Full Length Review Article

Deep Insights into Neuroprotective Effects of some Imperative Herbal Resources: A Compressive Review Perspective

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ABSTRACT
Even the simplest medical systems have a history of using medications derived from plants. Due to wide spread acceptance and the common impression of their safer profile compared to traditional pharmaceuticals, they are the most often used medicines. Herbal supplements and medications are growing in popularity throughout the globe as people look for caffeine-free options and healthy ways to cut calories. There has been a rise in interest in traditional medicine in recent years. Alzheimer's disease and other nerves system illnesses are treated with a variety of herbs in traditional medicine. The term "neuroprotection" is used to describe measures used to safeguard neurons in the CNS against demage. The remedies found in nature are still available to humans. Drug like vincristine, artemisinin and gentamcine own thire effectiveness in part to their origins in nature or to their structural similarities to naturally occurring compound. For countries several plants extract have been used in traditional medicine for their purported neuroprotective, memory-enhancing, and anti-aging properties. Several example of such as herbs include ginseng, ginkgo, bacopa, curcuma, and sage this traditional clam was investigated to determine whether it held water, and the herbs' neuroprotective benefits and their method of action were also explored.

Keywords: *Neurodegenerative, Plants, Neuroinflammation, Neuroprotection, Herbal, Hallmarks.*

INTRODUCTION

Neuroprotection

The term "neuraptotection" is used to describe measures taken to prevent damag to neurons in the brain from neurodegenerative disorders (such as Alzheimer's and Parkinson's) and other source is conginative and intellectual decline conditions are common outcome of this acute and chronic condition which originate in the destruction and degeneration of neurons in the CNS. Loss of short term memory, trouble learning, impaired motor coordination, and many other functional loses are common yearly indicators ND. NDs have been discovered to have a strong correlation with aging, which is characterized as a complicated physiological process including both morphological and biochemical changes that gradually unfold as we age Among the many potential causes of NDs, including as high blood pressure, infectious agents and inherited or environmental factors, aging stands out as a key contributor. Protein aggregation, inflammation, oxidative stress, and neurotransmitter loss are all hallmarks of the pathogenesis of NDs, and they tend to become more frequent as we age. nature is steel a reliable pharmacy from which humans may draw vincristine, artemisinin and gentamcine are only a few of the many effective medications that have their origins in nature are based on the structural finger prints of naturally occurring molecules several estimates put the percentage of people who rely on traditional medicine for their primary health care at about 80% in several developing countries (such as Nigeria, Ghana, China and India) a growing interest in the creation of novel medication candidate from natural sources

has been spared by the rising prevalence of resistance (particularly to antibiotics and antimalarial), unwanted side effect, high caused , and loss of effectiveness after extended use of the present treatment in use. Clinically available medicine for the therapy of NDs, including as amantadine, memantine, donepizile may at base alleviate symptoms.

Neurodegenerative diseases

Neurodegenerative disease is a term used to refer to various conditions which occurs are salt of neuronal cell death, particularly, those of the CNS. This deterioration is often associated with gradual onset of progressive symptoms, a major symptom being loss of memory. The NDs include Alzheimer's disease (AD), Parkinson's disease (PD), Lewy body dementia, multiple sclerosis, amyotrophic lateral sclerosis (ALS), and spongiform encephalopathy. Of these NDs, AD is the most prevalent, accounting for over 60–70% of all forms of dementia. Protein aggregation, inflammation, excitotoxicity, oxidative stress, and neurotoxicity have been implicated in the pathophysiology of NDs**.**

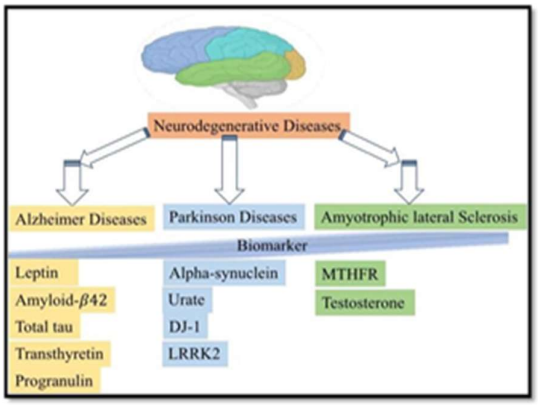

Figure No-1: Neurodegenerative Diseases

Alzheimer's Disease

The AD is the most prevalent and devastating disorder of the NDs. It is an incurable disease of cognition and behavioral impairment that affects social and occupational activities and is also a leading cause of institutionalization in the elderly. Clinically, AD is characterized by a progressive and irreversible memory deficits, cognitive deterioration, and personality changes, with a mean duration of about 8.5 years between onset of clinical symptoms and death. Memory impairments are first to appear in the early stage of the disease, after which motor and sensory functions are affected as the disease progresses. The onset of AD is usually above 65 years of age, with risk from this age doubling every 5 years. Hence, it has been suggested that the risk for AD for persons living into their eighties rises to 20–40% depending on a variety of factors such as population dynamics and geography. As the world population continues to age in parallel with economic development, the number of people with NDs and the associated dementia also continues to increase. This increase has in turn prompted an enormous increment in research Interest and efforts on the discovery of new therapeutic agents for primary, auxiliary, or tertiary prevention of these diseases**.**

Parkinson's disease

The PD is the second most common ageing-related neurodegenerative diseases that can greatly impair quality of life with significant consequences in terms of cost of patient care. Primarily a movement disorder, as opposed to AD which is mainly a cognitive disease, PD affects approximately 1% of the human population over the age of 60. Its classical signs include resting tremors, bradykinesia, extra pyramidal rigidity, and loss of postural reflexes such as disturbance in walking or equilibrium. The PD involves loss of dopaminergic neurons of the pars compact a region of their terminals in the corpus striatum. Since neurodegeneration is not restricted to the basal ganglia, PD is also linked with non-motor disorder like dementia. The association between PD and oxidative damage of neuronal cells has been well established. For example, the breakdown of dopamine (DA) by auto oxidation has been shown to be linked to semi quinone metabolism and the generation of superoxide anion, hydrogen peroxide (H2O2), and monoamine oxidase (MAO) expression**.**

Other Neurodegenerative Diseases

Amyotrophic lateral sclerosis is thought to be caused by the mutation of the gene coding for the enzyme superoxide dismutase (SOD) and also by the misfolding of the same enzyme. The ALS is incurable and has generally a median survival of three years from onset to death. Its symptoms include tripping or stumbling when running, foot and wrist drop, slurred speech, and depression. Huntington disease (HD) is another incurable ND. It has an adult onset with auto somal dominant inherited disorder characterized by progressive brain degeneration, causing rapid deterioration and eventually death. Symptoms of the diseases include involuntary movement, dementia, and behavioral changes. Prion diseases refer to a group of rare NDs caused by the aggregation of misfolded prion proteins. Prion proteins are known to be infectious and are presumed to cause some type of NDs referred to as spongiform encephalopathy: for example,

Creutzfeldt-Jacob disease and kuru in humans, Scrapie in sheep, and bovine spongiform encephalopathy in pigs collectively referred to as prion diseases. A major feature of these diseases is that they are transmissible**.**

Cerebrovascular diseases such as stroke cause acute degeneration of the CNS unlike the previously discussed chronic NDs. About 85% of stroke cases are of ischemic origin and have a slightly different etiology from the chronic ND. Interruption of blood supplies to the brain leads to a cascade of events that causes irreversible neuronal damage. Stroke is said to be the second leading cause of death in industrialized countries and has been reported to lead to dementia in 25% of patients within three months after a stroke. Interestingly, the deposition of both Aβ and APP in the cortical and subcortical brain area so from dementia patients follow in stroke has been reported**.**

LPS-induced Neuroinflammation

Neurodegenerative diseases are devastating conditions for which there is no cure so far. In general, the mechanisms involved in disease onset and development are still poorly understood. Therefore increasing efforts are being made to better compare end their pathogenesis. Among the different factors involved in these conditions, inflammation is considered a key contributor. Several lines of experimental evidence have demonstrated that neuronal cell death may induce an inflammatory process, and inflammation by itself may lead to cell death. Thus, it is necessary to induce inflammation in models of neuro degeneration in order to evaluate its intricate consequences. Induction of inflammation may be achieved in different manners, and lipopolysaccharide (LPS) is an important tool for this purpose. LPS is a molecule present in the outer membrane of Gram-negative bacteria. Its main target is the toll-like receptor (TLR) 4, although it is known to act on other receptors. The activation of TLR4 by LPS recruits a series of downstream adaptors, such as myeloid differentiation primary response protein 88 (MyD88), TIR-domain-containing adaptor-inducing interferon-β (TRIF) and TRIF-related adaptor molecule (TRAM), which are crucial for the signaling of the receptor. The recruitment of these adaptors can further activate downstream pathways which culminate in the activation of transcription factors, which, in turn, induce a plethora of pro-inflammatory genes. The TLR4 signaling pathway has been fully reviewed elsewhere. Although most of the work in this field uses LPS in order to stimulate glialcells, mainly microglia, it is known that neurons also express TLR4. Indeed, activation of this receptor leads to the neuronal production of different inflammatory mediators. LPS is used in a variety of *in vivo* and *in vitro* protocols. This compound not only is used to stimulate cell cultures, but also is injected either in the central nervous system (CNS) or in the periphery by single or multiple injections.

Hall mark of neuro inflammation Protein Mis folding and Aggregation

For proteins to properly function in the biological system, they must maintain their three- dimensional conformation. The process by which polypeptide chains fold into this three- dimensional structure is termed prote in folding. The correct three-dimensional structure, which is dependent on the sequence of amino acids, is very essential in the proper functioning of the protein. This in step wise process can how ever go wrong leading to thread option of abnormal configuration by the protein, a process called protein misfolding. Misfolded proteins lose their natural activity and in several cases become delete various and are unable to return to their native conformation. These protein sex pose hydrophobic terminals that are supposed to be buried in their core leading to the formation of insoluble aggregates. Since misfolded conformation can be generated spontaneously at low rate throughout life, their aggregates gradually accumulate as we age. These aggregates form distinct a DOB servable structures in the brain which are generally known as amyloid deposits in the brain. Furthermore, some form of mutation increases the chance of misfolding in proteins which is the case in the genetic or familial case of NDs**.**

As described in the preceding texts, two microscopic features resulting from the misfolding of proteins are observed in AD: extracellular amyloid plaques (senile plaque) consisting of amorphous extracellular deposits of Aβ and the NFTs of the hyper phosphorylated microtubule- associated tau protein. Amyloid deposits consist of aggregates containing 40 or 42 amino acid residues. Aggregates of 42 residues are more likely to form and are also overproduced when there is a genetic mutation. In rare cases of early onset of PD which runs in some families, mutations in a synaptic protein called α-synuclein that was originally identified from smaller peptides isolated in amyloid-containing fractions of AD brains are observed. The α-synuclein proteins are synaptic proteins that are able to aggregate and

form fibrils and are the major component of the Lewy body lesions, characteristic of PD as well as certain cases of AD and several other neurodegenerative conditions. In the HD, mutation of hunting tin, a cytoplasmic protein, leads to its aggregation and forms inclusions in cell nucleus in the brain. These aggregations, alongside the interaction of mutated huntingtin protein with regulatory caspases, are believed to be component of the pathophysiology of HD. In the case of ALS, it is the SOD that aggregates. There is evidence to suggest that the accumulation of SOD aggregate may lead to inflammation and neurotoxicity**.**

Oxidative Stress

Oxidative stress occurs when the body's antioxidant defense system can no longer cope with the neutralization of free radicals and/or reactive oxygen species (ROS) produced in the body. Free radicals have incomplete electron shells making them more chemically reactive than molecules with complete electron shells. They are formed in the course of normal cellular respiration and metabolism, especially under the influence of certain environmental chemical sand sunlight.

When an oxygen molecule (O_2) becomes electrically charged, it tries to steal electrons from neighboring molecules, causing damage to the DNA and other molecules. This damage may over time become irreversible, thereby leading to damage of cells and the body. The ROS are highly reactive molecules produced in the course of oxygen metabolism in the mitochondrial respiratory chain. The term ROS when used implies superoxide radicals, hydroxyl radicals (•OH), hydrogen peroxide (H_2O_2), and hydroperoxyl radicals (•HO_2). Other ROS include reactive sulphur species and the reactive nitrogen species such as nitric oxide (NO) and peroxynitrite (O=N–O–O-). The brain with only 2% of the body mass but responsible for about 20% of the oxygen utilization is particularly susceptible to oxidative damage. Furthermore, the brain tissues are readily susceptible to lipid peroxidation reactions due to the high amount of PUFAs present in neuronal membranes. The result of this is the formation of cytotoxic aldehydes, such as malondialdehyde (MDA) and 4-hydroxynonenal. Several studies have shown that cellular damage arising from free radicals and/or ROS is implicated in the etiology and pathophysiology of NDs and several other diseases**.**

Neurotransmitter Level

A number of neurotransmitters and associated biochemical processes are involved in the pathology of NDs. These include ACh, DA, and MAO. Low level of neurotransmitters such as ACh and DA characterized the two major neurodegenerative diseases, AD and PD, respectively. A loss or downregulation of the neuronal nicotinic acetylcholine receptors (nAChRs) as well as loss of the central cholinergic neurons is associated with the pathogenesis of the AD brain. The MAO catalyzes oxidative deamination of monoamines leading to the production of H_2O_2, aldehyde, ammonia, and amine, all of which have been found to be toxic at high concentrations and contribute to the pathology of NDs. Accordingly, MAO-B inhibitors have been reported to provide mild symptomatic effects and to reduce the incidence of motor fluctuations in PD with fewer side effects. They also modify the disease state thus making them ideal candidates for the early treatment of the disease**.**

The DA is a neurotransmitter synthesized by me encephalic neurons of the substantia nigra and ventral segmental area and by hypothalamic neurons of the actuate and per ventricular nuclei. Proper control of the DA levels and DA receptor interaction is important for normal functioning of the brain and several neurological and psychiatric disorders results from dysfunctional dopaminergic system. The dopaminergic pathways are implicated in several neurological and psychiatric diseases: for example, reduced levels of DA in PD, degeneration of selected DA neurons in HD, and dysfunctions of the dopaminergic system in ischemia and epilepsy. Dopamine has also been shown to have either neuroprotective or neurotoxic effects in different physiological and pathological condition.

HERBAL RESOURCES WITH NEUROPROTECTIVE EFFECTS

Bellisperennis

Bellis perennis's impact on a healthy neuronal cell line's capacity to survive was studied. When cells were exposed to 90% alcohol, their viability dropped dramatically to 18% compared to the 100% seen in the negative control group. Bellis perennis at 2 /ml, 4 V/ml, and 8 I/ml proved effective in counteracting the intoxicating effects of alcohol. The cell viability was dramatically improved.

Calendula-officinalis

Galendula officinalis Linn. Floral extract (COE) was tested for its neuroprotective effects against Monosodium Glutamate (MSG)-induced neurotoxicity in rats. In this study, adult Wistar rats were injected intraperitoneally with MSG and then given COB\@I00 and 200 mg/kg) orally 1 hour following the last MSG injection throughout

the course of 7 days. At the conclusion of the treatment period, the animals were evaluated for their level of mobility and then'slaughtere their brains were then extracted for histological examination and the measurement of LPO, GSH, CAT, TT, GST, and nitrite. Animal behavior, oxidative defense (increased levels of LPO and nitrite concentration and decreased antioxidant levels), and hippocampus neuronal histology were all significantly altered by MSG. Animals given MSG showed substantial behavioral changes, oxidative stress, and hippocampus damage; however, {fatment with COE greatly reduced all three. By monitoring for behavioral abnormalities, oxidative (Stress, and striatal damage in the brains of 3-NP-induced rats, researchers were able to assess the neuroprotective impact of Calendula officinalis flower extract (COE). Cotreatment with 3-NP (15 mg/kg, intraperitoneally) was administered to adult female Wistar rats 7 days after they had been pretreated with vehicle or COE (100 and 200 mg/kg) for 7 days. Changes in sensory motor capabilities and short-term memory were assessed in treated rats at the conclusion of the study period. In order to measure lipid peroxidation (LPO), glutathione, total thiols, glutathione S-transferase, catalase, and nitrite, brain homogenates were extracted from slaughtered animals. Neuronal damage in the striatum was assessed using a series of brain slices. Significant changes in behavior, oxidative defense system (as seen by increased levels of LPO and nitrite concentration), and antioxidant levels were induced by 3-NP. It also caused a decline in striatal Reuronal cell number. COE treatment dramatically reduced the abnormalities in behavior, oxidative damage, and striatal neuron loss seen in rats given 3-NP.

Carthamus-tinctorius

Hydroxysafflor yellow A (HSYA)jwas studied for its neuroprotective effects and potential mechanism of action against the neurotoxicity of glutamate in primary cultured rat cortical neurons. Neuronal death caused by excitotoxicity was significantly reduced by HSYA therapy.Restoring a healthy equilibrium between pro- and anti-apoptotic proteins, HSYA reduced Bax expression. In addition, HSYA dramatically down-regulated NR2A-containing NMDA receptor expression, whereas. upstegulating NMDA receptors containing NR2B was unaffected by NMDA exposure. Astragali, Ligusticum wallichii, Angelica (sinensis, and Carthamus tinctorius) were examined for its neuroprotective effects on reducing brain infarction(aind global ischemia and halting neurodegeneration in the wake of ischemia, Because of the increase in blood flow to the brain, there is hope that neurodegenerative disorders like Parkinson's and Alzheimers could be lessened in severity.

Coriandrum sativum

Brain ischemic-reperfusion injury was used \to test Coriandrum sativum's neuroprotective properties. Ischemic brain damage was caused in albino rats by blocking their common carotid arteries for 30 minutes, followed by reperfusion for 45 minutes. Histological altera Peroxidation, superoxide dismutase, catalase, glutathion, calcium, and total protein levels were assessed after the reperfusion period concluded. Lipid peroxidation, calcium, and infarct size all increased significantly after bilateral common carotid artery closure, whereas lowered glutathion, superoxide dismutase, and catalase levels all decreased. The endogenous enzyme levels of SOperoxide dismutase, glutathion, catalase, and total protein were enhanced after 15 days of pretreatment with methanolic extract of leaves of Coriandrum sativum (200 mg/kg, po), while cerebral infarct size, lipid peroxidation, and calcium levels were decreased. Reactive alterations in brain histology such as gliosis, lymphocyte infiltration, and cellular edema were also mitigated. In light of this information, we may conclude that Coriandrum sativum has a preventive effect against ischemic-reperfusion damage and cerebrovascular insufficiency.

Crocus sativus

Saffron aqueous extract was tested for its ability to prevent aluminuim chloride (AICI3)-induced neurotoxicity in mice. AICI3 (40 mg/kg/day) was administered subcutaneously into Balb/c and C57BL/6 mice for 45 days. Four groups of mice were used, two of which received AICI3 treatment and the other two received AICI3 treatnién with either water saffron extract (200 mg/kg bw once a day for 45 days) or honey syrup (500 mg/kg bw once a day for 45 days). No treatment was given to the control group. Brain oxidative stress and antioxidant status. Were evaluated, and mRNA expression in the treated and untreated groups was compared using differential display in both mouse strains, In addition, clones and sequences were created for up-and down-regulated genes. Comparisons were made between the sequenced gene and those listed in GenBank. Antioxidant enzymes such superoxide dismutase, catalase, and glutathione peroxidase were shown to have significantly lower activity in the AICI3 groups of both mouse strains (p0.001). Lipid peroxidation was significantly elevated in the AICI3 groupsyias measured by the concentration of thiobarbituric acid reactive compounds in the brain, Serum tumor indicators such as arginase and a-I-fucosidase were found to be elevated in the AICI3 treated group, suggesting carcinogenicity. Approximately 22 up-and down-regulated genes were found among the over 350 band pattems obtained; Three up-

regulated genes were identified, and their sequence analysis indicated similarities to B-cell lymphoma 2 (Bcl-2), R-spondin, and the inositol polyphosphate 4-phosphatase genes (INPP4B). All animals tested (save the controls) showed an increase in R-spondin expression, but only those given AICI3 and honey syrup showed increases in the other two genes. The neurotoxicity of AICI3 in mouse brains was confirmed by biochemical and molecular analyses, the scientists concluded. Saffron extract and honey syrup also showed some protective effects against the neurotoxicity of AICI3. The discovered molecular data revealed that AICI3 induced the genes for cell proliferation, R-spondin and inositol polyphosphate 4-phosphatase, as well as the anticancer gene, BCL-W, which may be a part of the brain cell's DNA repair mechanism.

Cyperus rotundus

In order to determine whether or fit a water extract of Cyperus rotundus rhizoma can prevent neurons from being damaged by'}6-hydroxydopamine (6-OHDA), an animal model of Parkinson's disease was used. The cell viability of PC12 cells was significantly protected by a
water extract of Cyperus rotundus rhizoma at concentrations of 50 and 100 microg/ml. Cyperus rotundus rhizoma water extract blocked 6-OHDA-induced mitochondrial membrane potential decrease, caspase-3 activity, mitochondrial reactive oxygen species production, and caspase-3ity. Dopaminergic neurons in primary mesencephalic culture were similarly significantly protected by a water extract of Cyperus rotundus rhizoma.

Dalbergia sissoo

Brain weight, antioxidant levels, histological examinations, and TTC staining were used to determine Whether or not the ethanolic extract of Dalbergia sissoo leaves has neuroprotectiv properties in rats with cerebral ischemia. Negative control (global cerebral ischemia rats) was used to evaluate the effects of the extracts (ethanolic 300, 600 mg/kg). Brain weight, antioxidant levels, and normal levels were significantly recovered after pretreatment with Dalbergia sissoo extract (DSE) (300 mg/kg and 600 mg/kg, po for 10days) compared to ischemia-reperfusion- induced oxidative stress groups. Histopathological and staining investigations on coronal brain slices of extract-treated groups showed they were protected against ischemia brain injury.

Geum urbanum

The neuroprotective potential of extracts from three Romanian medicinal plants (E. planum, G. firbanum, and C. benedictus) was studied in vitro by measuring their ability to inhibit acetylcholinesterase and tyrosinase. The ACHE inhibitory activities of the Geumu rbanum aqueous extract were 27.031 5, 36.481.7, and 79.113.9% at concentrations of 0.75 mg/ml.

Hyoseymus niger

Extracts of Hyoscyamus niger seeds were tested in a I-methyl-d-phenyl-1,2,36- tetrahydropyridine (MPTP) model of Parkinson's disease in mice for their neuroprotective effects. Motor functions and striatal dopamine levels were evaluated in Parkinsonian mice that were given the extracts twice daily (125-500 mg/kg, po.) for two days. Motor impairments (akinesia, catalepsy, and lower swim score) and striatal dopamine loss in MPTP-treated mice were considerably alleviated by administration of the aqueous methanol extract (containing 0.03% wiw of L-DOPA), but not the petroleum ether extract. When isolated mitochondria were treated with I-methyl-4-phenyl pyridinium (MPP+), the extract significantly reduced the production of hydroxyl radicals (OH) by the mitochondria. The capacity of the methanolic extract of Hyoscyamus niger seeds to suppress enhanced OH generation in the mitochondria ‘may account for the protective effect it has against parkinsonism.

Juglans regia

Walnuts (6%) were tested for their potential to protect rats’ brains from the neurotoxicity caused by cisplatin. The effects of chronic cisplatin therapy (5 mg/kg/week for 5 consecutive Weeks) on male rat hippocampus- and cerebellum-related behavior were studied. dietary walnut (6%) was included in the research. Cisplatin treatment significantly reduced the rats’ exploratory activities and their ability to remember previously seen objects. Memory and motor skills in cisplatin-treated rats were enhanced by eating walnuts, although walnuts alone had no discernible effect compared to a saline control group. Walnut counteracted cisplatin’s impact of prolonging the time it took for a person to react to pain.

Lagerstroemia speciosa

Lagerstroemia speciosa alcoholic extract (50 and po, for 58 days) was tested for its neuroprotective effects on streptozotocine-induced diabetic neuropathy in rats, which causes painful neuropathy. It was determined how much nitric oxide, reduced glutathione, and lipid peroxidation were present in the sciatic nerve. Both the lowered body weight and the increased blood sugar level were considerably recovered by the extract. Mechanical, cold, and thermal hyperalgesia tests all revealed a dose-dependent decrease in pain threshold when the extract was used.

Lithospermum officinale

In.a mouse model of ischemia/reperfusion injury, shikonin was shown to have a neuroprotective effect, reducing neurological impairment scores, infarct size, and levels of malondialdehyde, carbonyl, and reactive oxygen species. Shikonin's antioxidant properties may play a role in explaining why it protects nerve cells. Microglial cells, which

play a crucial role in regulating the body's immunological and inflammatory responses, have also been shown to benefit from shikonin and its derivatives in studies of neuroprotection. Isobutyryl- and isovalerylshikonin, two shikonin derivatives, were more efficient than shikonin in suppressing LPS-induced activation of microglia. Additionally, shikonin rescued dopaminergic neurons from the neurotoxicity caused by6-hydroxydopamine.

Lycium barbarum

Light-exposed mice retinas were subjected to oxidative stress, and the neuroprotective eff Lycium barbarum polysaccharides) (LBP, 150 mg/kg or 300 mg/kg) on photoreceptor degeneration were evaluated. The electroretinography (ERG) amplitudes of the - and -waves, which had been diminished by light exposure, were greatly enhanced by LBP. Photoreceptor cell death, nuclear condensation, an increase in mitochondrial vacuoles, outer membrane disc enlargement, and cristae fractures were all light-induced alterations that were markedly mitigated by LBP. In addition, it greatly reduced ROS (reattive oxygen species) production. LBP-treated animals showed dramatic increases in the mRNA levels of both nuclear factor erythroid 2-related factor 2 (Nrf2) and thioredoxin reductase (TrxR1). The DNA repair gene Poly (ADP-ribose) polymerase (PARP14) had considerably lower messenger RNA levels in LBP-treated animals.

Mangifera indica

Mangifera indica leaf extract (100, 200, 300 mg /kg bw, orally for 28 days) was tested for its protective effects against cadmium-induced neurotoxicity in ras. Malondialdehyde, nitric Oxide, the oxidized form of glutathione, and 8-hydroxy-2-deoxyguanosine were all elevated in the brains of Cd-exposed rats, as were the inflammatory mediators tumor nétrosis factor alpha and interleukin-1. And in the prefrontal cortex, Cd significantly reduced AChE activity and the biogenic amines tested while increasing the metabolites tested. All altered cortical parameters were normalized after extract coadministration. The extract appears to have protective effect against Cd-induced neurotoxicity at medium and higher doses, possibly as a result of its antioxidant and anti-inflammatory properties.

Matricaria chamomilla

Ethyl! alcohol extract of Matricaria chamomilla (50, 100, and 200 mg/kg. bw) was tested in rats for its neuroprotective effects against cerebral ischemia-induced motor dysfunctions. Motor dysfunction caused by ischemia and subsequent reperfusion was greatly alleviated by Matricaria chamomilla extract. Ischemia/reperfusion was also shown to drastically lower serum malondialdehyde (MDA) levels. Serum nitric oxide (NO) level and brain (hippocampus and cortex) total antioxidant capacity were unaffected.

Medicago sativa

Mice were studied to see whether a Medicago' Sativa methanol extract might prevent brain damage caused by ischemia and/feperfusion. Short-term memory and motor coordination impairments were mitigated, and reduced) glutathione, superoxide dismutase, and total tissue sulfhydryl levels were restored following pre-treatment with Medicago sativa methanolic extract (100 or 200 mg/kg, orally). Directly, the extract scavenged free radicals from reactions involving 1, -diphenyl-2-picrylhydrazyl and O2 from phenazine methosulfate-nicotinamide adenine dinucleotide systems, and indirectly, it blocked the conversion of XD to XO, preventing the formation of O2. The therapeutic impact of Medicago sativa in neurodegenerative illnesses was investigated using a molecular docking and network analysis combination. The triterpenesaponins found in Medicago sativa have been linked to the plant's memory-enhancing and nervous system-protecting properties.

Melilotus officinalis

Melilotus officinalis extract (100, 250, and 500 mg/kg. daily for 3 days) was tested for its protective effects on brain tissues in rats suffering from acute cerebral ischemia generated by carotid artery blockage. Biochemical indices in the plasma, including 6-keto-PGF1 and TXB2, as well as cytokine concentration, oxidative stress, apoptosis ratio, and Bel2 and Bax protein expressions in brain tissues, were used to corroborate the diagnosis of cerebral ischemia. When compared to the negative control group, the extract considerably reduced both the size of the fracture and the severity of the resulting neurological loss. The plasma concentration of 6-keto-PGFI also rose, while oxidative stress and cytokine levels in brain regions were dramatically reduced. The extract significantly increased plasma TXB2 levels. Extract also reduced cell death caused by cerebral ischemia.

Melissa officinalis

Researchers looked at whether or not Melissa officinalis may protect neurons from the ecstasy or 3.4-methylene dioxy methamphetamine (MDMA) used in hippocampus primary culture. In hippocampal neuronal culture, a high dose of ecstasy led to severe mitochondrial dysfunction, with values about 40% lower than the control value, and incféased apoptotic neuronal death, with values about 35% higher than the control value. However, co-treatment with Melissa officinalis significantly reversed these damages, with values

about 15% lower and 20% higher than the MDMA alone group, respectively.

Mentha-longifolia

The essential oils and ethyl acetate fraction of Mentha longifolia showed significant acetylcholinesterase inhibitory") activity (ICS0=123g/ml), indicating they may have neuroprotective effects against Alzheimer's disease. Brain ischemia in a rat model of stroke led researchers to examine the neuroprotective effects of Mentha longifolia ethanol extract (50, 100, and 200 mg/kg/day for 21 days). Total infarct volume, brain water content, and Evans Blue extravasation in the ischemic hemisphere were all significantly decreased after pretreatment with Mentha longifolia ethanol extract compared to the control group. The antioxidant capacity of the brain was improved by Mentha longifolia ethanol extract (100 and 200 mg/kg/day). The blood antioxidant capacity and MDA level of the 100 mg/kg/day group were both considerably greater than those of the control group.

Momordica charantia

Against cerebral ischemia/reperfusion damage, Momordica charantia polysaccharide (MCP) was investigated for its neuroprotective effects by scavenging superoxide (02-), nitric oxide (NO), and peroxynitrite (ONOO-) and inhibiting c-Jun N-terminal protein kinase (JNK3) signaling cascades. Because of its direct scavenging activities and inhibition of lipid peroxidation, MCP was shown to diminish infarction volume in ischemic brains in vivo and to attenuate apoptotic cell death in neural cells under OGD condition in vitro. The activation of the INK3/cJun/Fas-L and INK3/cytochrome C/caspases-3 signaling cascades was likewise reduced in ischemic brains in vivo by MCP.

Morusnigra

The PI3K/AKUGSK-3 signaling pathway was also examined for its potential involvement in mediating the antidepressant-like effects of Morus'inigra and syringic acid against glutamate-induced harm. Similarly to fluoxetine (10 mg/kg), Morus nigra (3 mg/kg) and syringic acid (1 mg/kg) treatment for 7 days had an antidepressant-like effect. Both cerebrogortical and hippocampal slices were protected from glutamatergic excitotoxicity after therapy. Morus nigra and syringic acid's neuroprotective action was mediated, at least in part, through the PISK/AKUGSK- 3 signaling pathway.

Myrtuscommunis

Myrtle's potential to protect nerve cells from damage was investigated in a rat model of neurotoxicity caused by lipopolysaccharides (LPS). Rats were tested to see what levels of nitric oxide, malondialdehy: 1 beta, tumor necrosis factor beta, estrogen, 5-lipoxygenase, se, lipoxin A4, asymmetric dimethyl arginine (ADMA), and von Willebrand factor (VWF) were in their blood and brain tissue after being put through a series of challenges. The estrogen level in LPS-imtoxicated rats dropped significantly, while the stress measures studied rose significantly. All of the biomarkers that were looked at showed significant improvement.

Neriumoleander

Neriumfoleander (PBI-05204) supercritical CO2 extract significantly reduced neuronal injury caused by oxygen and glucose deprivation during ischemic stroke. PBI-05204's neuroprotective effects persisted for hours after oxygen and carbohydrate deprivation were applied. Oleandrin and/or other glycoside components of PBI0S204 were responsible for its neuroprotective effects. Authors concluded that PBI-05204 has therapeutic promise for treating ischemic stroke and preventing the related neuronal death.

Nigellasativa

Nigella sativa was examined in relation to the corticosteroid methyl prednisolone in the context of rat spinal cord injury models. In addition to lowering tissue MDA and protein carbonyl levels, both therapies protetted tissue SOD, GSHPx, and CAT enzymes from inhibition. Neurons were shielded effectively in methyl prednisolone and Nigella sativa-treated groups.

Ocimumbasilicum

After inducing cerebral injury by blocking the bilateral common carotid artery and then re-opening it, mice were given Ocimum basilicum leaf extract (200 and 400 mg/kg, orally, once day for 7 days) to see whether it may prevent further damage to the brain. Morris Water Maze, Elevated Plus Maze, and Neurological Severity Score were used to measure cognitive results and sensorimotor abnormalities, respectively. Memory and motor skills'were significantly enhanced after treatment with the extract. The extract significantly reduced oxidative stress and the extent of brain infarcts in mice. The extract has strong antioxidant properties due to its high total phenol content.

Oxaliscorniculata

Alcoholic extract of Oxalis'comiculata was tested for its neuroprotective properties by observing its impact on MPTP (1-methyl-4-phenyl-1,2.3,6-tetrahydro_pyridine)-induced Parkinson's disease in mice. The actophotometer, raised plus maze, rota rod, hole board, step down, and step through tests were used to examine the animals' behaviors. When given Oxalis corniculata, MPTP-induced Parkinsonic mice regained their normal motor and motor-coordination abilities. Oxalis comiculata, withivarying dosages, substantially improved memory retention and retrieval. 'The authors found that the presence of antioxidants such flavonoids, coumarins, tocopherols, and phenolic acids in

Oxalis comiculata extract contributed to its ability to improve memory retention-and-retrieval.

Table 1. Mechanism of neuroprotection of some imperative herbal resources

S. No	PLANT	MECHANISM OF NEUROPROTECTION
1	Carthamus tinctorius	Down-regulated NR2A-containing NMDA receptor expression
2	Cyperus roundus	Blocked 6-OHDA-induced mitochondrial membrane potential decrease, caspase-3 activity, mitochondrial reactive oxygen species production, and caspase-3 activity
3	Geum urbanum	Inhibit acetylcholinesterase and tyrosinase
4	Hyoscymus niger	enhanced -OH generation in the mitochondria
5	Lycium barbarum	Increases in the mRNA levels of both nuclear factor erythroi 2-related factor 2 (Nrf2) and thioredoxin reductase (TrxR1)
6	Medicago sativa	02 from phenazine methosulfate-nicotinamide adenine dinucleotide systems
7	Momordica charantia	Scavenging superoxide (Or) peroxynitrite (ONOO-) and inhibiting c-Jun N-terminal protein kinase (JNK3) signaling cascades
8	Morus nigra	PI3K/AKUGSK-3 signaling pathway

Conclusion

Herbal remedies are extensively used in developing countries, not only because they are perceived as safe, but also due to limited access to modern medical care. In Western countries, there is an increasing demand for effective treatments for severe metabolic and neurological disorders, a need that has traditionally been addressed by plant-based remedies. A wide variety of plants produce bioactive secondary metabolites derived mainly from polyphenols, including alkaloids, terpenoids, and other compounds synthesized through the shikimic acid and/or acetate pathways. Despite the large volume of data available on plant-derived neuroprotective compounds, there remains a strong need for further investigation, particularly regarding efficacy trials in humans. Secondary metabolites represent a class of bioactive compounds present in medicinal and food plants and are known to exert beneficial effects on human health. Western industrialized countries are rich sources of phytochemicals such as phenylpropanoids, isoprenoids, and alkaloids, which play a protective role against chronic neurodegenerative diseases.

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