Chapter

Bioactive Molecules from Indian Medicinal Plants as Possible Candidates for the Management of Neurodegenerative Disorders

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Abstract

The present review gives an account of various bioactive molecules obtained from Indian medicinal plants for neurological degenerative disorders. Emphasis is laid on their correlation with the plants used in traditional system of medicine in India. The methodology involved in present review was enlisting of medicinal plants used for neurodegenerative disorders followed by their chemistry. A correlation with the chemical constituents and their recent findings has been done. Many medicinal plants such as *Aloe vera* and *Bacopa monnieri* have documented correlations and also need to be explored more. Molecules like garcinol **(34)**, which was originally an anti-cancer compound, have good correlation as neuroprotective agent. Likewise many plants that have not been explored but are used in traditional system of medicine have also been listed. *Jaggery* and honey, which are used in traditional formulations in large quantity, also have natural products that are used as neuroprotective agents. In conclusion, a lot more study is required to correlate the medicinal plants and herbal formulations to have much more natural products for neurodegenerative disorders.

Keywords: ayurvedic formulations, Indian medicinal plants, aloin, garcinol

1. Introduction

Neurodegeneration is defined as a complex process that involves progressive damage to the brain with neuronal loss leading to incurable and devitalizing consequences. The neurons, which get degenerated, are not restored, which result in impaired cognition and neurological disorders leading to depression, schizophrenia, Alzheimer's disease, dementia, epilepsy, cerebral ischemia, and parkinsonism [1, 2]. These diseases involve various characteristic pathological and molecular features affecting neurons in various regions of the brain. Neurodegenerative diseases are accelerated by the way we live our daily lives. As per recent report by Indian Council of Medical Research (ICMR), the proportion of deaths estimated due to lifestyle diseases has increased from 37.09% in 1990 to 61.8% in 2016 [3]. Thus, there is an immense need for the development of strategies for its prevention as a number of patients suffering from lifestyle diseases are increasing day by day. Ayurveda is considered an old age traditional medicine of Indian practice involving considerable usage of plants and herbal preparations, which are known to cure

various disorders. Various classical formulations for neurodegenerative diseases are listed in Ayurvedic Formulary of India (AFI), which also provides a file of information regarding single drugs of plant, animal, and mineral origin, providing their official names and English equivalents for their easy identification [4]. In present review, the major plants listed in the formulations indicated as neuroprotective is discussed. Present review outlines the chemical constituents and pharmacology of the listed plants. The sole aim of present review is to extract the hidden potential ancient formulations supported by modern findings so as to enhance their acceptability in masses. Further, a systematic approach for their chemical standardization is a need as it will be supportive in identifying therapeutic molecules, stating the need for combining scientific interpretations and traditional knowledge.

2. Indian medicinal plants and neurodegenerative diseases

The present sections describe plant material along with their chemical constituents and related pharmacology pertaining to neurodegenerative disorders. Few molecules with prominent activity have also been discussed.

3. *Aloe vera* (L.) Burm.f.

A. vera is a succulent, evergreen, perennial herb, which is being cultivated all over the world mainly for the purpose of agricultural and medicinal uses. Anthraquinones (aloe-emodin (**1**), chrysophanol (**2**), and a bitter reddish-yellow exudate containing majorly anthrones (aloin A and B (**3**)), aloe-emodin (**4**) [5], and few aloe resins such as aloeresin (**5**) and aloenin (**6**)) [6] are the major constituents in aloe (**Figure 1**). Aloe-emodin **4** is reported to enhance cognition against scopolamine-induced cognitive impairment in mice [7]. Aloin **3** is shown to decrease intracellular ROS generation and reduced Ca^{2+} production, which is responsible for depolarization and death of the neuron, suggesting it as a useful and alternative therapy for cerebrovascular diseases [8]. *A. vera* gel demonstrated antioxidant and anti-inflammatory activities when given to the rats with sciatic nerve reperfusion injury [9].

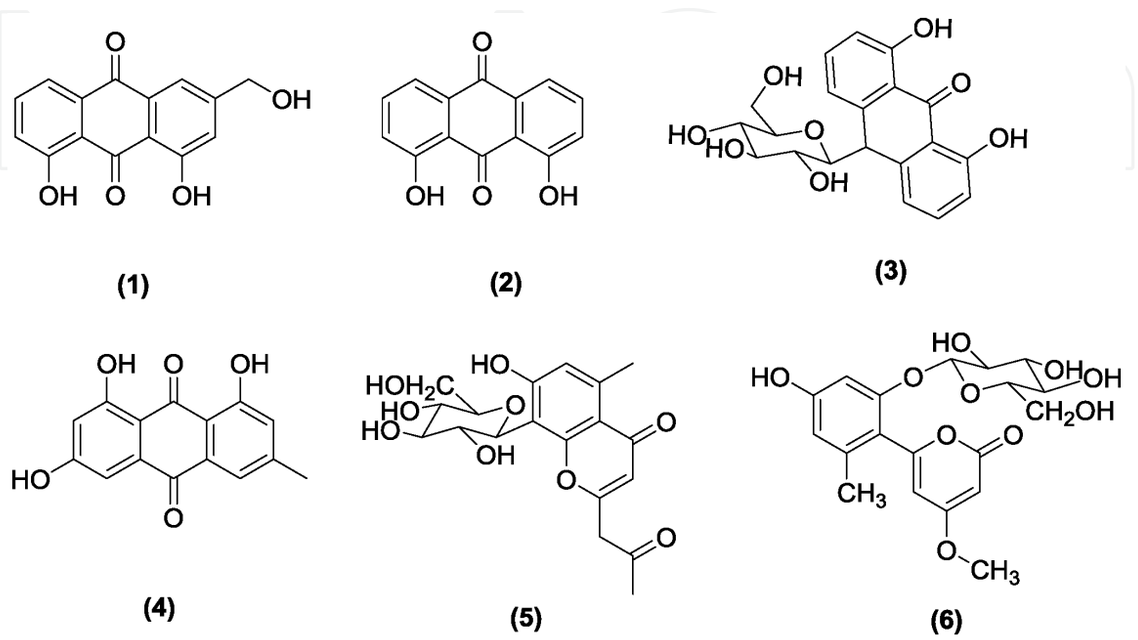

Figure 1.
Structures of compounds present in A. vera.

4. *Terminalia chebula* Retz

Terminalia chebula (Combretaceae) commonly called *Haritaki*, is used in ayurvedic formulations, also reported to demonstrate neuroprotective activities. The principle constituents in pericarp of *T. chebula* fruits are phenolics (chebulic acid (**7**), chebulagic acid (**8**), chebulinic acid (**9**), ellagic acid (**10**), gallic acid (**11**)) [10] and triterpenoid glycosides chebuloside II (**12**) (**Figure 2**) [11]. Pericarp of fruits of *T. chebula* constitutes *Triphala* (one of the popular formulations of ayurvedic system of medicine). The methanolic (70%) extract of the fruit *Fructus chebulae* has been shown to rescue cerebral ischemia by protecting neurons from degeneration. The in-vitro study and in-vivo studies have shown promising results [12]. Also, there is a promising decrease in the levels of malondialdehyde (MDA), NO, and microglial death stimulated by lipopolysaccharide (LPS) in the cells after treating with the extract [13]. The underlying mechanism might be the inhibition of inflammatory and oxidative processes. *T. chebula* constituents such as chebulagic acid, chebulinic acid, and ellagic acid have shown to be neuroprotective on various cell lines by showing its effect on various targets [14–16].

5. Honey and *Jaggery*

Both Honey and *Jaggery* are used in making of many ayurvedic preparations, and they constitute major part of many formulations [4]. Honey, a sweet and viscous substance, is produced by the honey bees (*Apis* spp.). It contains sugar and others such as minerals, proteins, essential oils, and flavonoids. Dietary polyphenols found in honey as well as other food and plant materials can prevent neurodegenerative disease in various ways [17–22]. These include oxidative protection of neurons [17], enhancement of neuronal function and regeneration [18], protection of neurons from Aβ-induced neuronal injury and neurotoxicity [19], protection of hippocampal cells against nitric oxide-induced toxicity [20], and modulation of neuronal and glial cell signaling pathways [21]. Luteolin (**13**) shows neuroprotective activity via prevention of microglia-associated inflammation in the hippocampus of aged rats [22]. Other flavonoids such as quercetin (**14**) and kaempferol (**1**) have also shown to be neuroprotective in various models. Kaempferol's (**15**) neuroprotective effect was confirmed by the histochemical findings where it prevented the loss of TH-positive neurons induced by MPTP [23–25]. Luteolin **13,** a flavone, has a significant role in treating CNS disorders through various mechanisms [26]. The activity of luteolin **13**

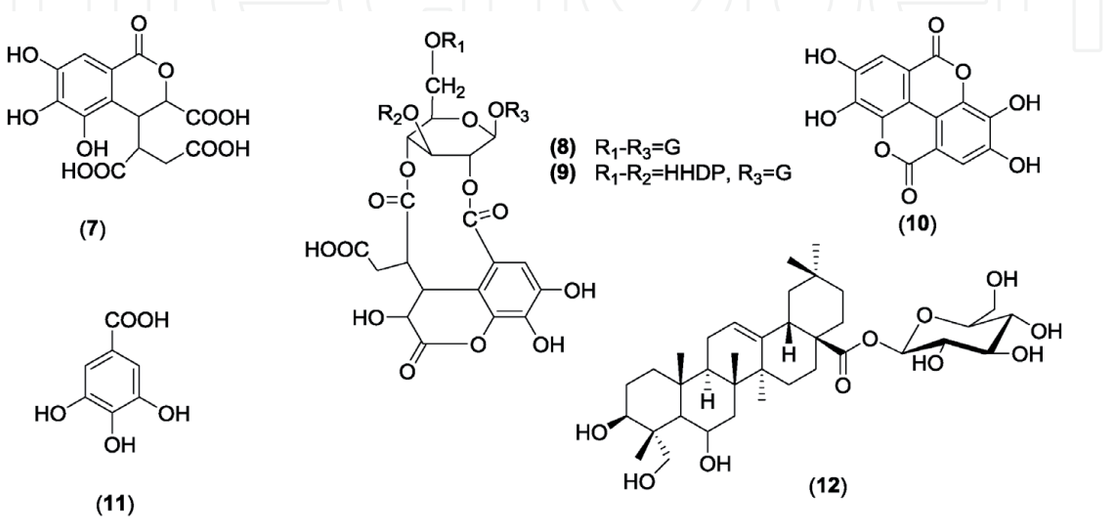

Figure 2.
Structures of compounds present in T. chebula.

was also reported at its microglial transcriptome level for the treatment of CNS disorders via anti-inflammatory activity [27]. Pretreatment of mice with luteolin **13** was expected to reduce the frequency of seizure in the PTZ mice model [28]. Luteolin **13** also has the potential to improve the activity of oxygen-glucose deprivation/reperfusion (OGD/R) induced neurons in a dose-dependent manner by enhancing the Na+/K+-ATPase activity suggesting a potential molecule to treat cerebral ischemia [29]. Apigenin (**16**), a trihydroxyflavone, was reported to inhibit the release of glutamate from hippocampal nerve terminals, which might be useful in treating epilepsy [30]. The role of apigenin (**16**) in the treatment of cognition was demonstrated by attenuating the Aβ-induced cytotoxicity in rat cortical neurons but having no intervention with oxidative stress. The biological activities of the flavonoids might be due to hydroxyl groups at R2 and R3 position influencing various cellular events eventually leading to apoptosis [27–30]. Other phenolics such as ferulic acid (**17**) exert neuroprotective effect through middle cerebral artery occlusion [31] and by decreasing the number of microglia/macrophages after cerebral ischemia/reperfusion injury in rats [32]. Chlorogenic acid (**18**) present in honey exerts a neuroprotective effect against methyl mercury-induced apoptosis in pheochromocytoma-12 (PC12) cell lines. It prevents the generation of reactive-oxygen species (ROS), suppressing the decreasing action of glutathione peroxidase (GPx) and GSH and attenuating apoptosis by the activation of caspase-3 [33] and also inhibits the activity of acetylcholine esterase and MDA in the hippocampus as well as in the frontal cortex in mice [34]. Honey as such has also shown to be neuroprotective in male Sprague-Dawley rats, and there was a decrease in the thiobarbituric acid reactive substance levels in the rats, which were pretreated with honey [35]. Chrysin (**19**) improved the morphological integrity of nigrostriatal neurons and increased the endogenous levels of BDNF, S100B, NGF, and GDNF in mice striatum improving behavioral and better muscular coordination [36]. Its lipophilic nature and bioflavonoid nucleus confers an added advantage to grow as a compelling therapeutic agent for neurological disorders. Pinocembrin

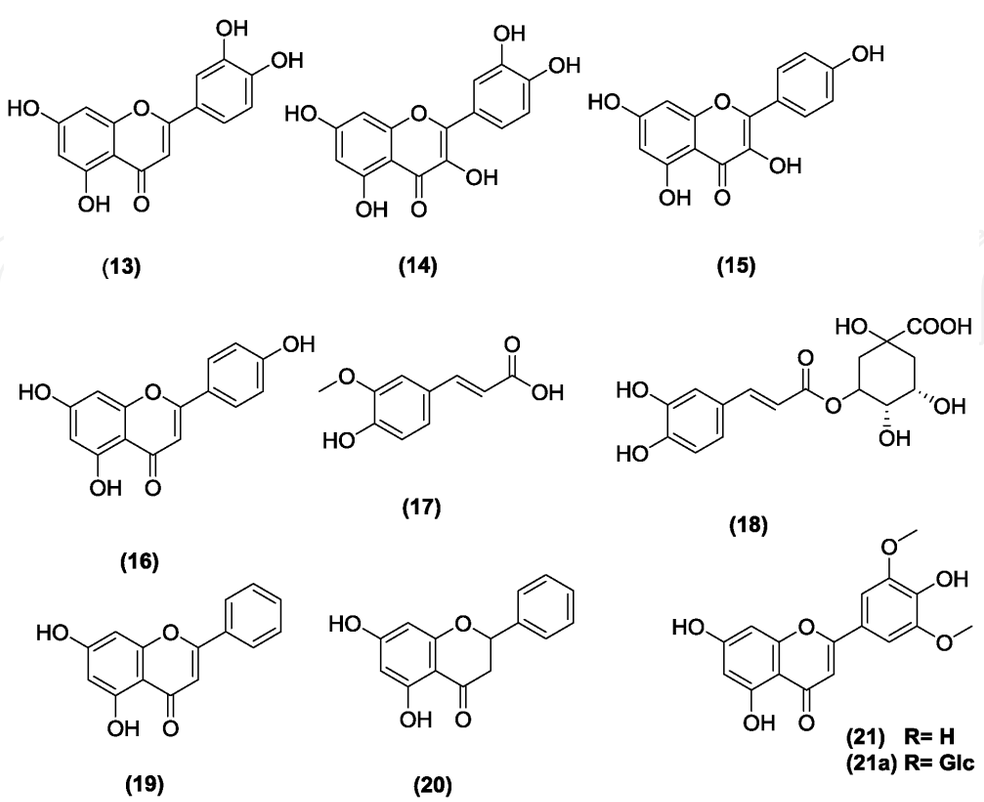

Figure 3.
Structures of compounds present in Jaggery *and honey.*

(**20**) elevated glutamate level, which was an important excitatory neurotransmitter produced by global cerebral I/R [37].

Jaggery is used in most of the ayurvedic formulations [4]. Traditionally, it is indicated for treating neurodegenerative disorders. The chemistry of sugar cane reveals that it is rich in phenolics and their glycosides [38], flavonoid glycosides, and flavones [39]. Tricin-7-glucoside **(21)** was reported to possess neuroprotective activity against cerebral ischemia via reduced expression of NF-κB and HMGB1. SH-SY5Y cells, which were pretreated with tricin **(21a**), reduced the apoptosis induced by OGD. Attenuation of histopathological damage reduced brain edema was reported in animal models of ischemia along with reduced NF-κB and HMGB1 expression [40]. It also has potential for Alzheimer's disease [41] (**Figure 3**).

6. *Bacopa monnieri* L.

Bacopa monnieri L. (Scrophulariaceae) is notable ayurvedic medicinal plant and referred to have impact on brain function and is a neural tonic to improve intelligence and cognition [42]. Normal formulation Illumina® containing *B. monnieri* (leaf dry extract 43%, containing bacoside, 20%) decreased of 8-iso-PFG2α and ROS/RNS generation in the rat brain, consequently, decreasing the basal and H_2O_2 and amyloid β peptide-incited oxidative stress [43]. In another study, standardized extract of *B. monnieri* (Bacoside A (**22**) content 82 ± 0.5%) when given in the doses of 5 and 10 mg/kg, orally, shows a dose-related increment in superoxide dismutase, catalase, glutathione peroxidase activities in the frontal cortex, striatum, and hippocampus [44]. *B. monnieri*, when administered orally, improves cognitive impairment and neurodegeneration in rats. Immunohistological recognition of superoxide dismutase (Cu/Zn-SOD) and histopathological changes in the CA1 region of the hippocampus were observed [45]. An extract containing 5% (w/w) of the saponins, which contains bacoside A3, bacopasaponin X, bacopasaponin C (**23**), bacopaside II **(24),** and bacopaside I **(25)**, shows improvements in cognitive abilities and neuroprotective impacts in Alzheimer's disease model [46, 47]. When rats treated with bacoside A (**22**), huge changes were found in the degrees of both nonenzymatic and enzymatic antioxidants, which recommends that bacoside A **22** improves *B. monnieri* antioxidant status in rat brain [48]. Other saponins such as **(26-28)** reported from this plant have been shown in **Figure 4**. A survey of 10 years of research at Swinburne University done by Con Stough et al. recommends that an extract of *B. monnieri* (CDRI 08: KeenMind) is a safe and effectual cognitive enhancer [49]. *B. monnieri* extract suppressed the generation of free radical levels and indicated critical assurance against 3-nitropropionic acid (3-NPA)-mediated cytotoxicity in dopaminergic (N27 cell lines) [50]. *B. monnieri* standard extract containing 55.34% of bacosides indicated a defensive impact on ischemia-induced memory hindrance and diminished the infarct size in the ischemic brain. It additionally demonstrated a critical increment in catalase action and exhaustion in lipid peroxidation, nitrite, and nitrate activity [51]. Neuronal cell cultures when treated with *B. monnieri* extract shielded neurons from β-amyloid-induced cell toxicity. The extract gave protection to cell cultures against glutamate-induced excitotoxicity since it was not able to repress glutamate-mediated toxicity [52]. In Alzheimer's disease animal model (C57/Bl6 mice), *B. monnieri* extract has decreased lipoxygenase action and hydrogen peroxide-induced lipid peroxidation. *B. monnieri* has neuroprotective mechanisms, and it lessens β-amyloid deposits in the brain of C57/Bl6 mice Alzheimer's disease animal model [53]. *B. monnieri* extract have also shown to have protective effect against rotenone induced Parkinson's disease in PC-12 cell lines [54].

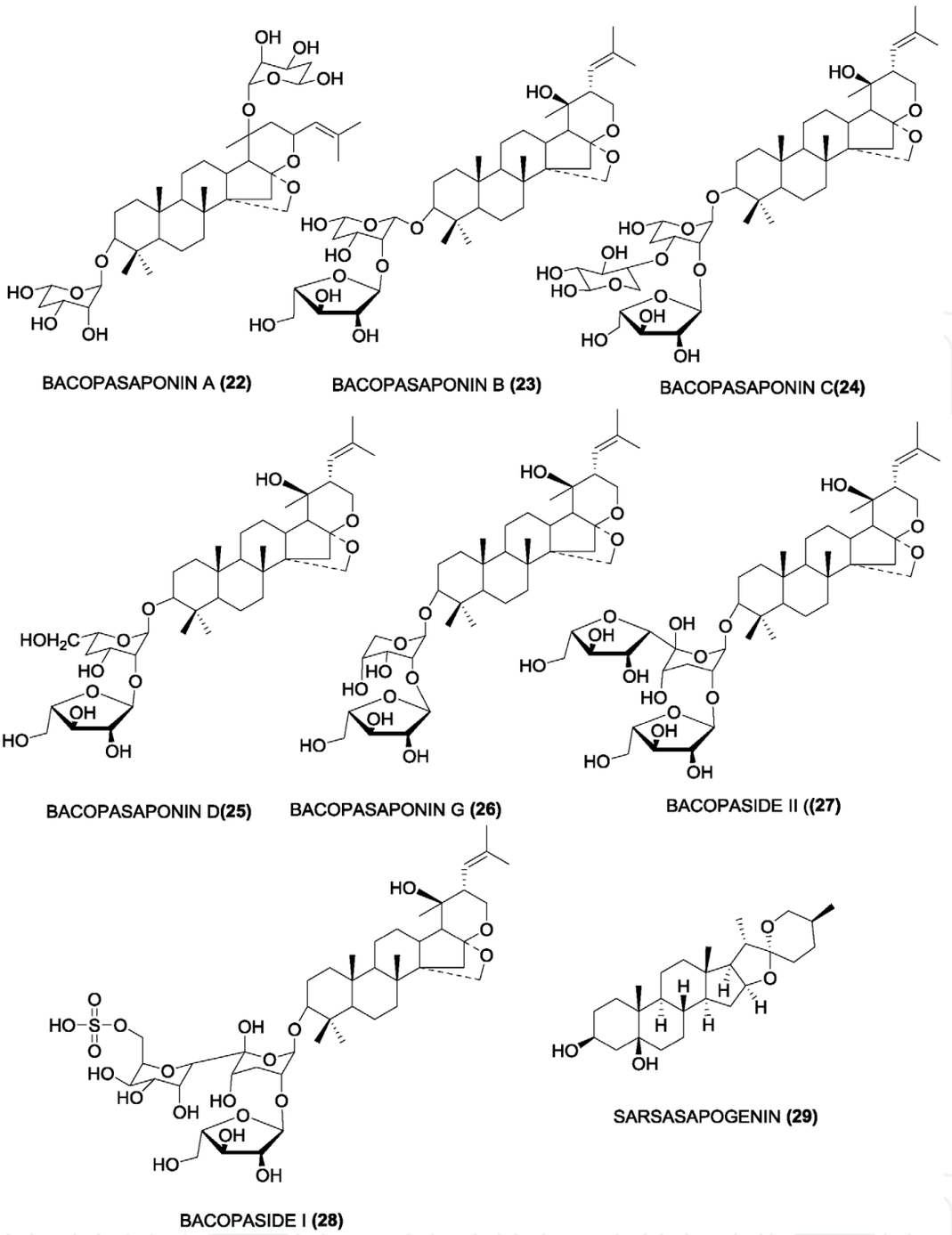

Figure 4.
Structures of compounds present in B. monnieri.

7. *Asparagus racemosus* Willd.

Methanolic extract of *Asparagus racemosus* decreased the degrees of cytokines, malondialdehyde (as a marker of lipid peroxides formation), and nitric oxide with a critical increment in the levels of catalase, superoxide dismutase, and glutathione, concluding its neuroprotective activity [55]. Its root extract (100 mg/kg) cured region-specific neurodegeneration created in Swiss albino mice [56] and also demonstrated dose-dependent improvement in memory after histochemical and behavioral studies. A noteworthy decrease in transfer latency time and a significant increment in acetylcholinesterase (AchE) staining in histochemical identification were observed suggesting antioxidant, cholinergic, and neuroprotective properties of *A. racemosus* [57]. EuMil, a formulation containing standardized extracts *A. racemosus* Willd., has

been used for stress-related problems and has been found to re-establish modified degree of nor-adrenaline, 5-hydroxytryptamine, and dopamine normal (100 mg/kg, p.o. 14 days) [58]. *Withania somnifera* and *A. racemosus* together have shown noteworthy impacts in cell viability test, lactic dehydrogenase, malondialdehyde, glutathione disulfide, glutathione, nerve growth factor, pro-brain-derived growth factor levels, and reactive oxygen species generation [59]. Ovariectomized adult female Wistar rats showed noteworthy upregulation of estrogen receptors (ERα and ERβ) in hippocampus and frontal cortex area alongside enhancement in the levels of brain-derived neurotrophic factor. Upregulation of estrogen receptors and enhancement in the levels of brain-derived neurotrophic factor can be filled in as proof for neuroprotective impact of ethanolic concentrate of *A. racemosus* roots [60, 61]. Significant protection is seen after the supplementation of Mentat (BR-16A) is an herbal psychotropic preparation, containing *A. racemosus* against ethanol withdrawal-induced decrease of pentylenetetrazole threshold in rats and mice [62]. Sarsasapogenin, a steroidal saponin from *A. racemosus,* has been studied for neuroprotective impact in Alzheimer's disease. Sarsasapogenin **(29)** indicated noteworthy restraint of butyrylcholinesterase, monoamine oxidase-B, beta-secretase 1, and acetylcholinesterase, key enzymes related to the pathogenesis of Alzheimer's disease. At the point when tested against Aβ42 and H_2O_2-interceded cytotoxicity, sarsasapogenin showed a huge neuroprotective impact on PC12 cells. These discoveries recommended that sarsasapogenin can go about as a multi-target directed ligand and as a reasonable lead compound for treating different elements engaged with the pathogenesis of Alzheimer's disease [63]. Alterations in the normal levels of neurotransmitters, glutamate, acetylcholinesterase, dopamine, and protein because of worldwide cerebral ischemia were normalized by standardized *A. racemosus* Willd. root methanolic extract, appeared by the abatement in the degree of glutamate, acetylcholinesterase, and increment in dopamine levels and protein levels. Group treated with methanolic root extract of *A. racemosus* Willd. shown 85% neuronal protection in the CA1 area of the hippocampus. This demonstrated the cerebroprotective role of *A. racemosus* Willd. [64].

8. *Foeniculum vulgare* Mill.

Foeniculum vulgare extract reduced the amnesic effect and memory deficits in mice induced due to aging. *F. vulgare* extract demonstrated inhibition of acetylcholine, and in the exteroceptive behavioral model, it increased the step-down latency in mice significantly [65]. Fennel essential oil inhalation inhibits beta-amyloid (1-42)-induced depression and anxiety and also indicates that it may have further clinical applications [66]. There were improvements in Parkinson's disease in the animal model produced by *F. vulgare* Mill. essential oil [67]. Clinically fennel supplementation to obese middle-aged women decreased bodyweight, reduction in serum Aβ protein along with improvements in cognitive functions and metabolic profiling [68]. It normalized the expression levels of oxidative stress markers [Superoxide dismutase and Peroxiredoxin-6 (Prdx6)] and APP isoforms (APP common, 770 and 695) and also improved the Pb-induced morphological deterioration of cortical neurons [69].

9. *Azadirachta indica* A. Juss.

Commonly known as *Neem* in Indian subcontinent, *Azadirachta indica* has been shown to attenuate cisplatin-induced neurotoxicity in rats, and it also had neuroprotective effect on cerebral post-ischemic reperfusion and hypoperfusion [70, 71]. *A. indica* extracts have shown to be anti-oxidative and anti-apoptotic

neuroprotective in Parkinson-induced functional damage [72]. *A. indica* standardized leaf extract (total bitters 4.3%) has shown to be neuroprotective in partial sciatic nerve injury in rats as evidenced from anti-inflammatory, antioxidant, and anti-apoptotic studies [73].

10. *Picrorhiza kurroa* Royle ex Benth

Picrorhiza kurroa, an ayurvedic herb, has been shown to potentiate photochemotherapy in vitiligo [74]. Apocynin **(30)** from *P. kurroa* has shown to be neuroprotective *in vivo* [75]. It also shows protective effect in a mouse model of chemically induced colitis [76]. It (4-hydroxy-3-methoxy-acetophenone, **30**) mediates long-lasting memory recovery, helps in hippocampal neuroprotection, and reduces glial cell activation after transient global cerebral ischemia in rats [77]. Interestingly, the concentration of picrosides I **(31)** and II **(32)** and apocynin **30** (iridoid rich fraction) in plasma (C_{max}) was found to be 244.9, 104.6, and 502 ng/ml with half-life ($t_{1/2}$) 14, 8, and 6 h, respectively [78]. *P. kurroa* also prevents memory deficits by inhibiting NLRP3 Inflammasome Activation and BACE1 Expression in 5xFAD Mice [79]. Acylated iridoid glycosides with hyaluronidase inhibitory activity from the rhizomes of *P. kurroa* Royle ex Benth have recently been isolated [80]. Therapeutic potentials of plant iridoids in Alzheimer's and Parkinson's diseases have separately been reviewed recently [81].

11. *Berberine* from *Berberis aristata* DC

Berberine **(33)** has been shown to be neuroprotective through the Nrf2 upregulation and also alleviates rotenone-induced cytotoxicity by antioxidation and activation of PI3K/Akt signaling pathway in SH-SY5Y cells [82]. Neuroprotective effects of berberine have also been confirmed in animal models of Alzheimer's disease [83]. Berberine nanoparticles have shown protective effect against LPS-induced neurodegenerative changes [84]. Berberine confers neuroprotection in coping with focal cerebral ischemia by targeting inflammatory cytokines [85]. Berberine had also shown protective effect against the altered intrinsic properties of the CA1 neurons induced by Aβ neurotoxicity [86]. There are many pathways by which berberine acts to protect neurons and has recently been reviewed. Authors have concluded that it being a potential candidate for combating neurodegenerative diseases [87, 88].

12. Garcinol from *Garcinia indica* Choisy

Garcinol **(34)** is one of the major constituents of *Garcinia indica* (a plant found in the region of Western Ghats of India). Garcinol can effectively restore the balance between the neurotransmitters glutamate and the γ-aminobutyric acid (GABA), rescue neural precursor cells, and promote their rapid growth. It regulates the expressions of glutamic acid decarboxylase 65 and GABAA receptors, preventing hyperactivation of NMDA receptor and the resultant excitotoxicity. It enhances memory and cognition in C57BL/6 mice, significantly lowering epileptic seizure scores [89, 90]. It also serves as a strong inhibitor of histone acetyltransferases (HAT), thus contributing protection against rapid neurodegeneration in parkinsonian brain [91, 92]. Garcinol helps in restoration of dopamine potency and has homocysteine lowering ability as well as have been shown to counter LDOPA-induced dyskinesia in PD model, demonstrate its worthiness as a potential drug candidate against Parkinson's Disease [93, 94]. Garcinol also exhibits desirable anti-cholinesterase properties by inhibiting the enzyme acetyl

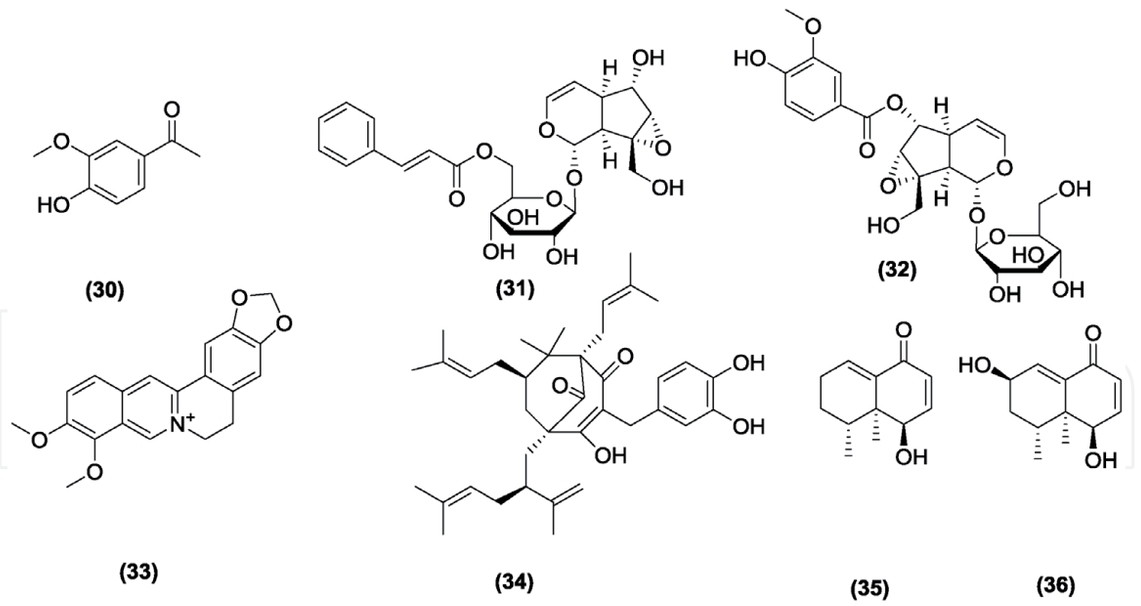

Figure 5.
Structures of compounds present in various plants for neuroprotective activity.

cholinesterase with an IC50 value of 0.66 μM, and it improves the neuronal count in hippocampal regions following administration of pentylenetetrazole (PTZ). In cultured rat cortical progenitor cells, garcinol can reduce cell death associated with growth factor deprivation. It also promotes neurite outgrowth in epidermal growth factor-responsive neural precursor cells and supports the survival of neurons [90]. In unilaterally 6-hydroxydopamine (6-OHDA)-lesioned hemi parkinsonian mice, 5 mg/kg of garcinol co-treatment with L-DOPA effectively controlled the axial, limb, and orofacial (ALO) score for dyskinesia analysis. Following the administration of garcinol, a decreased expression of c-Fos, FRA-2, and ARC genes has been visualized [94], which is usually over-activated in L-DOPA induced dyskinesia [95]. Moreover, methanolic extract of *G. indica*, which is known to contain garcinol, effectively elevates dopamine level in the striatum and confers neuroprotection to dopaminergic neurons in 6-OHDA lesioned experimental rats [96]. Even pharmacological inhibition of HATs by garcinol can notably suppress MPP+-induced cell death due to reduction in ATP content [97]. *In silico* studies on the molecular interaction between garcinol and the active sites of COMT and MAO-B revealed that garcinol can potentially inhibit the activity of the two enzymes, similar to their known inhibitors [93]. In conclusion, garcinol may prove to be a dependable remedial measure in PD therapeutics since its inhibition of MAO-B and COMT can be correlated to increase the availability of dopamine as well as prevent the generation of toxic dopamine metabolites including homocysteine, 3-omethyldopa, 3-methoxytyramine, and 3,4-dihydroxyphenylacetaldehyde [98] (**Figure 5**).

13. *Nardostachys jatamansi* (D. Don)DC. (Jatamansi)

The plant *Nardostachys jatamansi* is well exploited in Ayurvedic system of medicine for its role in neurological disorders. Various phytochemicals have been reported from this plant by various authors. Its sedative and antidepressant activity, its mechanism (inhibition of MAO and GABA), and its role in rat cerebral ischemia have been documented [99]. Anticonvulsant activity and neurotoxicity profile of the plant have been generated [100]. The extracts of *N. jatamansi* have been found to attenuate 6-hydroxydopamine-induced parkinsonism in rats, as proven by behavioral,

neurochemical, and immunohistochemical studies [101]. It also improves learning and memory in mice. It also has stress modulating antioxidant effect. Its formulation was also found to enhance the learning and memory process in rats [102–104]. It has shown neuroprotective efficacy in conjunction with selenium in cognitive impairment [105]. *N. jatamansi* root extract was found to modulate the growth of IMR-32 and SK-N-MC neuroblastoma cell lines through MYCN-mediated regulation of MDM2 and p53 [106]. Novel Sesquiterpeniods and Anti-neuroinflammatory metabolites from *N. jatamansi* have also been isolated [107]. Compounds such as Desoxo-narchinol A **35** and Narchinol B **36** isolated from *N. jatamansi* have been shown to exert anti-neuroinflammatory effects by upregulating nuclear transcription factor erythroid-2-related factor 2/heme oxygenase-1 signaling [108].

14. Other plants

Many plants, which have been used in traditional formulations for neurological disorders, need to be phytochemically explored and correlated with the modern findings. **Table 1** gives the list of those plants with reported neuroprotective activity.

Plant name	Part used	Reports on neuroprotective activity	Reference
Fumaria indica (Hausskn.) Pugsley	Leaf	Significant activity of ethanolic extract on rat cognitive dysfunctions. Potential antianxiety activity of leaf extract; preclinical study	[109, 110]
Alhagi pseudalhagi (M. Bieb) Desv. ex B. Keller & Shap.	Whole plant	Traditionally used for neuroprotective disorders. Compounds having neuroprotective activity like flavanone glycosides and alkaloids like β-phenethylamine and tetrahydroisoquinoline have been reported	[111–114]
Pluchea lanceolata (Oliver & Hiern.)	Leaf	Protection of hippocampal neurons from endothelin-1 induced ischemic injury to ameliorate cognitive deficits; protective effect against aluminum chloride-induced neurotoxicity in Swiss Albino mice; protective effect on LPS-induced neuro-inflammation in C6 rat glial cells	[115–117]
Premna mucronata Roxb.	Whole plant	Luteolin and apigenin are reported, and they are reported to be neuroprotective	[118]
Semecarpus anacardium L.f.	Fruits	Stress induced neuroprotective activity	[119]
Sida cordifolia L.	Whole plant	Ameliorative effect in parkinsonism	[120]
Tinospora cordifolia (Thunb.) Miers.	Stems	Suppresses neuro-inflammation in Parkinsonian Mouse Model; potential neuro-regenerative candidate against glutamate induced excitotoxicity: an *in vitro* perspective	[121–123]
Trichosanthes dioica Roxb.	Rhizome	Neuropharmacological properties of root	[124]
Strobilianthes ciliatus (Nees.)		No such reports	—

Table 1.
List of plants whose exploration is required, as they are used tremendously in traditional system of medicine in India.

15. Conclusions

In present review we focus on evidence to prevent neurodegenerative disorders in various studies (*in vitro* and *in vivo*). The mentioned medicinal plants play their protective roles *via* increased SOD and catalase levels, restoration of GSH, and decreased MDA levels and also protect neurons against ROS as antioxidant activities. The neuroprotective effects of the mentioned plants occur *via* reduction of inflammatory cytokines as well as enhancement of anti-inflammatory cytokines, inhibition of the acetylcholinesterase activity, and decreased MDA levels in the neural system via modulating GABAergic and glutamatergic neurons and also increasing amount of amino acids and serotonin (5-HT) in the neurotransmitters systems. Based on the evidence produced, it is suggested that more exploration of traditional formulations is required, and also repurposing in natural products is also required to a greater extent, as is evident from recent reports on garcinol and berberine.

Conflict of interest

Authors do not have any conflict of interest.

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