

Role of Traditional Plant Compounds in the Treatment of Neuropsychiatric Diseases

Praveen Halagali¹, Rohan Singadi², Hunsur Ranganath Arjun³, Gundada Sivaraj Rakshana³,
Salini Parameswaran Nair³, Prashant Halagali⁴, Preethi Somanna^{1,*}

¹Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Mysuru, Karnataka, INDIA.

²Department of Pharmaceutical Chemistry, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi, Karnataka, INDIA.

³Department of Pharmacology, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Mysuru, Karnataka, INDIA.

⁴Department of Pharmaceutical Quality Assurance, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi, Karnataka, INDIA.

ABSTRACT

Natural elements from nature along with their bioactive components are being extensively studied in recent times for their therapeutic efficacy in treating a variety of degenerative disorders. These diseases are specifically characterized by their progressive nature of dysfunction caused by gradual loss of function. Even though there is a shoot in technology and impressive breakthroughs in properly understanding neurodegenerative disorders, the progress and process in designing an efficient treatment were very few. In the process of prevention and therapy of neuropsychiatric diseases NDs. The use of natural products in the prevention and treatment of neurodegenerative disorders are known, though many clinical issues have been emerging regarding their usage pattern, primarily based on the lack of evidence of scientific evidence and also the proof of their efficacy and patient safety. Neurodegeneration is basically a myriad of various pathological processes, hence, targeting multiple mechanisms of action and neuroprotective approaches that include cell death prevention and restoring the function of damaged neurons must be focused on.

Keywords: Plant compounds, Neuropsychiatric diseases, Traditional medicines, Natural bioactive compounds.

Correspondence:

Ms. Preethi S

Lecturer, Department of Pharmaceutics,
JSS College of Pharmacy, JSS Academy of
Higher Education and Research, SS Nagar,
Mysuru-570015, Karnataka, INDIA.
Email: preethis@jssuni.edu.in

Received: 04-07-2023;

Revised: 27-07-2023;

Accepted: 20-10-2023.

INTRODUCTION

Conventionally, traditional plant compounds were used for the treatment of psychotic diseases. As time went by, after the conquer by globalization and modern medicine or 'allopathy', traditional medicines and methods were slowly forgotten.¹ Though, in recent times, the importance and impact of traditional medicines were being figured out. Though quintessential traditional legacy need not an introduction, Aarts M *et al.* conducted a study and discovered that Glutamate is responsible for central excitatory neurotransmission found mainly in the survival of neurons, synaptogenesis and neuronal plasticity.² Even though, higher than required concentrations of glutamate can lead to fatal neuronal dysfunction. Glutamate-induced neurotoxicity can be noticed in several neuropathological disorders, for instance, Alzheimer's disease, Ischemic stroke, Parkinsonism, and spinal cord trauma.³ Thus, it was suggested after a few studies that

neuroprotection against glutamate-induced neurotoxicity can be used as a therapeutic strategy to treat neurodegenerative diseases. As already known, Alzheimer's disease AD is a progressive neurodegenerative disease where oxidative stress was observed as a major cause of the condition. Y. Matsuoka *et al.*, conducted a study and found out that the source of oxidative damage in the brain actually leads to the condition.⁴ Various inflammatory responses originating in the CNS can be named as neuroinflammatory state due to the accumulation of glial cells by activation of the immune component. But in recent times, after the emergence of modern medicines, Non-steroidal anti-inflammatory drugs NSAIDs, opioid antagonists, cox inhibitors, NMDA receptor antagonists, and in very rare conditions, antibiotics too are being used. There are many factors contribute to neuropsychiatric disorder susceptibility which are depicted in Figure 1.⁵

Treatment

Rostom A *et al.* conducted a study and provided the result of importance of vigilance is each medication ingested and brought to the topic of undesirable effects caused by allopathic medicines



DOI: 10.5530/ijpi.14.1.7

Copyright Information :

Copyright Author (s) 2024 Distributed under
Creative Commons CC-BY 4.0

Publishing Partner : EManuscript Tech. [www.emanuscript.in]

though they are immensely useful in treatment of pain and inflammation.⁶ Considering of importance of pharmacovigilance and better patient care and survival, traditional drugs are being brought back since they are known to have least no side effects when compared to allopathic medicines.⁷ In addition to their antioxidant effect, natural bioactive compounds namely phenolics, flavonoids, terpenoids, lignans, alkaloids and saponins have essential properties to modulate proper neuronal function. A Davalos *et al.* brought in the importance of various factors playing roles in the process of neuro-degeneration, free radical formation and the presence of reactive oxygen species ROS. Excess of these species in the body may lead to cumulative damage in cells resulting in increased oxidative stress.⁸

Neurons and the brain cells are selectively vulnerable and submissive to free radicals present and oxidative stress is found to be one of the main causes in late onset disorders. Oxidative damage caused by neuronal cells can be a reason for endogenous production of ROS, and the amyloid beta peptide may increase ROS production even more leading to further impairment of brain's cellular structure. Amyloid beta is known to be the major component of senile plaques and is vastly engaged in the progression of neurodegenerative diseases. Molecules including phenolics act by inhibiting the initial propagation of oxidative chain reaction and in maintaining the brain's chemical balance by acting upon the receptor function. M. A. Ansari *et al.* and C. Riviere *et al.* conducted a study and found out that these

compounds hence prevent the aggregation and attenuate amyloid beta toxicity, oxidation of proteins and the process of apoptosis in primary hippocampal cultures.^{9,10} Elufioye TO *et al.*, mentioned in his study that nature is the best chemist the universe has provided and it can hence effortlessly treat almost any medical problem faced by the mankind. Only if one closely watches the details being studied, it can easily cure any disease ever occurred. One WHO estimates that 80% of the population of some Asian and African countries presently relies on herbal medicine for various aspects of primary health care.¹¹

Ayurveda, Unani and Siddha which are quintessential complementary and alternative systems of medicine provide a health care facility where more than 70% of the population exist in rural areas. Herbal medicine treatment for these neurodegenerative diseases is relatively less common the clinical setting in countries like USA and Europe.¹² It has also become very popular in recent times because of their effect against these diseases by slowing down their gradual or sudden onset progression. Recently, since the importance of herbal medicines have been researched and benefits derived from various plants were found to be quite promising. These herbs are also very affordable for obvious reasons and can be easily available too. Patel K C *et al.* stated in his study that these herbal medicines are rising in use and also they are being studied to the root because of the least amount of side effects with their affordability and easy accessibility.¹³

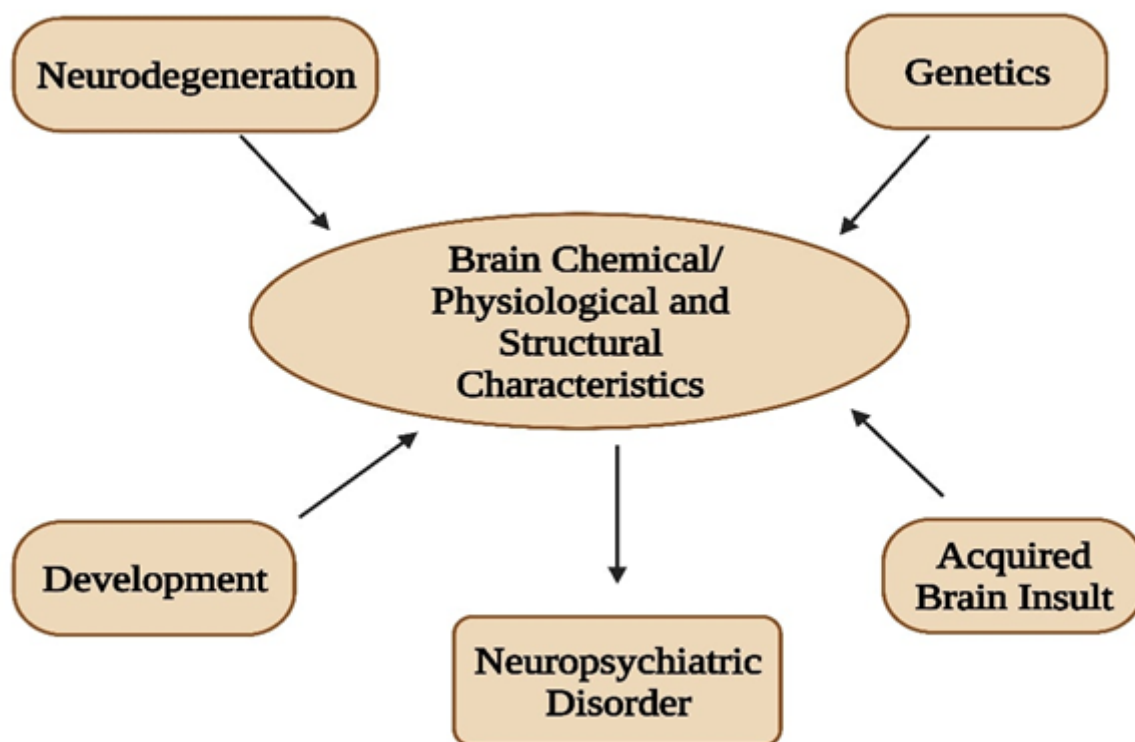


Figure 1: Factors contribute to neuropsychiatric disorder susceptibility.⁵

Lin MT *et al.*, mentioned in his study the actual process of neuronal degeneration where it is progressive in nature which results in neuronal death. For example, Alzheimer's disease, Huntington disorder etc. Considering the risk factors, most important factor would be aging which in turn was caused by the mutation of mitochondrial DNA and oxidative stress. There is major role by the etiology of any neuronal degeneration.¹⁴ The neuronal degeneration is mainly caused by mutations of genes mostly located in completely unrelated gene entities. In most conditions, it is encoded with CAG nucleotide triplet that supposedly codes for amino acid glutamine. The repeated units of CAG nucleotide leads to a polyglutamine tract poly Q by which these diseases are known as polyglutamine diseases.¹⁵

The question arises where did polyglutamine emerged from and it is known that the extra glutamine residues are able to acquire toxic properties through variety of ways, including irregular protein folding and degradation pathways, altered subcellular localization and abnormal interaction with other cellular proteins. In recent times, some neurodegenerative diseases are classified into the class of diseases called as proteopathies and they are named so because they are linked systematically with aggregation of misfolded protein pigments.¹⁶ There are various Intracellular mechanisms occurring in the background of all neurodegenerative diseases and these are clearly Protein degeneration pathways. Parkinsonism and Huntington diseases and other major neurodegenerative diseases are very much linked with an accumulation of intracellular toxin proteins in the cytosol.¹⁷

There are various mechanisms revolving around neuronal degeneration which includes excitotoxicity which is one of the most valuable mechanisms to cause cell death in case of CNS disorders. A sudden over excitation of these receptors especially the NMDA receptors causes more influx of calcium ions due to the opening of ion channel and glutamate binding. As the accumulation takes place the buffering level increases which is considered to be the major consequence of neuron.¹⁸ Calcium is the known secondary messenger and the accumulation of these ions causes improper regulation resulting in cell death and it also triggers neuroinflammation which is a key component in all kinds of CNS disorders. Special components called as Glutamate antagonists takes up the main goal of inhibiting the binding of glutamate to NMDA receptors and hence the accumulation of calcium and thus excitotoxicity can be prevented.¹⁹

There are various Approaches for neuroprotection and it refers to the relative preservation and protection of neuronal structure and its functionality. It focuses mainly to prevent or slow the disease progression and secondary injuries by pausing or at the least manner, slowing the loss of neurons. Oxidative stress and excitotoxicity are two major processes that triggers the cell death of neuron but when combined, they have synergistic effects that are able to cause even more degradation than on their own. Hence,

keeping a limit on excitotoxicity and oxidative stress would be considered as a very important aspect of neuroprotection.²⁰

Excitotoxicity can be inhibited by various elements including estrogen, ginsenoside and progesterone. 17 beta estradiol regulates excitotoxicity by inhibiting those NMDA receptors and other glutamate receptors. Ginsenoside attenuates the excitotoxicity. Progesterone helps in prevention of secondary injuries in patients with traumatic brain injury and stroke. NMDA receptor modulation is done by Simvastatin which is neuroprotective as well as anti-inflammatory effects due to NMDA receptors modulation. Secondly, there is equal importance for Memantine and it inhibits NMDA induced excitotoxicity while still preserving and protecting a certain degree of NMDA signaling.^{21,22} Another very important process is Free radical scavenging by antioxidants wherein they play an important role in controlling the oxidative stress levels. They act by eliminating those reactive oxygen species which are supposedly the main cause of neurodegeneration. Some antioxidants which reduce the oxidative stress are:

Crocin which is a potent neuronal antioxidant. Fish oil containing n-3 polyunsaturated fatty acids which is known for the offset of oxidative stress and dysfunction of mitochondria. Minocycline, which is a semi synthetic tetracycline compound that can cross the blood brain barrier and was found to be very effective in treatment of Parkinson's and Alzheimer's disease. Resveratrol prevents the condition of these antagonistic oxidative stress by attenuating the hydrogen peroxide induced cytotoxicity and further intracellular accumulation of reactive oxygen species. Vitamin E which is most effective in alzheimers disease.^{23,24}

The study also vividly talks about the importance of neuroprotection in traditional medicines. To begin with, the very known Indian medicine system, called The Ayurveda, is gaining greater and better deserved attention in recent times. Ayurveda is technically disease preventive and overall health promotive with least or no side effects and hence is gaining acceptance at a very large scale. There is a specific revitalization and enhanced rejuvenation treatment therapy in Ayurveda and is called the 'Rasyanachikitsa'. Rasayana, which is the applied group of drugs that act inside the human body by modulating the neuro-endocrino and immune systems and is also a powerhouse of antioxidants. Pushpagandan P *et al.* and Brahma SK *et al.* conducted years long study on these medicinal plants and shows that these represents a great deal of untapped drug reservoir and a structural diversity of their internal molecules makes a very valuable source of novel essential compounds. Researches had earlier proved that certain non-nutritive chemicals obtained from plants namely vizterpenoids and flavonoids possess exemplary antioxidant properties. The unfortunate absence of effective and applicable pharmacological treatments in the system of modern medicine for the correction of neurodegenerative disorders may promote and enhance the growing interest of the population in the traditional medicines furthermore.^{25,26}

Wasik J *et al.* and Esenberg DM *et al.* made statements based on their study which includes the herbal extract to be considered as the traditional crude which can be then isolated and synthesized. Ayurveda points out, Alzheimer's disease, affecting millions worldwide is an imbalance of the three components namely *vaatha*, *pitha* and *kapha* which are the three main components that holds the soul of the body. Medhya herbs such as, *Convolvulus microphyllus*, *Centella asiatica*, *Bacopa monnieri*, *Acorus calamus* and *Celastrus paniculatus* are known to be beneficial in cognitive disorders.²⁷ Sing S *et al.* talks about the infamous *Hemidesmus indicus*, colloquially called the Indian sarsaparilla or anantmool. It is widely accepted and recognized in the folk medicine system, grown wealthy in parts of Orissa and is being used as a major ingredient in the Ayurvedic and Unani preparations against various diseases. The roots of anantmool is said to be having extra-ordinary antioxidant properties and various studies have reported memory enhancing potential.²⁸

Kirtikar KR *et al.* and Ambikar DB *et al.* says about *Trapa bispinosa*, the floating herb which can be used as a nerve tonic and is proved to be neuroprotective which acts by the mechanism of reducing the antagonistic oxidative stress induced by D-galactose through the medium of activating glutathione peroxidases and catalases consequently reducing the lipid peroxide concentration.²⁹

Gajare *et al.* have reported the exemplary neuroprotective effect of *Bacopa monniera* on lipofuscinogenesis and the fluorescence byproduct in the brains of D-Galactose induced aging process accelerated in mice. The study demonstrated efficiently that D-Galactose reacts with the amino group side chain of proteins and lead to the formation of amadori products which finally results in to advanced glycation end product or the AEGs, which are very rich sources of free radicals and cause oxidative stress by chemical oxidation of these AEGs. Proteins and lipids are essential macromolecules which when damaged by any source of aluminum, it results in the interference with functioning of various cell organelles like mitochondria and lysosomes making them less efficient in activity. The BM protects these macromolecules and thereby exhibits extensive neuroprotection. The conservation of endogenous antioxidants with the treatment of *Bacopa monniera* enzymes further indicated the neuroprotection from the free radicals induced toxicity.³⁰

Vinutha B *et al.* brings out the fact that *Withania somnifera* has been in use for more than a span of 2500 years for treating various clinical conditions and its root extracts were shown to exhibit nootropic effects in mice and cause an inhibition of AChE, and this inhibition suggested indirect facilitation of cholinergic transmission which may be of enormous value in the process of neurodegeneration states associated with cholinergic associated deficiencies.³¹ Joshi H *et al.* brought out the importance of *Centella asiatica*, showed significant improvement in terms of learning ability and memory power and the study later reported significant reduction in the malondialdehyde MDA levels, with

simultaneous decreased levels of glutathione. The increased levels of MDA further support the enormous potential of the herb.³² *Brahmi* extracts, since ages had been protecting and preserving the neurons from the beta-amyloid induced death of major cells, but not the glutamate induced excitotoxicity. This mechanism of neuroprotection was probably, due to the herb's ability to suppress cellular stage of acetyl-cholinesterase activity but not in the case of inhibition of glutamate mediated toxicity says Stahl SM *et al.* in his study about *Brahmi* extracts.³³

Rutvi H Vekaria *et al.* brought into light the facts about coriander where it can improve the circulation to head part and thereby improving mental health, concentration and memory capabilities. There are various other studies that showcase the importance of traditional medicine in curing neurodegenerative diseases. Zanolli P *et al.* talks about *Acorus calamus* which contains the active ingredient Asarone belonging to the phytochemical group of monoterpene and brings out the important activity status which includes sedative property, memory power enhancer etc.³⁴⁻³⁶ Nalini K *et al.* in her study on traditional medicine, studied about *Centella asiatica* which contains the active ingredients namely Asiaticoside, Centelloside, Madecassoside and Asiatic acid all belonging to the phytochemical group called the triterpenoid saponins which can act brilliantly as brain tonic, cognition and anti-anxiety agents.^{37,38}

Clitoria ternatea is a reputed and used drug in the well-known Indian system of ayurveda. Vyawahare *et al.*, in a study, reported the effects of alcoholic root extract of CT on scopolamine induced memory disturbance using radial arm maze. The study later reported significant prevention of the idiopathic memory disruption, and thereby their validated traditional claim.³⁹

Panax ginseng is yet another traditionally medicinal plant that has been in use since time immemorial to fight diseases including neurodegenerative conditions linked with aging says Limpeanchob N *et al.* in their study about herbal remedies. A while later Limpeanchob proposed his study, Kennedy DO *et al.* show that animals when treated for disorders with either ginseng extract or preparations containing ginseng claimed to improve learning ability and memory power. The Wang *et al.* documented the recorded dose dependent reduction in the β amyloid deposition or glutamate induced excitotoxicity and followed by neuron death.^{40,41}

Kumar V *et al.*, a scientist of Indian origin and his team once focused on *Coridalis longa* with its active constituent being protropine which belongs to the phytochemical group of alkaloids. They had focused on the structures and found it has anticholinesterase and anti-anesthetic properties. He, had also studied about *Curcuma longa*, which is very similar to *Corydalis longa*, as it's the same family and it has been in household usage since time immemorial. Curcumin, found in the basic Indian spices including turmeric and chilli pepper has the most

appreciated activity of protection against synaptic dysfunction. Hence it clearly shows that daily intake curcumin can be extremely beneficial by all means.⁴²⁻⁴⁴ Joseph J A *et al.*, studied about *Embllica officinalis* and observed its active constituent which is Vitamin C hence the plant containing valuable ascorbic acid and phyllembin belonging to the phytochemical group of vitamin polyphenol exhibiting tremendous anti cholinesterase activity. Gupta P *et al.*, studied about the essential memory enhancing agent used in the treatment of dementia which is betaine, sankhaphushpine and evolvine containing active phytochemical group of alkaloids named the *Evolvulus alsinoides*.^{45,46}

Chandrasekaran K *et al.*, studied and proposed his findings on one of the most appreciated traditionally benefitting called Ginkgo biloba. Belonging to the family of Ginkgoaceae, it has got various colloquial names called ginkgo or gingko and also is known as maidenhair tree. This species of maidenhair trees are actually native to China. Ginkgo biloba dates back to over 290 million years ago from where it first appeared. Traditionally, it has been used vividly as a part of Chinese medicine for centuries wherein the leaves are used to treat brain, circulatory and respiratory conditions. Other than leaves, the nuts can be used for cough, fever, diarrhea, toothaches and even for gonorrhoea. In recent times, there had been studies showing various other health benefits of *Ginkgo biloba* and is being sold in the market commercially as supplements for memory support, brain health and weight loss. Out of which, it has gained wide popularity regarding boost of weight loss. Other infamous benefits of Ginkgo are that consuming an amount of Ginkgo 30 to 60 min to sleep have shown to help reduce stress, enhance relaxing ability and induce sleep.^{47,48} *Glycyrrhiza glabra* was found to improve learning ability and memory especially on scopolamine induced neurogenerative disorders. Belonging to the phytochemical group of triterpenoid saponins and containing the active constituent of Glycyrrhizin, it is a herbaceous perennial legume having enormous other health benefits. It is commonly known as Liquorice or Licorice native to Western Asia, Southern Europe and North Africa. It has been in use as a herbal medicine since ages owing to its anti-cancerous, antiviral and anti-inflammatory properties.^{49,50}

Nalini K *et al.* once did a study pairing up with Sakira MR *et al.* about the action of *Huperzia serrata* containing active ingredients namely Huperzine A and B with their phytochemical alkaloids acting on the neuromuscular systems related to cholinesterase activity.⁵¹⁻⁵³ *Llexpara guariensis* has memory enhancing activity with its core ingredients being chlorogenic acid, caffeine, theophylline and theobromine with theobromine quercetin and kaemferol. It also has its phytochemical group of polyphenols, xanthines and flavonoids says Rui DS *et al.* in a study conducted in 2003.^{54,55}

Magnolia officinalis, as the name suggests is a species of Magnolia native in the mountains, hills and valleys of China. Scientist Lee

H *et al.* once conducted a study on the family *Magnoliaceae* and observed that it can be used for the treatment of various neural disorders including neurosis, anxiety, stroke and dementia.^{56,57} Liu RH *et al.* did a study about *Uncaria rhynchophylla* with its active constituents observed to be Rhynophylline, Corynoxine, Isorhynchophylline and isocorynoxine with its vast phytochemical group of alkaloids and provided the database as these herbs are neuroprotective in nature particularly against ischaemia induced neuronal loss.⁵⁸⁻⁶⁰

CONCLUSION

Therapeutic efficacy of products of natural source and their bioactive compounds to be neuroprotective in nature has been in support by number of researches and studies in recent times. The need for natural compounds and their essential bioactive compounds are found to be exponentially increasing for the purpose of prevention and treatment of various neurodegenerative disorders without causing harmful adverse effects with regard to the current pharmacovigilant population. Considering the complex functional pathways found in neurodegenerative disorders, preventive methods and therapeutic approaches have a consistent and ever-lasting role to play. Hence, it is of utmost importance to develop innovative methods and techniques, for instance, nanotechnology, for an accurate and intact delivery of natural drugs into the systemic circulation.

ACKNOWLEDGEMENT

The authors express heartfelt gratitude towards the JSS College of Pharmacy, JSS Academy of Higher Education and Research JSSAHER, Mysuru, for providing all the obligatory facilities for completion of this piece of writing.

AUTHOR CONTRIBUTION

PH, RS, AHR, GSR, SPN, PS, and made significant contribution to the work reported, whether that is in the conception, execution, or the acquisition, analysis, or interpretation of data, or all the areas; took part in drafting, revising, or critically reviewing the article; and gave final approval of the version to be published. All have read and agreed to the published version of the manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ND: Neuropsychiatric Diseases; **AD:** Alzheimer's disease; **ROS:** Reactive oxygen species.

ORCID ID

ORCID ID: 0000-0002-6420-7436

REFERENCES

- Aarts MM, Tymianski M. Novel treatment of excitotoxicity: targeted disruption of intracellular signalling from glutamate receptors. *Biochem Pharmacol*. 2003;66(6):877-86. doi: 10.1016/s0006-2952(03)00297-1, PMID 12963474.
- Abramov AV, Canevari L, Duchon MR. β -amyloid Peptides Induce mitochondrial Dysfunction and Oxidative Stress in Astrocytes and Death of Neurons through Activation of NADPH oxidase. *J Neurosci*. 2004;24(2):565-75. doi: 10.1523/JNEUROSCI.14042-03.2004, PMID 14724257.
- Ambikar DB, Harle UN, Khandare RA, Bore VV, Vyawahare NS. Neuroprotective effect of hydroalcoholic extract of dried fruits of *Trox* on lipofuscinogenesis and fluorescence product in brain of d-galactose induced ageing accelerated mice. *Indian J Exp Biol*. 2010;48(4):378-82. PMID 20726336.
- Amos S, Adzu B, Binda L, Wambebe C, Gamaniel K. Neuropharmacological effect of the aqueous extract of *Sphaeranthus senegalensis* in mice. *J Ethnopharmacol*. 2001;78(1):33-7. doi: 10.1016/s0378-8741(01)00316-6, PMID 11585685.
- An H, Kim IS, Koppula S, Kim BW, Park PJ, Lim BO, et al. Protective effects of *Gastrodia elata* Blume on MPP⁺-induced cytotoxicity in human dopaminergic SH-SY5Y cells. *J Ethnopharmacol*. 2010;130(2):290-8. doi: 10.1016/j.jep.2010.05.006, PMID 20470875.
- Ansari MA, Abdul HM, Joshi G, Opii WO, Butterfield DA. Protective effect of quercetin in primary neurons against A β 1-42: relevance to Alzheimer's disease. *J Nutr Biochem*. 2009;20:4269-75.
- Aoyama K, Matsumura N, Watabe M, Wang F, Kikuchi-Utsumi K, Nakaki T. Caffeine and uric acid mediate glutathione synthesis for neuroprotection. *Neuroscience*. 2011;181:206-15. doi: 10.1016/j.neuroscience.2011.02.047, PMID 21371533.
- Arias C, Montiel T, Quiroz-Báez R, Massieu L. β -amyloid neurotoxicity is exacerbated during glycolysis inhibition and mitochondrial impairment in the rat hippocampus *in vivo* and in isolated nerve terminals: implications for Alzheimer's disease. *Exp Neurol*. 2002;176(1):163-74. doi: 10.1006/exnr.2002.7912, PMID 12093093.
- Beal MF, Lin MT. Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. *Nature*. 2006;443(7113):787-95. doi: 10.1038/nature05292, PMID 17051205.
- Bhattacharjee SK. Handbook of medicinal plants; 2001.
- Bhattacharya SK, Bhattacharya A, Kumar A, Ghosal S. Antioxidant activity of *Bacopa monniera* in rat frontal cortex, striatum and hippocampus. *Phytother Res*. 2000;14(3):174-9. doi: 10.1002/(sici)1099-1573(200005)14: 3<174::aid-ptr624>3.0.co;2-o, PMID 10815010.
- Brahma, S.K. PKD. Therapeutic importance of rasayana drugs with a special reference to their multidimensional actions. *Aryavaidyan*. 2003;163:160-3.
- Casson RJ, Chidlow G, Ebnetter A, Wood JP, Crowston J, Goldberg I. Translational neuroprotection research in glaucoma: a review of definitions and principles. *Clin Exp Ophthalmol*. 2012;40(4):350-7. doi: 10.1111/j.1442-9071.2011.02563.x, PMID 22697056.
- Cervo L, Rozio M, Ekalle-Soppo CB, Guiso G, Morazzoni P, Caccia S. Role of hyperforin in the antidepressant-like activity of *Hypericum perforatum* extracts. *Psychopharmacology*. 2002;164(4):423-8. doi: 10.1007/s00213-002-1229-5, PMID 12457273.
- Chandrasekaran K, Mehrabian Z, Spinnewyn B, Chinopoulos C, Drieu K, Fiskum G. Neuroprotective effects of bilobalide, a component of *Ginkgo biloba* extract EGB 761[®] in global brain ischemia and in excitotoxicity-induced neuronal death. *Pharmacopsychiatry*. 2003;1;Suppl 1:365SUPPL.
- Choi DW, Koh JY -y. J, Peters S. Pharmacology of glutamate neurotoxicity in cortical cell culture: attenuation by NMDA antagonists. *J Neurosci*. 1988;8:185-96.
- Cyril-Oolutayo CM, Agbedahunsi JM, Elufioye TO, Oladele AT. Ethnomedicinal study and screening of plants used for memory enhancement and antiaging in Sagamu, Nigeria. 2012.
- Dávalos A, Gómez-Cordovés C, Bartolomé B. Extending applicability of the oxygen radical absorbance capacity ORAC-fluorescein assay. *J Agric Food Chem*. 2004;52:148-54.
- Denny Joseph KM, Muralidhara M. Fish oil prophylaxis attenuates rotenone-induced oxidative impairments and mitochondrial dysfunctions in rat brain. *Food Chem Toxicol*. 2012;50(5):1529-37. doi: 10.1016/j.fct.2012.01.020, PMID 22289576.
- Dhawan K, Kumar S, Sharma A. Anti-anxiety studies on extracts of *Passiflora incarnata* Linnaeus. *J Ethnopharmacol*. 2001;78(2-3):165-70. doi: 10.1016/s0378-8741(01)00339-7, PMID 11694362.
- Dhingra D, Parle M, Kulkarni SK. Memory enhancing activity of *Glycyrrhiza glabra* in mice. *J Ethnopharmacol*. 2004;91(2-3):361-5. doi: 10.1016/j.jep.2004.01.016, PMID 15120462.
- Dunnett SB, Björklund A. Prospects for new restorative and neuroprotective treatments in Parkinson's disease. *Nature*. 1999;399(6738):Suppl:A32-9. doi: 10.1038/399a032, PMID 10392578.
- Epstein FH, Lipton SA, Rosenberg PA. Excitatory amino acids as a final common pathway for neurologic disorders. *N Engl J Med*. 1994;330(9):613-22. doi: 10.1056/NEJM199403033300907.
- Feltenstein MW, Lambdin LC, Ganzera M, Dharmaratne HRW, Nanayakkara NPD, Khan IA, et al. Anxiolytic properties of *Piper methysticum* extract samples and fractions in the chick social-separation-stress procedure. *Phytother Res*. 2003;17:3210-6.
- Ge P, Luo Y, Wang H, Ling F. Anti-protein aggregation is a potential target for preventing delayed neuronal death after transient ischemia. *Med Hypotheses*. 2009;73(6):994-5. doi: 10.1016/j.mehy.2008.10.041, PMID 19560879.
- Govindarajan R, Vijayakumar M, Pushpangadan P. Antioxidant approach to disease management and the role of "Rasayana" herbs of Ayurveda. *J Ethnopharmacol*. 2005;99(2):165-78. doi: 10.1016/j.jep.2005.02.035, PMID 15894123.
- Gupta P, Akanksha SKB, Ahmad A, Palit G, Arora A, et al. Anti-stress constituents of *Evolvulus alsinoides*: an ayurvedic crude drug. *Chem Pharm Bull*. 2007;55:771-5.
- Halliwell B. Free radicals, antioxidants, and human disease: curiosity, cause, or consequence? *Lancet*. 1994;344(8924):721-4. doi: 10.1016/s0140-6736(94)92211-x, PMID 7915779.
- Hinz B, Cheremina O. Acetaminophen paracetamol is a selective COX 2 inhibitor in man; 2008.
- Hosseinzadeh H, Parvardeh S. Anticonvulsant effects of thymoquinone, the major constituent of *Nigella sativa* seeds, in mice. *Phytomedicine*. 2004;11(1):56-64. doi: 10.1078/0944-7113-00376, PMID 14971722.
- Hoyer S, Lannert H, Nöldner M, Chatterjee SS. Damaged neuronal energy metabolism and behavior are improved by *Ginkgo biloba* extract EGB 761. *J Neural Transm*. 1999;106(11-12):1171-88. doi: 10.1007/s007020050232.
- Ji MH, Yong JL, So YL, Eun MK, Moon Y, Ha WK, et al. Protective effect of sulforaphane against dopaminergic cell death. *J Pharmacol Exp Ther*. 2007;321:249-56.
- Joseph JA, Shukitt-Hale B, Casadesu G. Reversing the deleterious effects of aging on neuronal communication and behavior: beneficial properties of fruit polyphenolic compounds. *Am J Clin Nutr*. 2005;81(15):3135-6S. doi: 10.1093/ajcn/81.1.313S, PMID 15640496.
- Kasture VS, Deshmukh VK, Chopde CT. Anticonvulsant and behavioral actions of triterpene isolated from *Rubia cordifolia* Linn. *Indian J Exp Biol*. 2000;38(7):675-80. PMID 11215310.
- Kelton MC, Kahn HJ, Conrath CL. The effects of nicotine and caffeine against Parkinson's disease.
- Kim HJ, Moon KD, Oh SY, Kim SP, Lee SR. Ether fraction of methanol extracts of *Gastrodia elata*, a traditional medicinal herb, protects against kainic acid-induced neuronal damage in the mouse hippocampus. *Neurosci Lett*. 2001;314(1-2):65-8. doi: 10.1016/s0304-3940(01)02296-0, PMID 11698148.
- Lee H, Kim YO, Kim H, Kim SY, Noh HS, Kang SS, et al. Flavonoid wogonin from medicinal herb is neuroprotective by inhibiting inflammatory activation of microglia. *FASEB J*. 2003;17:131-21.
- Li W, Lee MK. Antiapoptotic property of human α -synuclein in neuronal cell lines is associated with the inhibition of caspase-3 but not caspase-9 activity. *J Neurochem*. 2005;93(6):1542-50. doi: 10.1111/j.1471-4159.2005.03146.x.
- Liao JF, Hung WY, Chen CF. Anxiolytic-like effects of baicalin and baicalin in the Vogel conflict test in mice. *Eur J Pharmacol*. 2003;464(2-3):141-6. doi: 10.1016/s0014-2999(03)01422-5, PMID 12620506.
- Limpeanchob N, Jaipan S, Rattanakaruna S, Phrompittayarat W, Ingkaninan K. Neuroprotective effect of *Bacopa monniera* on beta-amyloid-induced cell death in primary cortical culture. *Journal of Ethnopharmacology*. 2008;120:1120(1):112-7. doi: 10.1016/j.jep.2008.07.039, PMID 18755259.
- Lin YC, Wu CR, Lin CJ, Hsieh MT. The ameliorating effects of cognition-enhancing Chinese herbs on scopolamine- and MK-801-induced amnesia in rats. *American Journal of Chinese Medicine*. 2003;31(4):543-9. doi: 10.1142/S0192415X03001302, PMID 14587877.
- Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *American Journal of Clinical Nutrition*. 2003;78(3):517S-20S. doi: 10.1093/ajcn/78.3.517S, PMID 12936943.
- Liu SB, Zhang N, Guo YY, Zhao R, Shi TY, Feng SF, et al. G-protein-coupled receptor 30 mediates rapid neuroprotective effects of estrogen via depression of NR2B-containing NMDA receptors. *Journal of Neuroscience*. 2012;32:14(14):4887-900. doi: 10.1523/JNEUROSCI.5828-11.2012, PMID 22492045.
- Liu T, Bitan G. Modulating self-assembly of amyloidogenic proteins as a therapeutic approach for neurodegenerative diseases: strategies and mechanisms. *Chem Med Chem*. 2012;7(3):359-74. doi: 10.1002/cmdc.201100585, PMID 22321314.
- Lu YJ, Zhou J, Zhang SM, Zhang HY, Zheng XX. Inhibitory effects of jujuboside A on EEG and hippocampal glutamate in hyperactive rat. *Journal of Zhejiang University Science B*. 2005;6(4):265-71. doi: 10.1631/jzus.2005.B0265, PMID 15754424.
- Luoma JI, Stern CM, Mermelstein PG. Progesterone inhibition of neuronal calcium signaling underlies aspects of progesterone-mediated neuroprotection. *Journal of Steroid Biochemistry and Molecular Biology*. 2012;131(1-2):30-6. doi: 10.1016/j.jsbmb.2011.11.002, PMID 22101209.
- Mahendra P, Bisht S. Anti-anxiety activity of *Coriandrum sativum* assessed using different experimental anxiety models. *Indian Journal of Pharmacology*. 2011;43(5):574-7. doi: 10.4103/0253-7613.84975, PMID 22022003.
- Matsuoka Y, Picciano M, La Francois J, Duff K. Fibrillar β -amyloid evokes oxidative damage in a transgenic mouse model of Alzheimer's disease. *Neuroscience*. 2001;104(3):609-13. doi: 10.1016/s0306-4522(01)00115-4, PMID 11440793.
- Morris T, Stables M, Hobbs A, de Souza P, Colville-Nash P, Warner T, et al. Effects of low-dose aspirin on acute inflammatory responses in humans. *The Journal of Immunology*. 2009;183(3):2089-96. doi: 10.4049/jimmunol.0900477, PMID 19597002.

50. Nalini K, Aroor AR, Karanth KS, Rao A. Effect of *Centella asiatica* fresh leaf aqueous extract on learning and memory and biogenic amine turnover in albino rats. *Fitoterapia*. 1992;633:232-7.
51. Ohta H, Matsumoto K, Watanabe H, Shimizu M. Involvement of β_1 but not β_2 -adrenergic systems in the antagonizing effect of paeoniflorin on scopolamine-induced deficit in radial maze performance in rats. *The Japanese Journal of Pharmacology*. 1993;622:199-202.
52. Papandreou MA, Kanakis CD, Polissiou MG, Efthimiopoulos S, Cordopatis P, Margarity M, *et al.* Inhibitory activity on amyloid- β aggregation and antioxidant properties of *Crocus sativus* stigmas extract and its crocin constituents. *Journal of Agricultural and Food Chemistry*. 2006;5423(23):8762-8. doi: 10.1021/jf061932a, PMID 17090119.
53. Patel K, Pramanik S. *Sci VPWJ Pharm Pharm*, 2014 undefined. Ayurvedic approach with a prospective to treat and prevent Alzheimers and other cognitive diseases. *Research gate Net*. 2014.
54. Perry NSL, Houghton PJ, Theobald A, Jenner P, Perry EK. *In vitro* Inhibition of Human Erythrocyte acetylcholinesterase by *Salvia lavandulaefolia* Essential Oil and Constituent Terpenes. *Journal of Pharmacy and Pharmacology*. 2010;527:895-902.
55. Prediger RDS, Fernandes MS, Rial D, Wopereis S, Pereira VS, Bosse TS, *et al.* Effects of acute administration of the hydroalcoholic extract of mate tea leaves *Ilex paraguariensis* in animal models of learning and memory. *Journal of Ethnopharmacology*. 2008;1203:465-73.
56. Qian YH, Liu Y, Hu HT, Ren HM, Chen XL, Xu JH. The effects of the total saponin of *Dipsacus asperoides* on the damage of cultured neurons induced by beta-amyloid protein 25-35. *Anatomical Science International / Japanese Association of Anatomists*. 2002;773(3):196-200. doi: 10.1046/j.0022-7722.2002.00029.x, PMID 12422413.
57. Rao VS, Rao A, Karanth KS. Anticonvulsant and neurotoxicity profile of *Nardostachys jatamansi* in rats. *Journal of Ethnopharmacology*. 2005;1023(3):351-6. doi: 10.1016/j.jep.2005.06.031, PMID 16095854.
58. Rivière C, Richard T, Vitrac X, Mérillon JM, Valls J, Monti JP. New polyphenols active on β -amyloid aggregation. *Bioorganic and Medicinal Chemistry Letters*. 2008;182(2):828-31. doi: 10.1016/j.bmcl.2007.11.028, PMID 18042380.
59. Ross GW, Petrovitch H. Current evidence for neuroprotective effects of nicotine and caffeine against Parkinson's disease. *Drugs and Aging*. 2001;18(11):797-806. doi: 10.2165/00002512-200118110-00001, PMID 11772120.
60. Rostom A, Dube C, Wells G, Tugwell P, Welch V, *et al.* 2002 Prevention of NSAID induced gastroduodenal ulcers; 2002.

Cite this article: Halagali P, Singadi R, Arjun HR, Rakshanaa GS, Nair SP, Halagali P, *et al.* Role of Traditional Plant Compounds in the Treatment of Neuropsychiatric Diseases. *Int. J. Pharm. Investigation*. 2024;14(1):48-54.