Authors declare no conflict of interest.

Author’s contributions

MB: study conception, editing and critical revision of the manuscript; KD, MCM, Paola C, PM, Pietro C; literature search, editing and critical revision of the manuscript. All authors have read and approved the final manuscript.

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