



PLANT BASED INDIAN TRADITIONAL MEDICINE FOR NEURODEGENERATIVE DISEASES - A NOVEL APPROACH TO TREAT ALZHEIMER

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ABSTRACT

As per the earlier reports, the most prevalent disease of Alzheimer's, a kind of dementia, affects approximately 24 million people worldwide. There may be many invisible reasons for the disease to be caused and the common evidences for the disease is due to a few reasons like aggregation of self-assembled fibrous proteins and variation in the level of Acetyl choline (ACh). Traditional Indian herbs which are rich in natural alkaloids and are an important source of acetyl-cholinesterase (AChE) which can restore the levels of acetylcholine. Bioactive compounds like Coumarins, flavonoids and other indirect sources from herbs can activate the complexes of the deadly disease, so that the derivatives work against the severity of the disease. The natural compounds derived from herbs can act as modulators and inhibitors for amyloid accumulation so that they can also suppress inflammation and neuronal cytotoxicity. These bioactive compounds have the advantage of being multi-targeted and hence are advantageous over the single target drugs in the treatment of such complex diseases. This review suggests the possibilities of using traditional Indian herbs which are a rich source of these compounds to effectively treat Alzheimer's disease and hence has attracted attention towards research and development of the therapies.

KEYWORDS: Alzheimer's, phyto-active agents, neurodegenerative diseases, plant extracts, antioxidants



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INTRODUCTION

Neurodegenerative diseases primarily affects the brain and leads to cognitive impairment combined with motor deficits mostly reported in the aged populations. Alzheimer diseases and Parkinson disease are the most prominent aging related neurodegenerative diseases. Among these Alzheimer disease is a common neurodegenerative disorder reported in many victims leading to dysfunction, memory loss, language deficits, depression and behavioral problems¹⁻². Several Indian medicinal plants have been used in the Indian traditional Ayurveda system called rasayana which has been one of the most extensive traditional systems to treat neurodegenerative diseases³. The early process of the Indian traditional system of medicine deals with the phenomena of endogenous or exogenous processes which cause physiological disequilibrium leading to the pathological state. Three different plant species have been analyzed for their neuroprotective effect to cure Alzheimers disease⁴. The development of traditional based medicine mainly focused on three approaches such as isolated single compound, poly-herbal mixture and pharmacological and therapeutic effects of herbal extracts on specific diseases. In this review we discuss the development of each approach along with the advantage and dis-advantage.

ISOLATION OF BIOACTIVE COMPOUNDS

Several parts of the herbal plants such as roots, leaves, stems, barks, flowers and fruits are commonly rich in phenolic and other secondary metabolite compounds⁵. The pharmacological property of each compound differed in their active principles and many Indian medicinal plant composites are represented as neuroprotective and neuro-pharmacologically active compounds. Reports suggest that the anti-inflammatory and anti-oxidant properties of the medicinal plants are optimal for neurodegenerative diseases like Alzheimer. Oxidative stress induced by ROS free radicals have been suggested to play a major role in ageing and neurodegenerative diseases by means of increase dopamine oxidation in nigral dopaminergic neurons⁶. The proteolytic cleavage of the transmembrane amyloid precursor proteins leads to the formation of Amyloid β -peptide which induced extensive oxidative stress in neurons by means of lipid peroxidation and protein oxidation⁷. More over, the extracellular deposits of Amyloid β -peptide and PrP amyloid fibrils induce non-immune mediated chronic inflammatory responses and over deposition of high level of fibrillary amyloid β -peptide which is associated with loss of synapses and impairment of neuronal function leading to the risk factor for Alzheimer⁸⁻¹⁰. These reports suggest the possibility of the antioxidant compounds from the herbal plant can reduce the risk of Alzheimer by suppressing the oxidative stress. The use of isolated compound calebin-A, curcumin, dimethoxy curcumin, bis-demethoxy curcumin from *Curcuma longa* L., Zingiberaceae has been described effectively against Alzheimer by means of protection from β A(1-42) through antioxidant pathway¹¹. Nongnut *et al.*, described the saponins and

glycosides isolated from perennial creeping plant *Bacopama nniera* Linn. which exhibited lipid peroxidation inhibitory activity and neuroprotection against Alzheimer disease¹². A flavonoid kaempferol isolated from *Ginkgo biloba* leaves were potentially neuro-protectant as described elsewhere¹³. The inhibition of noise stress induced changes in the rat brain was determined by a novel drug α -asarone from *Acorus calamus*¹⁴. Glabridin isolated from *Glyocyrrhiza glabra* (*liquorice*) showed neuroprotective effect on pathways associated with an apoptosis¹⁵. Reports are available on arabinogalactan polysaccharide isolated from *Tinospora cordifolia* (*Menispermaceae*) which revealed protection against iron-mediated lipid peroxidation in rat brain cellular glutathione¹⁶. The neuroprotective compound FrB from *Convolvulus Pluricaulis choi*. (*Convolvulaceae*) stimulates the antioxidant mechanism in brain has been reported¹⁷. 4-hydroxyisophthalic acid an antioxidant compound isolated from *Decalepis hamiltonii* roots are reported as neuroprotective agent¹⁸⁻¹⁹. An acetylcholinesterase (AChE) inhibitor compound catechol alkenyls from *Semecarpus anacardium* L. f. (*Anacardiaceae*) was reported in earlier studies²⁰. The saponin rich fraction of *Ficus religiosa* L. (*Moraceae*) showed anticonvulsant activity against epileptic seizures induced synchronous neuronal activity in the brain has been reported earlier²¹. The anti-depressant activity in mouse brain monoamine neurotransmitters by means of reduced monoamine oxidase (MAO)-A level has been demonstrated²². Another compound iso-curcumenol from *Cyperus rotundus* L. (*Cyperaceae*) acts as a benzodiazepine receptor against an allosterically modulated GABAergic neurotransmission²³. The asiatican triterpenoid and madecassic acid from *Centella asiatica urban* (*Umbelliferae*) were reported as neuro protective agent²⁴⁻²⁶. The anti-epileptogenic activity of thymol isolated compound from *Carum copticum Benth* (*Apiaceae*) by means of neuronal Na⁺ channel blocking, positive allosteric modulation of GABA_A receptor and also due to its antioxidant properties was studied²⁷. The neuro protective agent embelin isolated from *Embelia ribes* Burm. (*Myrsinaceae*) was reported as a good remedy to treat brain damage, stroke and depression. Another report suggests embelin can inhibit glioma by blocking NF- κ B activity²⁸⁻³⁰. A patent compound vicenin-2 was reported for its potential neurological activity to control Alzheimer³¹. It was stated that the acetylcholinesterase (AChE) inhibiting nature of coumarin isolated from *Lantana camara* (*Verbenaceae*)³². The polyphenol xanthone compound mangiferin isolated from *Mangifera indica* L. (*Anacardiaceae*) claims to be a potential agent in the treatment of Alzheimer's disease. Moreover another report suggests that mangiferin interacts with the central neural components as secondarily peripheral target specifically instead of direct interaction with the neural components³³. With the available background information, it has been suggested that the anti-depressant activity of *Hypericum perforatum* L. purified compound hyperforin will enhance the concentration of monoamines and glutamate in the synaptic cleft³⁴⁻³⁵. The neuroprotective effect of polysaccharides purified from *Momordica charantia* (*Cucurbitaceae*) which inhibits c-Jun N-terminal protein kinase (JNK3) signaling

pathway inducing intracerebral hemorrhage injury has been described³⁶. Another recent experimental study suggests that *Momordica charantia* polysaccharides inhibit JNK3 induced cerebral injury by means of its antioxidant activities³⁷. A steroidal saponin isolated from *Momordica cymbalaria Fenzl (Cucurbitaceae)* produced a potential neuroprotective compound which enhanced the neuronal degenerative changes³⁸. It has been stated that β -carotene, a compound from *Moringa oleifera Lam. (Moringaceae)* will promote neuritogenesis³⁹. Chun *et al.*, reported the neuroprotective effect of macelignan isolated from *Myristica fragrans Houtt. (Myristicaceae)* which significantly reduced the spatial memory impairment induced by the chronic lipopolysaccharide infusions. The results add that the macelignan may target therapeutic compounds to prevent Alzheimer's disease⁴⁰⁻⁴¹. The neuroprotectivity and anti-depressant effect of luteolin, carnosic acid, rosmarinic acid and polyphenol compound from *Rosmarinus officinalis (R. officinalis)* has been reported⁴². The anticonvulsant and anxiogenic activity of triterpene isolated from *Rubia cordifolia Linn (Rubiaceae)* and the possibility of its anticonvulsant activity is mediated by chloride channels of GABA/benzodiazepine receptor complex instead of the chloride channel of glycine receptors of rat brain is a recent study in this area⁴³. Another report pointed out that the polysaccharides from *Rubia cordifolia* enhanced the proteasome activity which inhibited A β aggregates⁴⁴. The active constituents from *Solanum nigrum* suppressed free radicals in the brain which are under psychological stress and neuronal diseases⁴⁵. The neuronal protectivity of arjunolic acid from *Terminalia arjuna Weight & Arn. (combretaceae)* against oxidative stress induced damage in focal cerebral ischemia and reperfusion has been identified⁴⁶. Chebulic acid has been isolated from *Terminalia chebula Retzius (Combretaceae)* which was demonstrated to have a potential active compound against the AGE-induced endothelial cell dysfunction⁴⁷. These endothelial cell dysfunction inhibition activities were necessary in case of Alzheimer disease stage. Since, recently it was reported that Alzheimer disease may process endothelial dysfunction in its pathogenesis stage⁴⁸. Reports on bacopaside I from *Bacopamonnieri (L.) Wettst* which exhibited a potential neuroprotective effect against OGD-induced neuronal cell damage by means of blocking the PKC inhibitor Ro-31-8220 and P13K inhibitor in mouse model has been referred⁴⁹. Another report supports the presence of anti-stress agents like bacopaside I by means of stimulating antioxidant activity in adverse stress conditions in rat brain⁵⁰. The acetylcholine esterase inhibiting activity of Huperzine A, an alkaloid from *Huperzia serrata (Lycopodiaceae)* is a recent report from pharmaceutical scientists⁵¹. A report on Huperzine A suggests that it can be a potential therapeutic compound to overcome the Alzheimer's disease⁵². The potentiality of crocin from *Crocus sativus L.* has revealed to boost the memory through inhibition of the oxidative stress inducing neuronal damage⁵³. The anticonvulsant activity of morusin isolated from *Morusalba L* was demonstrated⁵⁴. Another report points out that the neuroprotective effect of cyaniding-3-O- β -D-glycopyranoside isolated from *Morusalba L.* revealed a neuroprotective effect on the PC12 and cerebral

ischemic damage by means of its antioxidant activities⁵⁵. The anti-stress activity of ocimumosides A, B and ocimarine isolated from *Ocimum sanctum* which normalizes the hyperglycemia, corticosterone levels, creatine kinase and adrenal hypertrophy effects is an already proven experimental methodology⁵⁶. The anti-depression and anti-anxiety effects of glycol-withanolides from *Withania somnifera (L.) Dunal* has been considered as an important information⁵⁷. Another experimental study on sitoindosides IX and X compounds from *Withania somnifera (L.)* showed its potential anti-stress nature which had an enhancing learning and memory retention in rat⁵⁸.

STANDARDIZED EXTRACT FROM HERBS

CURCUMA LONGA L.

The enhancement of learning and spatial memory by the compounds from *Curcuma longa. L* was reported by Nam sung *et al.*, at the dosage levels of 300 mg/Kg through oral administration in the adult mice⁵⁹.

ACORUS CALAMUS LINN

Acorus calamus Linn belongs to the family *Acoraceae*, a common ethno pharmacological plant widely used in Indian traditional based medicinal system such as Ayurveda, Unani, Siddha and also in Chinese medicine to treat various diseases and disorders including depression⁶⁰. The neuroprotective effect of ethanol: water (1:1) extract of rhizomes of *Acorus calamus* against cerebral ischemia was described elsewhere⁶¹. The neuro-modulatory effect of methanol and acetone extracts of *Acorus calamus* in mice was reported earlier⁶². Another report suggests that the oral and intraperitoneal injection (100 mg/kg) of *Acorus calamus* extracts enhance the spatial recognition and memory in male rats⁶³. Reports on the anti-cholinergic and anti-histaminic effect of *Acorus calamus* leaf extract is available in literature⁶⁴.

PIPER NIGRUM L

Piper nigrum L belongs to family *Piperaceae* which is a well-known medicinal plant for its antioxidant, anti-inflammatory, anti-hypertension and anti-depressant activity⁶⁵⁻⁶⁶. Reports on the anti-oxidative stress and neurodegenerative activity of methanol extracts of *Piper nigrum* seeds in Alzheimer induced rat are available with experimentation proof⁶⁷. Another report suggests the anti-neuro inflammatory like activity of *piper nigrum* alcoholic extract in Alzheimer induced rat⁶⁸. A recent, report on the memory enhancing activity of methanolic extracts of *piper nigrum* fruit by means of inhibiting the oxidative stress in Alzheimer rat model is available⁶⁹. The methanolic extract of *Piper nigrum* fruit extract showed possible anxiolytic and antidepressant activity in Alzheimer rat model⁷⁰.

CONVOLVULUS CHOISY

The plant belongs to the family *Convolvulaceae*. It is widely used in traditional Ayurveda and Chinese medicine to treat central nervous system and epileptic diseases⁷¹. Earlier reports suggest that the ethanolic extracts of *Convolvulus pluricaulis* enhance the learning and memory in young and aged mice at the dosage (200 mg/kg)⁷². Another report by Syed et al., suggest that *C. pluricaulis* extract at dosage (150 mg/kg) can inhibit amyloid β (A β) and increased amyloid precursor protein (A β PP) level in rat⁷³.

PSIDIUM GUAJAVA (L.)

P. guajava comes under the family *Myrtaceae*. The medicinal values of *P. guajava* are noted to treat inflammation, diabetes and central nervous system depressant activity⁷⁴. The ethanolic extracts of *P. guajava* showed significant impact in behavioral activity like locomotion and memory retention in obsessive compulsive disorder mice⁷⁵. Another recent experimental studies shows the potential antiepileptic activity of ethanol extract of *P. guajava* in mice (400 mg/kg)⁷⁶.

GLYCYRRHIZA GLABRA LINN

Belonging to the family *Leguminosae*, it is a common medicinal herb from the Indian medicinal history of Ayurveda to cure various diseases including hyperdipsia, inflammation and also in the treatment of epilepsy and paralysis⁷⁷⁻⁷⁸. The learning and memory enhancing effect of aqueous extract root of *G. glabra* was reported in experimental rat at 150 mg/kg dosage administered orally⁷⁹. Another recent experimental report suggests that the *G. glabra* will be the source of potential drug for Alzheimer and other neurodegenerative disorders. In this, the aqueous *G. glabra* root extract at the dosage 150 and 225 mg/kg significantly improve the learning and memory in male rats⁸⁰.

TINOSPORA CORDIFOLIA (LOUR.) MERR

Belonging to the family *Menispermaceae*, there has been several reports on the pharmacological activity of this plant including anti-inflammatory, anti-oxidant and anti-stress properties⁸¹. The clinical reports were pointed on the *T. cordifolia* tonic which can significantly improve behavior disorders and memory enhancing in children⁸². Another clinical study with thirty healthy 18-30 year volunteers showed 500 mg of pure aqueous *T. cordifolia* extract significantly increase verbal learning and memory behaviors⁸³. Reports on the ethanol and aqueous extracts of *T. cordifolia* can inhibit the cyclosporine induced memory deficit and enhance the learning and memory in rats⁸⁴. Another report suggests that anti-inflammation and antioxidant properties of *T. cordifolia* play an important role in memory enhancement process⁸⁵.

DAECALEPIS HAMILTONII WIGHT & ARN

The herb belongs to the family *Asclepiadaceae*. The root extract is considered as the major medicinal properties to cure epilepsy and central nervous system disorders⁸⁶. Several recent experiment studies reveals the antioxidant properties of *D. hamiltonii* as key responsible agent for its neurodegenerative activity. Reports on the root extract of *D. hamiltonii* reduces the age-related decline in cognitive ability in *Drosophila melanogaster* means of its antioxidant properties⁸⁷. A very recent report on the antioxidant properties of *D. hamiltonii* extract promisingly enhance the climbing ability and circadian rhythm of locomotor activity in *Drosophila melanogaster* model after feeding the extract for twenty one days has been evaluated⁸⁸. Suggestion on the antioxidant properties of *D. hamiltonii* root extract can play a major contribution for its neuroprotective activity⁸⁹.

SEMECARPUS ANACARDIUM LINN

Belonging to the family *Anacardiaceae*, it is well known for various ailments in traditional system. The fruits and nuts of *S. anacardium* are considered to add major medicinal value to treat inflammation, central nervous system disorders and hypoglycemic activity⁹⁰. An important report an ethanolic extract of *S. anacardium* inhibits the neuronal degenerative disorder induced by stress in experimental rats which resembles the cytoprotective properties has been evaluated⁹¹. A detailed description on the central nervous system effect of *S. anacardium* nuts milk extract shows that it can enhance the locomotor and nootropic activity in various animals models by inhibit AchE leads to improving the half-life of acetylcholine effectively and enhancing the memory process⁹².

FLEMINGIA STROBILIFERA L (R.BR)

The plant belongs to the family *Leguminosae*. The root parts are applied to treat epilepsy and hysteria⁹³. The tribal people from Assam use *F. strobilifera* to cure ringworm infection by applying over the infected area⁹⁴. Only a few experimental data was available on *F. strobilifera* which deals with the neuro-pharmacological activities. Reports on the anticonvulsant activity of ethanol extract of the roots of *F. strobilifera* and ethyl acetate fraction revealed depressant like action in central nervous system in locomotor activity without inhibiting the motor coordination at the dose (400 and 600 mg/kg)⁹⁵.

CINNAMOMUM TAMALA (BUCH-HAM) NEES AND E BERM

Belonging to *Lauraceae* family, it was applied to treat various diseases and infection in the traditional medicinal system of Ayurveda and Yunani. Several experimental studies states its potential properties such

as anti-diabetics, anti-inflammation, anti-cancer and anti-oxidant activities properties⁹⁶. Recently, reports on the acetylcholinesterase inhibition activity of *C. tamala* methanol extract and its leaf oil cinnamon are available. Among this, cinnamon oil shows maximum acetylcholinesterase inhibition than the *C. tamala* extract⁹⁷.

CYPERUS ROTUNDUS

The plant belongs to the family *Cyperaceae*. It is well known for its traditional medicinal value to treat analgesic, malarial infection and inflammation⁹⁸. Several recent experimental data suggest that its free radical scavenging activity leads to neuroprotective properties. Reports are available on the neuroprotective effect of *C. rotundus* extract against ONOO- induced apoptosis by inhibiting NO generation by down regulating i-NOS expression⁹⁹. Same as the previous report, description on the neuroprotective activity of *C. rotundus* rhizome extracts through inhibiting H₂O₂ induced human neuroblastoma cell damage which increases the brain derived nerve growth factor resembling its neuro-regeneration properties has been proved by experimentation¹⁰⁰. Another recent experimental study on Alzheimer animal model suggests the learning and memory enhancing activity of *C. rotundus* tubers ethanolic extract. In this *C. rotundus* extract potentially inhibiting the loss of cholinergic neurons of the nucleus basalis of meynert which leads to overcome Alzheimer disorders in animal models¹⁰¹.

CENTELLA ASIATICA (L.) URBAN

Belonging to the family *Apiaceae*, *C. asiatica* traditionally is well known for its memory enhancement and also for neurological medicinal properties in many countries¹⁰². Reports on the inhibition of streptozotocin induced cognitive impairment in the Alzheimer model treated with 200 and 300 mg/kg of aqueous extract of *C. asiatica* is an effective means of suppressing the oxidative stress¹⁰³. Another report also suggests that *C. asiatica* extract shows significant neuroprotective in age related disorders by inhibiting lipid peroxidation and protein carbonyl in aged rat brain¹⁰⁴. A report on solvent of n-hexane, chloroform, ethyl acetate and n-butanol extract of *C. asiatica* shows increased in ATPases in different regions of rat brain epilepsy¹⁰⁵. A very recent report suggests that *C. asiatica* extract significantly inhibit the thiol oxidation induced by sodium nitroprusside and quinolinic acid in different regions of brain¹⁰⁶. Another experimental study suggests ethanolic extract of *C. asiatica* possess anti-oxidant defense mechanism to inhibit A β ₁₋₄₀ induced reactive oxygen species free radicals neurotoxicity in Alzheimer condition¹⁰⁷.

EMBELIA RIBES BURM.F

Belonging to the *Myrsinaceae* family, the dried fruits of *E. ribes* were used to treat helminthic, carminative and

inflammation¹⁰⁸. Reports on the neuroprotective effect of *E. ribes* ethanol extract which inhibits the oxidative stress in middle cerebral artery occlusion leads to focal cerebral ischemia in rats¹⁰⁹.

AERUALANATA (L.) JUSS. EXSCHULT

Belonging to the family *Amaranthaceae*, the plant is widely used in traditional system of medicine to cure helminthic, inflammation, skin diseases and headache¹¹⁰. Very recently, reports on the neuroprotective effect of *A. lanata* 70% ethanolic extracts against cisplatin induced neurotoxicity in male rats has been observed¹¹¹.

MANGIFERA INDICA L.

The tree belongs to the family *Anacardiaceae* and the ethno-pharmacological importance of *M. indica* has been reported to treat diarrhea, jaundice, pain and inflammations. The extracts which proved to have free sugars, saponin, tannins and flavonoids when treated chronically with vitamin C on mice reversed aging and memory deficits and hence suggests to contain memory enhancing pharmacologically active principles¹¹².

CONCLUSIONS

Alzheimer's the multifactorial complex disease which is a type of dementia causing mental disability and death among humans. Current therapy can relieve the symptoms of the disease and cannot prevent the progression as it uses acetylcholine esterase inhibitors. Hence use of bioactive agents derived from Indian traditional ayurvedic medicines have multi-targeted agents for therapy so as to specifically bind and deactivate the preformed complexes. These multifaceted drugs have to be structurally characterized and their pharmacokinetic activities are to be routed in order to establish the structure - activity relationship studies of individual compounds present in herbal complexes. More attention is required towards their derivatives and tissue restoration processes. Studies should be undertaken to overcome the clinical hurdles currently faced by the herbal drugs such as brain penetration and oral activities.

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CONFLICT OF INTEREST

Conflict of interest declared none.

REFERENCES

- Howes MJ, Houghton PJ. Plants used in Chinese and Indian traditional medicine for improvement of memory and cognitive function. *Pharmacology Biochemistry and Behavior*. 2003 Jun 30;75(3):513-27.
- Ho YS, So KF, Chang RC. Anti-aging herbal medicine—how and why can they be used in aging-associated neurodegenerative diseases?. *Ageing research reviews*. 2010 Jul 31;9(3):354-62.
- Auddy B, Ferreira M, Blasina F, Lafon L, Arredondo F, Dajas F, et al. Screening of antioxidant activity of three Indian medicinal plants, traditionally used for the management of neurodegenerative diseases. *Journal of Ethnopharmacology*. 2003 Feb 28;84(2):131-8.
- Anitha R, Lakshmi T, Geetha RV. Top three herbs in Alzheimers disease-A review. *International Journal of Pharma and Biosciences*. 2011 Oct;2(4):362-75.
- Surveswaran S, Cai YZ, Corke H, Sun M. Systematic evaluation of natural phenolic antioxidants from 133 Indian medicinal plants. *Food Chemistry*. 2007 Dec 31;102(3):938-53.
- Beal MF. Aging, energy, and oxidative stress in neurodegenerative diseases. *Annals of neurology*. 1995 Sep 1;38(3):357-66.
- Butterfield DA, Lauderback CM. Lipid peroxidation and protein oxidation in Alzheimer's disease brain: potential causes and consequences involving amyloid β -peptide-associated free radical oxidative stress 1, 2. *Free Radical Biology and Medicine*. 2002 Jun 1;32(11):1050-60.
- McGeer EG, McGeer PL. Neuroinflammation in Alzheimer's disease and mild cognitive impairment: a field in its infancy. *Journal of Alzheimer's Disease*. 2010 Jan 1;19(1):355-61.
- Eikelenboom P, Bate C, Van Gool WA, Hoozemans JJ, Rozemuller JM, Veerhuis R, et al. Neuroinflammation in Alzheimer's disease and prion disease. *Glia*. 2002 Nov 1;40(2):232-9.
- Hamaguchi T, Ono K, Murase A, Yamada M. Phenolic compounds prevent Alzheimer's pathology through different effects on the amyloid- β aggregation pathway. *The American journal of pathology*. 2009 Dec 31;175(6):2557-65.
- Kim DS, Park SY, Kim JY. Curcuminoids from *Curcuma longa* L.(Zingiberaceae) that protect PC12 rat pheochromocytoma and normal human umbilical vein endothelial cells from β A (1–42) insult. *Neuroscience Letters*. 2001 Apr 27;303(1):57-61.
- Uabundit N, Wattanathorn J, Mucimapura S, Ingkaninan K. Cognitive enhancement and neuroprotective effects of *Bacopa monnieri* in Alzheimer's disease model. *Journal of Ethnopharmacology*. 2010 Jan 8;127(1):26-31.
- Sloley BD, Urichuk LJ, Morley P, Durkin J, Shan JJ, Pang PK, et al. Identification of kaempferol as a monoamine oxidase inhibitor and potential neuroprotectant in extracts of *Ginkgo biloba* leaves. *Journal of pharmacy and pharmacology*. 2000 Apr 1;52(4):451-9.
- Manikandan S, Devi RS. Antioxidant property of α -asarone against noise-stress-induced changes in different regions of rat brain. *Pharmacological research*. 2005 Dec 31;52(6):467-74.
- Yu XQ, Xue CC, Zhou ZW, Li CG, Du YM, Liang J, et al. In vitro and in vivo neuroprotective effect and mechanisms of glabridin, a major active isoflavan from *Glycyrrhiza glabra* (licorice). *Life sciences*. 2008 Jan 2;82(1):68-78.
- Subramanian M, Chintalwar GJ, Chattopadhyay S. Antioxidant properties of a *Tinospora cordifolia* polysaccharide against iron-mediated lipid damage and γ -ray induced protein damage. *Redox Report*. 2013 Jul 19;7(3):137-143.
- Kaur M, Prakash A, Kalia AN. Neuroprotective potential of antioxidant potent fractions from *Convolvulus pluricaulis* Choisy. in 3-nitropropionic acid challenged rats. *Nutritional neuroscience*. 2016 Feb 7;19(2):70-8.
- Srivastava A, Rao LJ, Shivanandappa T. A novel cytoprotective antioxidant: 4-Hydroxyisophthalic acid. *Food Chemistry*. 2012 Jun 15;132(4):1959-65.
- Srivastava A, Shivanandappa T. Neuroprotective effect of *Decalepis hamiltonii* roots against ethanol-induced oxidative stress. *Food chemistry*. 2010 Mar 15;119(2):626-9.
- Adhami HR, Linder T, Kaehlig H, Schuster D, Zehl M, Krenn L. Catechol alkenyls from *Semecarpus anacardium*: acetylcholinesterase inhibition and binding mode predictions. *Journal of ethnopharmacology*. 2012 Jan 6;139(1):142-8.
- Singh D, Singh B, Goel RK. Role of saponins for the anticonvulsant effect of adventitious roots of *Ficus religiosa*. *Pharmaceutical biology*. 2012 Jul 1;50(7):816-22.
- Dhingra D, Valecha R. Evidence for involvement of the monoaminergic system in antidepressant-like activity of an ethanol extract of *Boerhaavia diffusa* and its isolated constituent, punarnavine, in mice. *Pharmaceutical biology*. 2014 Jun 1;52(6):767-74.
- Ha JH, Lee KY, Choi HC, Cho J, Kang BS, Lim JC, et al. Modulation of Radioligand Binding to the GABAA-benzodiazepine Receptor Complex by a New Component from *Cyperus Rotundus*. *Biological and Pharmaceutical Bulletin*. 2002 Mar 5;25(1):128-30.
- Krishnamurthy RG, Senut MC, Zemke D, Min J, Frenkel MB, Greenberg EJ, et al. Asiatic acid, a pentacyclic triterpene from *Centella asiatica*, is neuroprotective in a mouse model of focal cerebral ischemia. *Journal of neuroscience research*. 2009 Aug 15;87(11):2541-50.
- Grimaldi R, De Ponti F, D Angelo L, Caravaggi M, Guidi G, Lecchini S, et al. Pharmacokinetics of the total triterpenic fraction of *Centella asiatica* after single and multiple administrations to healthy volunteers. A new assay for asiatic acid. *Journal of ethnopharmacology*. 1990 Feb 1;28(2):235-41.

26. Lee MK, Kim SR, Sung SH, Lim D, Kim H, Choi H, et al. Asiatic acid derivatives protect cultured cortical neurons from glutamate-induced excitotoxicity. *Research communications in molecular pathology and pharmacology*. 1999 Dec;108(1-2):75-86.
27. Sancheti J, Shaikh MF, Chaudhari R, Somani G, Patil S, Jain P, et al. Characterization of anticonvulsant and antiepileptogenic potential of thymol in various experimental models. *Naunyn-Schmiedeberg's archives of pharmacology*. 2014 Jan 1;387(1):59-66.
28. Thippeswamy BS, Nagakannan P, Shivasharan BD, Mahendran S, Veerapur VP, Badami S. Protective effect of embelin from *Embelia ribes* Burm. against transient global ischemia-induced brain damage in rats. *Neurotoxicity research*. 2011 Nov 1;20(4):379-86.
29. Gupta G, Kazmi I, Afzal M, Upadhyay G, Singh R, Habtemariam S. Antidepressant-like activity of Embelin isolated from *Embelia ribes*. *Phytopharmacology*. 2013 Oct 6;4(1):87-95.
30. Park SY, Lim SL, Jang HJ, Lee JH, Um JY, Kim SH, et al. Embelin induces apoptosis in human glioma cells through inactivating NF- κ B. *Journal of pharmacological sciences*. 2013 Mar 20;121(3):192-9.
31. Buchwald Werner S, Fujii H, inventors; Amino Up Chemical Co., Ltd., assignee. Composition comprising vicenin-2 having a beneficial effect on neurological and/or cognitive function. United States patent US 14/361,012. 2012 Nov 29.
32. Rajashekar Y, Raghavendra A, Bakthavatsalam N. Acetylcholinesterase inhibition by biofumigant (Coumaran) from leaves of *Lantana camara* in stored grain and household insect pests. *BioMed research international*. 2014 Jun 15;2014:6.
33. Zajac D, Stasinska A, Delgado R, Pokorski M. Mangiferin and its traversal into the brain. In: Mieczyslaw Pokorski, editors. *Respiratory Regulation-The Molecular Approach*. Netherlands: Springer; 2013. p. 105-111.
34. Kaehler ST, Sinner C, Chatterjee SS, Philippu A. Hyperforin enhances the extracellular concentrations of catecholamines, serotonin and glutamate in the rat locus coeruleus. *Neuroscience letters*. 1999 Mar 12;262(3):199-202.
35. Mennini T, Gobbi M. The antidepressant mechanism of *Hypericum perforatum*. *Life sciences*. 2004 Jul 16;75(9):1021-7.
36. Duan ZZ, Zhou XL, Li YH, Zhang F, Li FY, Su-Hua Q. Protection of *Momordica charantia* polysaccharide against intracerebral hemorrhage-induced brain injury through JNK3 signaling pathway. *Journal of Receptors and Signal Transduction*. 2015 Nov 2;35(6):523-9.
37. Gong J, Sun F, Li Y, Zhou X, Duan Z, Duan F, et al. *Momordica charantia* polysaccharides could protect against cerebral ischemia/reperfusion injury through inhibiting oxidative stress mediated c-Jun N-terminal kinase 3 signaling pathway. *Neuropharmacology*. 2015 Apr 30;91:123-34.
38. Koneri RB, Samaddar S, Simi SM, Rao ST. Neuroprotective effect of a triterpenoid saponin isolated from *Momordica cymbalaria* Fenzl in diabetic peripheral neuropathy. *Indian journal of pharmacology*. 2014 Jan;46(1):76.
39. Hannan MA, Kang JY, Mohibullah M, Hong YK, Lee H, Choi JS, Choi IS, Moon IS. *Moringa oleifera* with promising neuronal survival and neurite outgrowth promoting potentials. *Journal of ethnopharmacology*. 2014 Feb 27;152(1):142-50.
40. Cui CA, Jin DQ, Hwang YK, Lee IS, Hwang JK, Ha I, et al. Macelignan attenuates LPS-induced inflammation and reduces LPS-induced spatial learning impairments in rats. *Neuroscience letters*. 2008 Dec 19;448(1):110-4.
41. Jin DQ, Lim CS, Hwang JK, Ha I, Han JS. Antioxidant and anti-inflammatory activities of macelignan in murine hippocampal cell line and primary culture of rat microglial cells. *Biochemical and biophysical research communications*. 2005 Jun 17;331(4):1264-9.
42. Sasaki K, El Omri A, Kondo S, Han J, Isoda H. *Rosmarinus officinalis* polyphenols produce antidepressant like effect through monoaminergic and cholinergic functions modulation. *Behavioural brain research*. 2013 Feb 1;238:86-94.
43. Kasture VS, Deshmukh VK, Chopde CT. Anticonvulsant and behavioral actions of triterpene isolated from *Rubia cordifolia* Linn. *Indian journal of experimental biology*. 2000 Jul 24;38(7):675-80.
44. Chakrabortee S, Liu Y, Zhang L, Matthews HR, Zhang H, Pan N, et al. Macromolecular and small-molecule modulation of intracellular A β 42 aggregation and associated toxicity. *Biochemical Journal*. 2012 Mar 15;442(3):507-15.
45. Zaidi SK, Hoda MN, Tabrez S, Ansari SA, Jafri MA, Shahnawaz Khan M, et al. Protective effect of *Solanum nigrum* leaves extract on immobilization stress induced changes in rat's brain. *Evidence-Based Complementary and Alternative Medicine*. 2014 Feb 9;2014.
46. Yaidikar L, Thakur S. Arjunolic acid, a pentacyclic triterpenoidal saponin of *Terminalia arjuna* bark protects neurons from oxidative stress associated damage in focal cerebral ischemia and reperfusion. *Pharmacological Reports*. 2015 Oct 31;67(5):890-5.
47. Lee HS, Koo YC, Suh HJ, Kim KY, Lee KW. Preventive effects of chebulic acid isolated from *Terminalia chebula* on advanced glycation endproduct-induced endothelial cell dysfunction. *Journal of ethnopharmacology*. 2010 Oct 5;131(3):567-74.
48. Kelleher RJ, Soiza RL. Evidence of endothelial dysfunction in the development of Alzheimer's disease: is Alzheimer's a vascular disorder. *Am J Cardiovasc Dis*. 2013 Oct 1;3(4):197-226.
49. Le XT, Pham HT, Van Nguyen T, Nguyen KM, Tanaka K, Fujiwara H, et al. Protective effects of *Bacopa monnieri* on ischemia-induced cognitive deficits in mice: The possible contribution of bacopaside I and underlying mechanism. *Journal of ethnopharmacology*. 2015 Apr 22;164:37-45.
50. Chowdhuri DK, Parmar D, Kakkar P, Shukla R, Seth PK, Srimal RC. Antistress effects of bacosides of *Bacopa monnieri*: modulation of

- Hsp70 expression, superoxide dismutase and cytochrome P450 activity in rat brain. *Phytotherapy Research*. 2002 Nov 1;16(7):639-45.
51. Konrath EL, Neves BM, Passos CD, Lunardi PS, Ortega MG, Cabrera JL, et al. Huperzia quadrifariata and Huperzia reflexa alkaloids inhibit acetylcholinesterase activity in vivo in mice brain. *Phytomedicine*. 2012 Nov 15;19(14):1321-4.
 52. Ved HS, Koenig ML, Dave JR, Doctor BP. Huperzine A, a potential therapeutic agent for dementia, reduces neuronal cell death caused by glutamate. *Neuroreport*. 1997 Mar 3;8(4):963-7.
 53. Hosseinzadeh H, Sadeghnia HR, Ghaeni FA, Motamedshariaty VS, Mohajeri SA. Effects of saffron (*Crocus sativus* L.) and its active constituent, crocin, on recognition and spatial memory after chronic cerebral hypoperfusion in rats. *Phytotherapy Research*. 2012 Mar 1;26(3):381-6.
 54. Gupta G, Dua K, Kazmi I, Anwar F. Anticonvulsant activity of Morusin isolated from *Morus alba*: Modulation of GABA receptor. *Biomedicine & Aging Pathology*. 2014 Mar 31;4(1):29-32.
 55. Kang TH, Hur JY, Kim HB, Ryu JH, Kim SY. Neuroprotective effects of the cyanidin-3-O- β -d-glucopyranoside isolated from mulberry fruit against cerebral ischemia. *Neuroscience letters*. 2006 Jan 2;391(3):122-6.
 56. Gupta P, Yadav DK, Siripurapu KB, Palit G, Maurya R. Constituents of *Ocimum sanctum* with antistress activity §. *Journal of natural products*. 2007 Sep 13;70(9):1410-6.
 57. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic-antidepressant activity of *Withania somnifera* glycowithanolides: an experimental study. *Phytomedicine*. 2000 Dec 31;7(6):463-9.
 58. Mir BA, Khazir J, Mir NA, Hasan TU, Koul S. Botanical, chemical and pharmacological review of *Withania somnifera* (Indian ginseng): An Ayurvedic Medicinal Plant. *Indian Journal of Drugs and Diseases*. 2012 Sep 1;1(6):147-60.
 59. Nam SM, Choi JH, Yoo DY, Kim W, Jung HY, Kim JW, et al. Effects of curcumin (*Curcuma longa*) on learning and spatial memory as well as cell proliferation and neuroblast differentiation in adult and aged mice by upregulating brain-derived neurotrophic factor and CREB signaling. *Journal of medicinal food*. 2014 Jun 1;17(6):641-9.
 60. Rajput SB, Tonge MB, Karuppayil SM. An overview on traditional uses and pharmacological profile of *Acorus calamus* Linn.(Sweet flag) and other *Acorus* species. *Phytomedicine*. 2014 Feb 15;21(3):268-76.
 61. Shukla PK, Khanna VK, Ali MM, Maurya R, Khan MY, Srimal RC. Neuroprotective effect of *Acorus calamus* against middle cerebral artery occlusion-induced ischaemia in rat. *Human & experimental toxicology*. 2006 Apr 1;25(4):187-94.
 62. Ka V, Ta G, Ra V, Ja N, Ma K. Neuromodulatory effect of *Acorus calamus* leaves extract on dopaminergic system in mice. *International Journal of PharmTech Research*. 2009;1(4):1255-9.
 63. Naderi GA, Khalili MO, Karimi ME, Soltani MA. The effect of oral and intraperitoneal administration of *Acorus Calamus* L. extract on learning and memory in male rats. *Journal of Medicinal plants*. 2010 Jun 15;2(34):46-56.
 64. Vijayapandia P, Annabathina V, SivaNagaSrikanth B, Manjunath V, Boggavarapu P, RajendraPrasad K, et al. In vitro anticholinergic and antihistaminic activities of *Acorus calamus* Linn. leaves extracts. *African Journal of Traditional, Complementary and Alternative Medicines*. 2013 Jan 1;10(1):95-101.
 65. Manoharan S, Balakrishnan S, Menon VP, Alias LM, Reena AR. Chemopreventive efficacy of curcumin and piperine during 7, 12-dimethylbenz (a) anthracene-induced hamster buccal pouch carcinogenesis. *Singapore medical journal*. 2009 Feb 1;50(2):139.
 66. Li S, Wang C, Wang M, Li W, Matsumoto K, Tang Y. Antidepressant like effects of piperine in chronic mild stress treated mice and its possible mechanisms. *Life Sciences*. 2007 Mar 20;80(15):1373-81.
 67. Mahdy K, Shaker O, Wafay H, Nassar Y, Hassan H, Hussein A. Effect of some medicinal plant extracts on the oxidative stress status in Alzheimer's disease induced in rats. *Eur Rev Med Pharmacol Sci*. 2012 Jul 1;16(3 Suppl):31-42.
 68. Hritcu L, Noumedem JA, Cioanca O, Hancianu M, Kuete V, Mihasan M. Methanolic extract of *Piper nigrum* fruits improves memory impairment by decreasing brain oxidative stress in amyloid beta (1–42) rat model of Alzheimer's disease. *Cellular and molecular neurobiology*. 2014 Apr 1;34(3):437-49.
 69. Ahmed HH, Salem AM, Sabry GM, Husein AA, Kotob SE. Possible Therapeutic Uses of *Salvia triloba* and *Piper nigrum* in Alzheimer's Disease-Induced Rats. *Journal of medicinal food*. 2013 May 1;16(5):437-46.
 70. Hritcu L, Noumedem JA, Cioanca O, Hancianu M, Postu P, Mihasan M. Anxiolytic and antidepressant profile of the methanolic extract of *Piper nigrum* fruits in beta-amyloid (1–42) rat model of Alzheimer's disease. *Behavioral and Brain Functions*. 2015 Mar 29;11(1):1.
 71. Agarwa P, Sharma B, Fatima A, Jain SK. An update on Ayurvedic herb *Convolvulus pluricaulis* Choisy. *Asian Pacific journal of tropical biomedicine*. 2014 Mar 31;4(3):245-52.
 72. Sharma K, Bhatnagar M, Kulkarni SK. Effect of *Convolvulus pluricaulis* Choisy. and *Asparagus racemosus* Willd on learning and memory in young and old mice: A comparative evaluation. 2010 May; 48(5): 479-485.
 73. Bihaqi SW, Singh AP, Tiwari M. Supplementation of *Convolvulus pluricaulis* attenuates scopolamine-induced increased tau and Amyloid precursor protein (A β PP) expression in rat brain. *Indian journal of pharmacology*. 2012 Sep 1;44(5):593.
 74. Chaudhary N, Tripathi S. A Review on Multipurpose Plant: *Psidium Guajava*.

- International Journal of Pharmacognosy and Phytochemical Research. 2014 Mar 1; 6(1); 118-121.
75. Krishna Mohan Chinnala, Swetha Jukanti, Madhan Mohan Elsani. Effects of ethanolic leaf extract of *Psidium guajava* Linn. on L-arginine induced obsessive compulsive disorder in mice. *Scholars Academic Journal of Pharmacy*. 2015; 4(3): 157-163.
 76. Pushpa VH, Shetty KP, Sushma N, Kalabharathi HL, Satish AM. EVALUATION OF THE ANTICONVULSANT ACTIVITY OF ETHANOL EXTRACT OF *PSIDIUM GUAJAVA* (GUAVA LEAVES) IN ALBINO MICE. *International Journal of Pharmaceutical Sciences and Research*. 2014 Oct 1;5(10):4288.
 77. Sheth A. *The herbs of India*. Edn 1, Vol 2, Hi Scan Pvt Ltd, Gujrat, 2005, pp. 566.
 78. Kaur R, Kaur H, Dhindsa AS. *Glycyrrhiza glabra*: a phytopharmacological review. *International Journal of Pharmaceutical Sciences and Research*. 2013 Jul 1;4(7):2470.
 79. Chakravarthi KK, Avadhani R, Narayan RS. Effects of *Glycyrrhiza glabra* root extract on learning and memory in Wistar albino rats. *Drug Invention Today*. 2012 Aug 5;4(4):387-90.
 80. Chakravarthi KK, Avadhani R. Enhancement of hippocampal CA3 neuronal dendritic arborization by *Glycyrrhiza glabra* root extract treatment in Wistar albino rats. *Journal of natural science, biology, and medicine*. 2014 Jan;5(1):25.
 81. Phukan P, Bawari M, Sengupta M. PROMISING NEUROPROTECTIVE PLANTS FROM NORTH-EAST INDIA. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2015 Jan 29;7(3):28-39.
 82. Singh SS, Pandey SC, Srivastava S, Gupta VS, Patro B, Ghosh AC. Chemistry and medicinal properties of *Tinospora cordifolia* (Guduchi). *Indian journal of pharmacology*. 2003 Mar 1;35(2):83-91.
 83. Bairy KL, Rao Y, Kumar KB. Efficacy of *Tinospora cordifolia* on learning and memory in healthy volunteers: A double-blind, randomized, placebo controlled study. *IRANIAN JOURNAL OF PHARMACOLOGY & THERAPEUTICS*. 2004 Dec 31; 3:57-60.
 84. Agarwal A, Malini S, Bairy KL, Rao MS. Effect of *Tinospora cardifolia* on learning and memory in normal and memory deficit rats. *Indian journal of pharmacology*. 2002;34(5):339-49.
 85. Dhingra D, Parle M, Kulkarni SK. Memory enhancing activity of *Glycyrrhiza glabra* in mice. *Journal of ethnopharmacology*. 2004 Apr 30;91(2):361-5.
 86. Murthy KS. A review on *Decalepis hamiltonii* Wight Arn. *Journal of Medicinal Plants Research*. 2013 Nov 3;7(41):3014-29.
 87. Haddadi M, Jahromi SR, Shivanandappa T, Ramesh SR. *Decalepis hamiltonii* root extract attenuates the age-related decline in the cognitive function in *Drosophila melanogaster*. *Behavioural brain research*. 2013 Jul 15;249:8-14.
 88. Jahromi SR, Haddadi M, Shivanandappa T, Ramesh SR. Attenuation of neuromotor deficits by natural antioxidants of *Decalepis hamiltonii* in transgenic *Drosophila* model of Parkinson's disease. *Neuroscience*. 2015 May 7;293:136-50.
 89. Srivastava A, Shivanandappa T. Neuroprotective effect of *Decalepis hamiltonii* roots against ethanol-induced oxidative stress. *Food chemistry*. 2010 Mar 15;119(2):626-9.
 90. Semalty M, Semalty A, Badola A, Joshi GP, Rawat MS. *Semecarpus anacardium* Linn.: A review. *Pharmacognosy reviews*. 2010 Jan 1;4(7):88.
 91. Shukla SD, Jain S, Sharma K, Bhatnagar M. Stress induced neuron degeneration and protective effects of *Semecarpus anacardium* Linn. and *Withania somnifera* Dunn. in hippocampus of albino rats: an ultrastructural study. *Indian journal of experimental biology*. 2000 Oct 28;38(10):1007-13.
 92. Farooq SM, Alla TR, Rao NV, Prasad K, Shalam NK. A study on CNS effects of milk extract of nuts of *Semecarpus anacardium* linn.(Anacardiaceae). *Pharmacologyonline*. 2007;1:49-63.
 93. Madan S, Singh GN, Kumar Y, Kohli K, Singh RM, Mir SR, et al. A new flavanone from *Flemingia strobilifera* (Linn) R. Br. and its antimicrobial activity. *Tropical Journal of Pharmaceutical Research*. 2008 Mar 1;7(1):921-7.
 94. Baruah M, Kalita D. Ethnomedicine used by Mishings tribes of Dibrugarh district, Assam. *Indian Journal of Traditional Knowledge*. 2007 Oct 1;6(4):595-8.
 95. Gahlot K, Lal VK, Jha S. Anticonvulsant potential of ethanol extracts and their solvent partitioned fractions from *Flemingia strobilifera* root. *Pharmacognosy research*. 2013 Oct;5(4):265.
 96. Sharma V, Rao LJ. An overview on chemical composition, Bioactivity and processing of leaves of *cinnamomum tamala*. *Critical reviews in food science and nutrition*. 2014 Jan 1;54(4):433-48.
 97. Dalai MK, Bhadra S, Chaudhary SK, Bandyopadhyay A, Mukherjee PK. Anti-cholinesterase potential of *Cinnamomum tamala* (Buch.-Ham.) T. Nees & Eberm. leaves. *Indian J Tradit Know*. 2014 Oct 1;13:691-7.
 98. Meena AK, Yadav AK, Niranjana US, Singh B, Nagariya AK, Verma M. Review on *Cyperus rotundus*-A potential herb. *International Journal of Pharmaceutical and Clinical Research*. 2010 Jan;2(1):20-2.
 99. Kumar KH, Tamatam A, Pal A, Khanum F. Neuroprotective effects of *Cyperus rotundus* on SIN-1 induced nitric oxide generation and protein nitration: ameliorative effect against apoptosis mediated neuronal cell damage. *Neurotoxicology*. 2013 Jan 31;34:150-9.
 100. Kumar KH, Khanum F. Hydroalcoholic extract of *Cyperus rotundus* ameliorates H₂O₂-induced human neuronal cell damage via its anti-oxidative and anti-apoptotic machinery. *Cellular and molecular neurobiology*. 2013 Jan 1;33(1):5-17.
 101. Rabiei Z, Hojjati M, Rafieian-Kopaeia M, Alibabaei Z. Effect of *Cyperus rotundus* tubers ethanolic extract on learning and memory in animal model

- of Alzheimer. *Biomedicine & Aging Pathology*. 2013 Dec 31;3(4):185-91.
102. Orhan IE. *Centella asiatica* (L.) Urban: from traditional medicine to modern medicine with neuroprotective potential. *Evidence-based complementary and alternative medicine*. 2012 May 14; 2012 (2012).
 103. Veerendra Kumar MH, Gupta YK. Effect of *Centella asiatica* on cognition and oxidative stress in an intracerebroventricular streptozotocin model of Alzheimer's disease in rats. *Clinical and Experimental Pharmacology and Physiology*. 2003 May 1;30(5-6):336-42.
 104. Subathra M, Shila S, Devi MA, Panneerselvam C. Emerging role of *Centella asiatica* in improving age-related neurological antioxidant status. *Experimental gerontology*. 2005 Sep 30;40(8):707-15.
 105. Visveswari G, Siva Prasad K, Lokanatha V, Rajendra W. The antiepileptic effect of *Centella asiatica* on the activities of Na⁺/K⁺, Mg²⁺ and Ca²⁺-ATPases in Rat brain during pentylenetetrazol-induced epilepsy. *Indian J Pharmacol*. 2010 Apr;42(2):82-6.
 106. Marques NF, Stefanello ST, Froeder AL, Busanello A, Boligon AA, Athayde ML, et al. *Centella asiatica* and Its Fractions Reduces Lipid Peroxidation Induced by Quinolinic Acid and Sodium Nitroprusside in Rat Brain Regions. *Neurochemical research*. 2015 Jun 1;40(6):1197-210.
 107. Chen CL, Tsai WH, Chen CJ, Pan TM. *Centella asiatica* extract protects against amyloid β 1–40-induced neurotoxicity in neuronal cells by activating the antioxidative defence system. *Journal of Traditional and Complementary Medicine*. 2015 Aug 1.
 108. Harish GU, Danapur V, Jain R, Patell VM. Endangered Medicinal Plant *Embelia ribes* Burm. f.-A Review. *Pharmacognosy Journal*. 2012 Feb 29;4(27):6-19.
 109. Nazam Ansari M, Bhandari U, Islam F, Tripathi CD. Evaluation of antioxidant and neuroprotective effect of ethanolic extract of *Embelia ribes* Burm in focal cerebral ischemia/reperfusion-induced oxidative stress in rats. *Fundamental & clinical pharmacology*. 2008 Jun 1;22(3):305-14.
 110. Kumar G, Karthik L, Rao KV. Phytochemical composition and in vitro antioxidant activity of aqueous extract of *Aerva lanata* (L.) Juss. ex Schult. Stem (Amaranthaceae). *Asian Pacific journal of tropical medicine*. 2013 Mar 31;6(3):180-7.
 111. Rao MA, Palaksha MN, Sirisha KN, Bhargavi VL, Manikandhar P. Effect of *Aerva lanata* on cisplatin induced Neurotoxicity in rats. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2014;3(2):2431-51.
 112. Kumar S, Maheshwari KK, Singh V. Effects of *Mangifera indica* fruit extract on cognitive deficits in mice. *Journal of Environmental Biology*. 2009 Jul;30(4):563-6.