Advantaging Neuroprotective Trees from North-East India

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Abstract: The word "neuroprotection" is broad and frequently used to describe treatment approaches that can stop, slow down, or even reverse neural damage. Throughout the world, herbal medicinesare extensively used as affordable, efficient, and secure substitutes for pharmaceuticals. Among the 34 global biodiversity hotspots, North-East (NE) India is home to a considerable number of medicinal plants and is part of the Indo-Burma global hotspot. People in this area employ a range of medicinal plants in traditional medicine to cure a variety of illnesses. This publication aims to evaluate plants from Northeast India that may have neuroprotective properties and to serve as a reference for future research on novel and alternative treatments for neurological conditions.

Keywords: Neuroprotection, North-East India, Herbal Medicine, Neurotoxicity, Neuroprotective plant.

INTRODUCTION

India's northeast (NE) region is one of the richest in terms of biological diversity; it has a highendemism rate and is home to numerous uncommon species that are currently facing grave threats. Joined to the main landmass via a slender corridor that runs between Bangladesh and Nepal. Arunachal Pradesh, Assam, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, and Tripura are the eight states that make up this region, which has a diverse spectrum of physiographic and ecoclimatic characteristics. Neighbour Of the 34 global biodiversity hotspots currently recognised (2005), India is includedin the Indo-Burma hotspot. The WHO has designated the entire Eastern Himalaya as a Global200 Eco-region of priority. The nervous system is an intricate network of nerve cells that controls both voluntary and involuntary bodily movements as well as the movement of nerve impulses throughout the body. The peripheral nervous system (PNS), which is made up of the remaining nervous system elements that are not located within the central nervous system (CNS), and the brain and spinalcord make up the CNS, which is divided into two main sections. Chemically, the brain and spinal cord is isolated by the so-called blood–brain barrier, which prevents most types of chemicals from moving from the bloodstream into the interior of the CNS. These protections make the CNS less susceptible in many ways than the PNS.

MECHANISMS OF NEUROTOXICITY

AMYLOID CASCADE HYPOTHESIS:

The amyloid cascade hypothesis has dominated the field of Alzheimer's disease (AD) researchand has provided the intellectual underpinning for therapeutic intervention [1]. According to this theory, the first pathogenic event in AD is the deposition of β-amyloid, which eventually causes senile plaques, neurofibrillary tangles, neuronal cell death, and dementia. According togenetic research, early-onset familial dementia and the buildup of βamyloid are caused by mutations in the presenilin 1 and presenilin 2 genes, as well as the amyloid precursor protein [2].

APOPTOSIS:

A series of biological events known as apoptosis or programmed cell death (PCD) cause cells to undergo distinctive morphological changes before dying. Cell shrinkage, nuclear fragmentation, chromatin condensation, and fragmentation of chromosomal DNA are among the alterations. It has been determined that caspase-3 is a crucial modulator of neuronal PCD. This protease is essential to the growth of the nervous system; it is activated early in the development of the neural tube and continues to

be active throughout the postnatal differentiation of the neural network. A significant aspect of the neuronal cell death programme, caspase-3 activation, is also present in a large number of chronic neurodegenerative disorders [3].

EXCITOTOXICITY:

Howard first proposed this idea in 1978. Neuronal degeneration brought on by excessive glutamate receptor stimulation is known as excitotoxicity. Ionotropic glutamate receptors, such as the AMPA and N-methyl-D-aspartate (NMDA) receptors on post synaptic neurons, are activated by glutamate released from the presynaptic neuron during glutamatergic neurotransmission. An action potential is eventually produced when these glutamate receptors are activated, which causes an influx of Na+ and Ca2+ ions into the cell and depolarization [4].Changes in glutamate homeostasis can have a substantial impact on neurons by generating neurotoxic or ex cytotoxic cascades, despite the fact that glutamate is essential for excitatory neurotransmission [5]. Continuous activation of large numbers of NMDA receptors leads to increases in intracellular calcium loads and catabolic enzyme activities, which can trigger a cascade of events eventually leading to apoptosis or necrosis [6]. Experimental evidences support that ex cytotoxicity could contribute to neuronal damage in stroke, neurotrauma, epilepsy, and a number of neurodegenerative disorders including amyotrophic lateral sclerosis[7].

OXIDATIVE STRESS:

A disruption in the equilibrium between the generation of reactive oxygen species (ROS) and antioxidant defences is known as oxidative stress. Excess ROS have detrimental effects on cellsdue to oxidative stress, which causes an accumulation of ROS. Lipid peroxidation (LPO) is mediated by ROS. LPO is a self-sustaining process, which amplifies the effects of the originalfree radical and leads to the activation of a cascade of toxic reactions resulting in extensive tissue damage. The brain is especially prone to LPO because of the way neuronal tissue is composed, which leaves the brain open to chain reactions that are mediated by free radicals and result in LPO products. The brain contains high levels of polyunsaturated fatty acids and high levels of redox transition metal ions in addition to its high oxygen consumption. On the other hand, levels of lower molecular weight and enzymatic antioxidants are relatively low and might contribute to the accumulation of oxidative damage [8]. LPO in the brain is one of the major factors of several neurological disorders.

PROINFLAMMATORY CYTOKINES:

Injury, ischemia, and infection are just a few of the pathogenic situations that cause microglia to become activated in the central nervous system. Proinflammatory cytokines such interleukin-1 (IL-1), IL-6, and tumour necrosis factor alpha are produced by activated microglia (TNF-α).Although the release of these substances is usually done so in an attempt to stop additional harm to the CNS tissue, neurons and other glial cells may find them hazardous.

While chronic activation of microglia has been suggested as a potential mechanism in neurodegenerative illnesses, short-term stimulation is generally acknowledged to play a beneficial effect. Growing research suggests that neurodegenerative illnesses may be influenced by chronic microglial activation in their onset and progression. Unfortunately, determining the role of pro-inflammatory cytokines in these disorders has been complicated by their dual roles in neuroprotection and neurodegeneration [9].

CHOLINERGIC THEORY:

One of the most prominent theories on the neurochemical underpinnings of AD is the cholinergic hypothesis. According to the hypothesis, the decline in cognitive function observed in AD patients can be attributed mostly to the death of cholinergic neurons in the basal forebrain and the ensuing loss of cholinergic neurotransmission in the cerebral cortex and other regions [10].

NEUROPROTECTION:

Any kind of therapeutic approach, typically pharmaceutical, that can stop, slow down, or even reverse neuronal damage—whether it be axonal degeneration, neuronal death, or any other type of neuronal injury—is referred to by the general term "neuroprotection." The use of acetylcholinesterase inhibitors, glutamate antagonists, calcium channel

blockers, nitric oxide synthase inhibitors, and other neuroprotective tactics is currently being studied.

HERBAL PROTECTION:

A different kind of treatment for various neurological conditions is the use of herbs. Numerousbioactive substances that have been extracted from herbs are being effectively employed to treat neurological conditions. Herbal therapies are becoming more and more popular as a resultof the negative consequences of chemical medications. Herbal extracts and active ingredients extracted from various herbs have been shown in numerous scientific studies to alleviate nervediseases and enhance memory and learning.

ACORUS CALAMUS:

Acorus calamus L. (AC), often known as Bach in Assamese and Sweet flag in English, is a perennial aromatic herb that is herbaceous and belongs to the Aceraceae family. For hundredsof years, the Indian traditional medical system has utilized the roots and rhizomes of AC treesas a rejuvenator for the nerve system and brain, as well as a treatment for stomach issues. Therhizome of AC, namely the compounds α and β-asarone, have been shown through scientific research to exhibit a variety of pharmacological properties, including sedative, CNS depressant, behavior-modifying, anticonvulsant, acetylcholinesterase (AChE) inhibitory, and memory-enhancing effects [11,12].AC is registered in the Pakistani Materia Medica where both the roots and rhizomes are used for nervous diseases and disorders, whereas the rhizome is especially indicated in cases of neurological symptoms of the brain [13]. AC also shows neuroprotective effect against stroke and chemically induced neurodegeneration in rats [14,15].

ASPARAGUS RACEMOSUS WILD:

The Asparagaceae family includes Asparagus racemosus Wild. (AR). It goes by the names Satmuli (Hindi) and Satumul (Assamese). This well-known Ayurvedic rasayana helps to ward off ageing, lengthen life, boost immunity, enhance mental clarity, give the body more energy, and enhance vigour. Additionally, dyspepsia, tumours, inflammation, neuropathy, and hepatopathy are treated with it [16]. Asparagamine, racemosol, polysaccharides, mucilage, steroidal saponins (shatavarins I–IV), isoflavones, folic acid, asparagamine, B1, B2, C, E, Mg, P, Ca, Fe, and mucilage are the main active ingredients in AR. Asparagine, arginine, tyrosine, flavonoids (kaempferol, quercetin, and rutin), tannin, resin, and essential oils are other main chemical components of AR [17, 18].According to reports, AR root extract has pharmacological properties that include immunomodulatory, antidiabetic, antiulcer, antioxidant, and antidiarrheal properties [21–22]. After being given to mice, methanolic extract significantly reduced the levels of brain monoamine Oxidase A (MAOA) and monoamine Oxidase B (MAO-B) activity. It has been discovered that the methanolic extract has antidepressant properties, most likely through inhibiting MAO-A and MAO-B as well as through interactions with the GABAergic (gamma amino butyric acid), adrenergic, dopaminergic, and serotonergic systems [23]. When compared to hexane and chloroform extracts, the methanolic extract of AR also strongly inhibited cholinesterase and acted as a non-selective competitive inhibitor [24]. Another study by Laddawan Lalert *et al.* on neuroprotective effects of the AR root extract on ovariectomized rats demonstrated that AR may be a beneficial agent for prevention of cognitive decline induced by ovariectomy [26].

BACOPA MONNIERI (L) WETTEST:

According to reports, AR root extract has pharmacological properties that include immunomodulatory, antidiabetic, antiulcer, antioxidant, and antidiarrheal properties [21–22]. After being given to mice, methanolic extract significantly reduced the levels of brain monoamine Oxidase A (MAOA) and monoamine Oxidase B (MAO-B) activity. It has been discovered that the methanolic extract has antidepressant properties, most likely through inhibiting MAO-A and MAO-B as well as through interactions with the GABAergic (gamma amino butyric acid), adrenergic, dopaminergic, and serotonergic systems [23]. When compared to hexane and chloroform extracts, the methanolic extract of AR also strongly inhibitedcholinesterase and acted as a non-selective competitive inhibitor [24].

CELASTRUS PANICULATUS WILD:

The Celastraceae family includes Celastrus paniculatus Wild (CP). Jyotishmati, Pokitai (Assamese) is the common name for it. Unani CP has been used in the traditional Ayurvedic medical system to treat joint pain, arthritis, mental disorientation, physical weakness, headaches, asthma symptoms, and tonicity. It has also been used as an emetic and a potent hunger stimulant [32]. According to phytochemical studies, the following compounds are present: evoninoate, sesquiterpene, wifornine F, alkaloids paniculatine A, B, and C, celastrine, celapanine, celapanigine, celapagine, polyalcohol (malangunin, malkanginnol, malkanguniol, and paniculatadiol), triterpenoids (pristimerin), and sterols (β-amyrin and β- sitosterol) [33–35]. Neuronal cells treated beforehand with CP seed oil showed a substantial reduction in glutamate-induced neuronal death. Whole-cell currents triggered by N-methyl-D-aspartate were considerably and reversibly reduced by CP seed.

The findings imply that via modifying glutamate receptor activity, water soluble extracts of CPseed (CPWSE) shielded neuronal cells from glutamate-induced damage. Both the shuttle-box and step-through paradigms demonstrated improvements in learning and memory with CPWSE(200 mg/kg body weight for 14 days). Step-through delay in the step-through apparatus and thenumber of avoidances in the shuttle-box were both increased by 100, 200, and 300 mg/kg bodyweight dosages of the aqueous extract. The step-down delay was significantly increased by theaqueous extract doses of 200 and 300 mg/kg body weight. Malondialdehyde (MDA) levels in the brain were significantly reduced by only 200 and 300 mg/kg body weight, while glutathione and catalase levels were significantly increased at the same time [36].

CENTELLA ASIATICA (L) URB:

In Ayurvedic medicine, Centella asiatica (L.) Urb. (CA) has been used for ages. It is sometimesreferred to as Indian pennywort (English) or Manimuni (Assamese). CA is a member of the Apiaceae family. Numerous biochemical components of CA, such as flavonoids, terpenoids, essential oils, alkaloids, carbohydrates, and amino acids, have been documented in scientific investigations [37, 38].

The application of CA to boost cognitive function and intellect dates back thousands of years. Furthermore, 28 human samples have undergone experimental verification that CA improves self-esteem and working memory [39]. Enhanced learning and memory capabilities were demonstrated by male Spraque-Dawley rats when exposed to Asiatic acids extracted from CA[40]. When given as an aqueous extract at a concentration of 200 mg/kg, it has also been demonstrated to enhance brain function in juvenile and young mice [41]. CA has demonstrated its ability to inhibit AChE, the primary enzyme involved in the pathophysiology of AD. This was demonstrated in vitro through testing of the plant's hydroalcoholic extract against AChE.

Since AD patients' brains have been shown to have deficits in the amount of acetylcholine (ACh), which is digested by AChE, inhibiting AChE and its sister enzyme butyrylcholinesterase (BChE) has emerged as a sensible target for AD medication development [42]. Using Ellman's spectrophotometric technique, the extract was reported to inhibit AChE with 50% of the inhibition rate at 150 µg/mL concentration [43]. Research conducted on rats in vivo has demonstrated that CA had a noteworthy antioxidant impact and can potentially lower MDA while raising glutathione and catalase levels.

In addition to neuroprotective effect of CA, it has been reported to own a wide range of biological activities such as wound healing [44], anti-inflammatory [45], ant psoriatic [46], antiulcer [47], hepatoprotective [48], anticonvulsant [49], sedative [50], immunostimulant cardioprotective, antidiabetic, cytotoxic and antitumor, antiviral, antibacterial, insecticidal, antifungal, antioxidant, and for leprosy and venous deficiency treatments.

CORIANDRUM SATIVUM L:

Coriandrum sativum L. (CS), a highly esteemed ayurvedic medicinal tree also referred to as the Dhanya, is a member of the Apiaceae family. Coriander is utilised to treat digestive, respiratory, and urinary system issues in traditional Indian medicine. Antioxidant activity, anti-diabetic activity,anti-mutagenicactivity,antihelmintic activity,sedative-hypnotic activity, anticonvulsant

activity, diuretic activity, cholesterol lowering activity,antifungal activity ,anti-feeding activity ,anticancer activity ,anxiolytic activity, hepatoprotective activity, anti-protozoal activity,anti-ulcer activity, post-coital anti-fertility activity,and heavy metal detoxification have all been reported to be displayed by CS. Mahendra and Bisht's study found that extracts at 100 and 200 mg/kg had anti-anxiety effects comparable to those of diazepam.

In experimental rats, pretreatment with a 200 mg/kg methanolic extract of CS leaves enhanced endogenous levels of superoxide dismutase, glutathione, catalase, and total protein levels. It also decreased the extent of brain infarcts, levels of calcium, and LPO. It also decreased reactivechanges in brain histology such gliosis, lymphocytic infiltration and cellular edema. In a different study, leaves of CS (5, 10 & 15% W/W of diet) improved memory scores in both young and old rats in a dose-dependent manner, according to Vasudevan Mani & Milind Parle. Additionally, the memory deficits caused by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.) were successfully restored by CS leaves. Cholesterol-lowering, anti-inflammatoryand antioxidant properties of leaves of CS may favorably contribute to its memory-enhancement effect.

CROCUS SATIVUS L

The Iridaceae family includes Crocus sativus L. (CS). Commercially known as saffron, the dried red stigma of CS is a kind of spice. The plant's stigmas are employed because they are rich in several chemical elements such as crocetin, crocin, and other flavonoids that provide them a variety of medicinal uses for different conditions. The traditional uses of CS include fever, galactagogue, inflammations, laxative, stimulant, stomachic, and as a tonic. It has also been used as an aphrodisiac, analgesic, anodyne, antispasmodic, bitter, cephalgia, diuretic, depression, and epilepsy. Numerous therapeutic properties of CS were also shown by scientific research, including antihypertensive, anticonvulsant, antitussive, antigenototoxic, anticancer, cytotoxic effects, anxiolytic, antioxidant, antidepressant, anti-inflammatory, and relaxing properties.

Hippocampal long-term potentiation, a kind of activity-dependent synaptic plasticity that may underpin learning and memory, was shown to be improved by ethanol-induced learning behaviour deficits in mice when aqueous extract of CS was used. In order to examine the neuromodulatory effects of crocetin in a 6-hydroxydopamine, Abdullah Shafique Ahmad et al. assessed Parkinsonism in a rat model. The findings indicated that crocetin could prevent both neurological disorders and Parkinsonism.Lower than its other ingredient dimethylcrocetin, the water: methanol (50:50, v/v) extract of CS stigmas reduced A-beta fibrillogenesis, which is generated by oxidation of the amyloid beta-peptide fibrils in AD, in a concentration and time dependent manner.

An abnormal feeling of worry and unease brought on by tenseness, a faster heartbeat, perspiration, etc. is called anxiety. It is also an unpleasant condition of internal conflict. Rat models were used in the study to check the anxiolytic properties in the presence of crocin and the authors N. Pitsikas et al., found that the crocin which is the active constituent of CS. Possess the anxiolytic-like effects in the rat.

CLITORIA TERNATEA L:

Clitoria ternatea L. (CT) is a herbaceous medicinal plant that is also referred to as Aparajita (Assamese) and Aparajit in Hindi. CT is a member of the Leguminosae family. It has long been utilised in Ayurvedic medicine for millennia as a nootropic, memory booster, antistress, anxiolytic, antidepressant, anticonvulsant, sedative, and tranquillizer. From CT, a variety of secondary metabolites have been identified, including as steroids, flavonol glycosides, anthocyanins, and triterpenoids. Numerous pharmacological activities, such as antimicrobial, antihelmintic, antipyretic, proteolytic, anti-inflammatory, larvicidal, analgesic, diuretic, local anaesthetic, antidiabetic, insecticidal, and vascular smooth muscle relaxing properties, have been confirmed by scientific studies to be present in its extracts. For a duration of 30 days, oral intubation with 100 mg/kg of aqueous root extract of CT has been shown to enhance memory and learning in rats.

Subsequent investigation of the dendritic arborization of CA3 pyramidal neurons in rat hippocampi revealed a notable rise in basal and apical dendritic branches. It has been observedthat rats and mice given an alcoholic extract of CT

intraperitoneally experience drowsiness and decreased attention. It has been observed that giving rats oral therapy with alcoholic extracts ofthe aerial and root sections of CT increases ACh concentration and AChE activity in the rat brain and enhances memory retention. According to certain research, influences on cholinergic activity in the central nervous system may be linked to memory retention and intellect promotion. A study investigating both the aerial parts and roots of CT showed alcoholic root extracts to bemore effective in attenuating memory deficits in rats compared to aerial parts. Enhanced memory retention following oral administration of the CT root extract was associated with increased levels of ACh and choline acetyltransferase in rat brain, but any relationship with inhibition of AChE activity was not established, and cortical AChE activity was actually found to be increased .An aqueous extract of the root also increased ACh levels in rat hippocampus following oral administration, and it was hypothesised that this effect may be due to an increasein ACh synthetic enzymes.

CURCUMA LONGA L:

Curcuma longa L. (CL), a member of the Zingiberaceae family of gingers, is believed to be native to the subcontinent of India. It goes by the name Haldi as well. Turmeric has been used extensively for millennia in indigenous medical systems, such as Ayurveda, to treat a wide range of inflammatory illnesses and conditions, including biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis. The volatile oils tumerone, atlantone, and zingiberene as well as the flavonoid curcumin are the active ingredients in CL. Resins, proteins, and carbohydrates are among the other ingredients. Curcumin crosses the blood-brain barrier.It was demonstrated that curcumin provided neuroprotection against ethanol-induced brain damage in vivo after oral treatment; this effect was linked to a decrease in lipid peroxide levelsand an increase in glutathione in the brain of rats .Certain chemicals from CL, such as calebin-A and some of its synthetic counterparts, curcumin, demethoxycurcumin, bisdemethoxycurcumin, and demethoxycurcumin, were demonstrated to shield PC12 cells from b-amyloid damage in vitro; it was also proposed that this protective action was caused by an antioxidant effect.Cell viability was greatly extended, antioxidant enzyme activity was elevated, and MDA content was lowered when cells were pretreated with an aqueous extract of CL (0.5 microgram/ml) before being exposed to hydrogen peroxide (H2O2). An additional activity that might be pertinent to the treatment of symptoms associated with diseases connected to cognition is antidepressant activity. Antidepressant activity is another activity that might be pertinent to the treatment of symptoms associated with diseases related to cognition. After oral administration, an aqueous extract of CL exhibited antidepressant action in rats, which was linked to the suppression of brain MAO-A.Curcumin has been shown to reduce ischemia-reperfusion injury in the heart and brain in animal studies [100,101]. As a result of curcumin's protection against alcohol-induced brain damage, oxidative stress and lipid peroxidation are reduced, and the glutathione level in brain tissue is raised. A low oral dose of 20 mg of curcumin per day for 75 days significantly reduced serum LPO in healthy individuals by 60%.

ECLIPTA PROSTRATA L:

In the Compositae family, Eclipta prostrata (L.)L (EP) is classified. Numerous phytochemicals,such as alkaloids, glycosides, coumarins, flavonoids, and sterols, are present in the plant and define its characteristics. EP has long been used to strengthen, encourage hair growth, and blacken hair. The leaf extract is regarded as a potent liver tonic and rejuvenator in Ayurvedic medicine. In addition to its nootropic potential, EP has been shown to have pharmacological activities that include analgesic activity, anti-aggression activity, anti-bacterial activity, anticancer activity, anti-diabetic activity, anti-helminthic activity, hepatoprotective activity, anti-inflammatory activity, and hair growth promoter activity.

Superoxide dismutase, glutathione peroxidase, reduced glutathione, catalase, glutathione-S-transferase, glutathione reductase, and MDA levels in the brain are all markedly increased uponpretreatment with hydroalcoholic extract of EP. When both common carotid arteries were blocked for 30 minutes, followed by four hours of reperfusion, the ischemic neuronal loss in the rat brain was significantly decreased by EP at higher doses.

ENHYDRA FLUCTUANT LOUR:

Enhydra fluctuans Lour. (EF) is a semi-aquatic, annual herbaceous plant that is locally referredto as Helechi (Assamese) or Water Cress (English). The species EF is widespread in northeastern India. The presence of alkaloids, saponins, flavonoids, triterpenoids, steroids, tannins, polysaccharides, and glycosides was discovered through phytochemical study of the EF extract. Indian medicine has utilised the herb to cure a variety of illnesses. Analgesic, cytotoxic, phagocytic, antibacterial, hepatoprotective, anti-inflammatory, anti-diarrheal, anti- oxidant, and anti-cancer properties have all been documented for EF. In addition, it may have neuroprotective properties. Using mice as models for the central and peripheral neurological systems, Roy et al. investigated the neuropharmacological effects of three fractions (benzene, chloroform, and ethyl acetate) of the aerial sections of EF. Significant spontaneous motility depressant, sedative, anticonvulsant, and anti-stress activity was demonstrated by the results.

GLYCYRRHIZA GLABRA L:

Glycyrrhiza glabra L. (GG) is a member of the Leguminosae family. GG is sometimes referredto as licorice, or Yashti-madhuh. It is reported to have antiviral, anticancer, anti-ulcer, anti- diabetic, antioxidant, immunomodulatory activity, antimicrobial activity, anti-inflammatory activity, anticonvulsant. One of GG's main flavonoids, glacirid, has a variety of therapeutic actions. Xue-Qing Yu et al. showed that Glabridin significantly attenuated the level of brain MDA induced by middle cerebral artery occlusion in rats, while it elevated the level of two endogenous antioxidants in the brain, i. e. superoxide dismutase and reduced glutathione. A study by P. Muralidharan aqueous extract administration restored the decreased levels of brain enzymes such as glutamate and dopamine and decreased AChE activity significantly in hypoxicrats induced by providing sodium nitrite drinking water to rats for 14 days.

Dinesh Dhingra and colleagues study how GG affects mice's memory and learning. To assess memory and learning, the passive avoidance paradigm and the elevated plus-maze were used. For seven days in a row, three doses (75, 150, and 300 mg/kg) of GG's aqueous extract were given to different animal groups. The learning and memory of mice were greatly enhanced byan aqueous extract of GG at a concentration of 150 mg/kg. Additionally, this dosage dramatically corrected the amnesia that was brought on by scopolamine (0.4 mg/kg) and diazepam (1 mg/kg). A. K. Teltumbde et al. conducted a study on male students to assess the impact of oral Yashtimadhu supplementation on memory and mental capacity.

HUPERZIA SERRATA (THUNB) TREVIS:

The traditional Chinese herb Huperzia serrata (Thunb.) Trevis (HS), also called QianCeng Ta/Jin Bu Huan in Chinese, Firmoss, or Club moss in English, is a member of the Lycopodiaceae family. Many species of Huperzia, including Huperzia serrata, are present in North-East India, and it has been proposed that HS and its other related species are also foundin India. HS are used in traditional Chinese medicine to treat a wide range of conditions, such as schizophrenia, myasthenia gravis, strains, contusions, and swellings.Huperzia's phytochemical investigations reveal substances such alkaloids, phenolic acids, flavones, and triterpenes. According to recent reports, China treats AD and organophosphate poisoning with the alkaloid Huperzine A (HupA), which was isolated from HS and proved to be a potent AChEinhibitor.

MORUS ALBA L:

Popular medicinal plant Morus alba L. (MA), which is a member of the Moraceae family, has long been utilised in many traditional medical systems, including Ayurveda. Mulberry leaves,root bark, and twigs have long been used in traditional medicine to treat fever, strengthen joints,protect the liver, enhance vision, ease urination, and lower blood pressure.MA contains variousphytochemicals, including alkaloids, flavonoids, glycosides, terpenoids, steroids, volatile oils and tannins .Numerous academic investigations demonstrate the significant pharmacological properties of MA, such as its antidiabetic, antihelmintic, antioxidant, antibacterial, anxiolytic, immunomodulatory, and nephroprotective properties. Tian et al. reported that the neurodegeneration is mostly caused by free radical production. Neurological disorders such as Parkinson’s disease (PD) and AD have been due to

the depletion of GABA in the brain.
In vitro and in vivo brain ischemia models are used to test the method that Kang et al. (2006) devised to raise the GABA level in MA leaves by a variety of anaerobic treatments. According to the findings, treating MA leaves anaerobically improves their neuroprotection against cerebral ischemia in vivo as compared to in vitro. Subsequent research was conducted to determine how cyanidin-3-O-β-dglucopyranoside (C3G) was extracted from MA fruit extract.When vivo and PC12 cells are exposed to hydrogen peroxide in vitro, C3G exerts a neuroprotective effect against cerebral ischemia damage. Parkinson's disease (PD) is a prevalent neurological illness caused by a loss of dopaminergic neurons in the substantia nigra pars compacta. The ethanolic extract of MA fruit was assessed in PD using both in vitro and in vivotests.

OCIMUM SANCTUM:
Ocimum sanctum (OS), a plant in the genus Ocimum that is a member of the Labiatae family,is significant due to its potential therapeutic uses. OS, sometimes referred to as "Holy Basil" in English, "Tulsi" in Hindi, and "Tulasi" in Assamese. Alkaloids, glycosides, saponins, tannins,a significant amount of vitamin C, and trace amounts of maleic, citric, and tartaric acids are also said to be present in the plant. Many medical benefits of OS have been demonstrated, including its ability to reduce pain, fight inflammation, treat arthritic pain, modulate immunity, treat asthma, reduce seizures, treat diabetes, reduce inflammation, reduce stress, and more. The impact of OS leaf ethanol extract on anxiety and depressive disorders was investigated by Chatterjee et al. in Swiss albino mice.
Forced swim tests and tail suspension tests were used to study depression. Experiments on anxiety included increasing light-dark together with the maze and hole-board tests. The OS extracts have the potential to treat mixed anxiety and depressive syndrome since they exhibit both antianxiety and antidepressant qualities at the same dosage. Mahmood Samim et al.'s work [168] demonstrated OS's neuroprotective potential in rats with rotenone-induced Parkinson's disease. The hydroalcoholic extract of OS (OSE) demonstrated potent antioxidant activity against hydroxyl radicals, 2,20-azinobis (3-ethylbenzothiozoline-6-sulfonic acid) radical, and DPPH with IC50 values of 395 ± 16.2, 241 ± 11.5, and 188.6 ± 12.2 lg/ml, respectively. This may be attributed to the extract's high polyphenol and flavonoid content.

SEMECARPUS ANACARDIUM L.F:
The plant Semecarpus anacardium L. f. (SA) belongs to the Anacardiaceae family and is commonly referred to as "Ballataka" or "Bhilwa." It is well-known for its medicinal value in the Ayurvedic and Siddha systems of medicine. Skin diseases, tumours, malignant growths, fevers, hemoptysis, excessive menstruation, vaginal discharge, inadequate lactation, constipation, intestinal parasites, and brain tonics were treated with the detoxified nut of SA in Ayurveda.
Since ancient times, it has also been used for non-medical purposes such as hair dye and fabricmarking. Phytochemical tests of SA reveal that it includes a range of components that are biologically active, including minerals, vitamins, amino acids, phenolic compounds, and biflavonoids. Anti-inflammatory, immunomodulatory, hypocholesterolemic, antioxidant, antibacterial, antispermatogenic, hair growth-promoting, and other properties have been shownin a number of research. According to Shukla et al., prolonged immobilisation stress results in considerable degradation of neuronal cells in the granule (Dg) and pyramidal (CA2) cells of the hippocampal subregions.
Studies using light microscopy revealed that there were a sizable number of black cell bodiesin both areas. The amount of degenerating cell bodies, or dark cells, in the pyramidal (CA2) and granule cell layer (Dg) was greatly decreased following treatment with the SA extract. In adistinct investigation on the CNS effects of SA nut milk extract, Farooq et al. demonstrated nootropic and locomotory effects in various experimental animal models. Neurotransmitter ACh is also lost when cholinergic cells, especially in the basal forebrain, are lost. By inhibitingAchE, the SA effectively extends the half-life of ACh. SA has a track record of helping to cure cognitive impairment and enhance memory.

SIDA CORDIFOLIA L:
Sida cordifolia L. (SC) is a perennial shrub that is found throughout the tropical and subtropicalplains of India. It is a member of the Malvaceae family. The

plant is tonic, astringent, emollient,aphrodisiac, and helpful in treating issues associated to the respiratory system, according to Ayurveda. Bark is thought to be calming. It helps with piles, blood, throat, and urinary system issues, among other things. Ephedrine, pseudoephedrine, quinazolines (vasicine, vasicinol), cryptoleptins, phytosterols (stearic and hexacosanoic acids, sterculic, malvalic, and fumaric acid), flavonoids, saponins, aspargine, and n-methyl tryptophan were detected by phytochemical screening of SC.Antioxidant activity ,analgesic activity ,anti-inflammatory activity ,hepatoprotective activity ,nephroprotective impact ,antidiabetic activity ,andantibacterial activity are only a few of the many therapeutic and pharmacological uses for it.

SC at 1000 mg/kg, there was drowsiness and a substantial ($p<0.001$) decrease in spontaneous locomotion [202]. Aqueous and hydro-ethanolic extracts of SC (AESC and EESC,respectively) were investigated by Navneet Khurana et al. in reserpine-induced orofacial dyskinesia and catalepsy, as well as LPO assessed by measuring the amounts of thiobarbituricacid like reactive substances (TBARS) in the rat forebrain. AESC (50, 100, and 250 mg/kg; p.)dose-dependently reversed the increased forebrain TBARS levels in rats, as well as the vacuouschewing movements, tongue protrusions, orofacial bursts, and catalepsy caused by repeated administration of reserpine (1 mg/kg) on alternate days (day 1, 3 and 5) for a period of 5 days.

TERMINALIA CHEBULA RETZ:

A member of the Combretaceae family, Terminalia chebula Retz. (TC) is one of the most significant medicinal plants utilised in homoeopathic, Siddha, Unani, and Ayurvedic medicine.In Tibet, it is referred to as the "King of Medicines." It is often referred to as Hilikha (Assamese)Black Myrobalan. Traditionally, TC has been used to treat kidney and urinary disorders, nervous disorders, colic pain, chronic cough, sore throat, asthma, etc. It is also used as laxative,antitussive, diuretic, digestive, antidiabetic, and as a cardiotonic remedy. It is reported to contain various biochemical compounds such as triterpenes arjun glucoside 1, arjungenin and the chebulosides 1 and 2.

Other constituents contains tannins, chebulic acid, chebulinic acid, tannic acid, ellagic acid, 2,4-chebulyi–β-D-gluco pyranose, gallic acid, ethyl gallate, punicalagin terflavin A, terchebin, luteolin, rutins, quercetin, and other flavonoids are purgatives of the anthraquinone nature. Research on TC has revealed that it possesses antioxidant, anticancer, antidiabetic, antimutagenic, antibacterial, and cardio-protective properties, among other properties. An assessment of the acute anxiolytic potential of the aqueous extract of TC fruits (AETC) using Light and Dark Arena in Swiss albino mice was conducted by Chandrashekar R. et al. According to their findings, AETC's behavioural disinhibitory effects demonstrated anxiolyticaction at doses of 1.3 and 2.6 mg/kg that were equivalent to those of the common medication diazepam. Acute doses of ethanolic extracts of TC improve mice's capacity for learning and memory recall in an inverse dose-dependent manner, according to a different study by Nageswara Rao et al.

TINOSPORA CORDIFOLIA (LOUR) MERR:

Tinospora cordifolia (Lour.) Merr. is a member of the Menispermaceae family. The plant is also referred to as Amarlata (Assamese), Gurcha (Hindi), and Giloe. Alkaloids, steroids, diterpenoid lactones, aliphatics, and glycosides are just a few of the active ingredients that havebeen extracted from the plant's various body parts, which include the root, stem, and entire plant.Anti-diabetic,anti-inflammatory,anti-arthritic,anti-oxidant,anti-stress,immunomodulatory, and anti-neoplastic effects are some of its documented therapeutic qualities.T.

cordifolia has high free radical scavenging properties against reactive nitrogen species and reactive oxygen species, according to a study by Avinash K. Rawal et al. that used electron paramagnetic resonance spectroscopy to analyse the plant. Additionally, the herb successfullyraises reduced glutathione levels, gammaglutamyl-cysteine ligase expression, and Cu-Zn superoxide dismutase gene expression. Furthermore, T. cordifolia markedly reduced the expression of iNOS After 48 hours, the (Inducible Nitric Oxide Synase) gene is expressed, andthis gene is important for brain damage during hypoxia/ischemia.By safeguarding dopaminergic neurons and lowering iron accumulation, T. cordifolia may be able to lessen thesymptoms of 6-hydroxy dopamine-induced Parkinsonism, according

to another study by AShanish Antony et al. Dopamine levels were increased in T. cordifolia ethanol extract.

Additionally, T. cordifolia improves memory and learning. Children with moderate-to-severe behavioural issues and mental deficits have shown significant responsiveness, as well as increase in IQ.It was discovered that the pure aqueous extract of the root improved logical memory and verbal learning in a 21-day randomised, double-blind, placebo-controlled research.It has also been demonstrated that T. cordifolia improves cognition in normal rats andreverses the memory loss brought on by cyclosporine. The Hebb William maze learning scoresand memory retention decreased in response to both the alcoholic and aqueous extracts of T. cordifolia, suggesting improved memory and learning. The histological analysis of the hippocampal regions of rats treated with cyclosporine revealed neurodegenerative alterations that T. cordifolia prevented.

TRAPA NATANS VARS BISPINOSA (ROXB) MAKINO:

Bispinosa Trapa Natans Vars. (Roxb.)Known locally as water chestnut, pani singori (Assamese), or singara (Hindi), Makino (TN) is a member of the Lythraceae family and is widely planted in India. It has been utilised for ages for a number of significant medicinal purposes in the traditional medical systems of Unani and Ayurveda. Its uses include nourishing, cooling, aphrodisiac, astringent, appetiser, tonic, and anti-diarrhea.

It is used in the Unani medical system to treat a variety of illnesses, including bronchitis, TB,renal calculi, weariness, sore throats, bilious affections, and sexual weakness. Modern researches have supported its traditional uses and also explored other important properties such as analgesic, immunomodulatory ,neuroprotective, antioxidant activity, anti-microbial activity, antibacterial activity, anti-ulcer activity, hepatoprotective activity .Analysis of chemical constituents of TN reveals the presence of flavonoids, tannins, glycosides, saponins, steroids, proteins, carbs, phenolic compounds, vitamins, and necessary minerals.

The effects of TN's hydroalcoholic extract on the fluorescent product and biochemical markersin the brains of female albino mice were investigated, including lipid peroxidation, catalase activity, and glutathione peroxidase activity. The use of 0.5 ml 5% D-galactose for 15 days accelerated the ageing process. In the cerebral cortex, this led to an increase in fluorescence product, an increase in LPO, and a decrease in antioxidant enzymes such glutathione peroxidaseand catalase. Following co-administration of 500 mg/kg of TN hydroalcoholic extract, the fluorescence product in the cerebral cortex decreased. Furthermore, in comparison to the ageing-accelerated control group, TN reduced the growth of LPO and restored the activities of glutathione peroxidase and catalase in the cerebral cortex.

WITHANIA SOMNIFERA (L) DUNAL:

Within the Solanaceae family is Withania somnifera (L.) Dunal (WS). WS, also referred to as ashwagandha, is frequently used interchangeably with Indian ginseng. It is categorised as a rasayana (rejuvenation) in Ayurveda and is supposed to improve both mental and physical health, revitalise the body in weakened states, and lengthen life. Steroidoidal alkaloids and steroidal lactones, which belong to a class of compounds known as withanolides, are the mainbiochemical components of ashwaganda root.A significant portion of ashwaganda's pharmacological effects have been linked to two primary withanolides: withanolide D and withaferin A. Several medicinal properties of WS include its ability to reduce inflammation, relax, hypnotise, narcotic, general tonic, diuretic (Fruits & Seeds), and aphrodisiac effects .In the brain, WS have an antioxidant impact.

LPO rises can be avoided by using WS extract.An analysis of biochemistry revealed important Elevation in the rat brain levels of catalase, glutathione peroxidase, superoxide dismutase, and other important free-radical scavenging enzymes.Both sitoindosides IX and X compounds hada strong anti-stress effect in albino mice and rats when administered orally (50-200 mg/kg). Additionally, they improved memory retention, learning, and acquisition in both young and oldrats .

Male Wistar rats' brain cholinergic, glutamatergic, and GABAergic receptors were the subjects of an investigation into the effects of sitoindosides VII–X and withaferin, which were separatedfrom an aqueous methanol extract of the roots of grown cultivars of

WS. The chemicals reduced AChE activity in the vertical diagonal band and slightly increased it in the globus pallidus andlateral septum.According to the experimental research, mice who get withanoside IV orally metabolise it into sominone, which enhances axonal and dendritic outgrowth as well as synaptogenesis and causes a notable recovery in neuritis and synapses .

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Phytochemicals and other active ingredients found in herbal plants are abundant and responsible for enhancing nootropic activity. Researchers are finding it difficult to provide effective treatments for patients suffering from neurodegenerative disorders due to the increasein incidence of these conditions and our limited understanding of their pathophysiology and process of development. Plants of different kinds have been utilised as neuroprotectants in traditional medicine. Through the use of an ethnopharmacological method, this publication hasidentified promising plant sources for the amelioration of various neurodegenerative illnesses.The paper indicates that certain herbs from northeastern India have potential as remedies for neurological conditions. Further experimental research is yet required to determine the precise mechanism at play and to isolate the active components.

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