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VASCULAR DEMENTIA-A PREVENTIVE APPROACH ON HERBAL THERAPY

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ABSTRACT

Vascular dementia is a syndrome usually occur Alzhemer's disease (AD) due to disease in brain, problems with blood circulation result in parts of the brain not receiving enough blood and oxygen. It associate's the impairment of memory, thinking, learning disability, orientation and judgement. Since, the drugs and natural remedies have been

prescribed to enhance the memory and protect the memory functioning in vascular dementia. These are popular all over the world due to their proven effective therapeutic effects. The drugs acting on the brain are called as nootropic drugs. The natural memory enhancing drugs controlled the activity on acetyl cholinesterase (AChE). AChE modulates acetylcholine (ACh) to proper levels by degradation accordingly excessive AChE activity produce to constant Ach deficiency leads to memory and cognitive impairments. These natural agents like *Acorus calamus, Centella asiatica, Clitorea ternatea, Gingko bioloba, Curcuma longa, Withania somnifera, Terminalia chebula, Polygala tenufolia, Rheum spp and Melissa officinalis* inhibit's the excessive AChE activity and protects the people suffering with dementia. This review focuses on medicinal plants as memory enhancing agents play a preventive role on curing the vascular dementia.

KEYWORDS: Alzhemer's disease, Nootropic drugs, Polygala tenufolia, AChE.

INTRODUCTION

Vascular dementia is a syndrome usually occur Alzhemer's disease (AD) due to disease in brain, problems with blood circulation result in parts of the brain not receiving enough blood and oxygen. It associate's the impairment of memory, thinking, learning disability, orientation and judgement. Changes in cognition occurs deterioration in the person's emotional control, social behaviours or motivation and other cognitive changes often include ataxia, agnosia, aphasia, depression, anxiety, agitation, restlessness, apathy and suspicion. Mainly dementia occurs in Alzheimer's disease (AD), Cerebrovascular disease, Lewy body weight disease (LBD), Frontotemporal dementia (FTD), parkinsons disease. The changes in behaviour associated with the level or stage of severity of the dementia is a Clinical Dementia Rating Scale (CDRS).

Vascular dementia occur three stages characterized by severe memory loss, disorientation time and place and inability to make judgements. Vascular dementia occur due to the cerebral ischemia, energy failure, calcium over load, glutamate mediated exitotoxicity, oxidative stress and structural and functional changes.^[1] The herbal drugs promote intelligence and memory enhancing is called Medhya. These drugs related to mind and mind resides in brain and nervous system and inhibition the memory loss.

Now drugs and natural remedies have been prescribed to enhances memories and prevent from memory deficits in the brain for curing the vascular dementia. The herbal drugs acting on the brain are called Nootropic herbs (Nootropic is derived from Greek and means acting on the mind) and their isolated constituents referred as smart drugs. The medicinal plants increase the blood circulation to the brain leads to normal functioning of brain. The medicinal plants affecting on cholinergic neurotransmitter (ACh) related to memory and learning. It will degraded by acetylcholinestrase (AChE) and this inhibited by the natural enhancing drugs.

Several treatments like drug therapy, mental exercises, nutrition mainly drug therapy shows major role in the treatment of vascular dementia. Advanced neuroprotective treatment options cover all of the molecular targets of dementia cascades, interesting, protective effects of cholinergic agents especially AChE inhibitors^[2] on multiple mechanisms energy failure, glutamate mediated exitotoxicity, intracellular death pathway, oxidative stress, calcium overload.

Symptoms

The impact of vascular dementia condition on thinking skills varies widely, depending on the severity of the blood vessel damage and the part of the brain it affects. Memory loss may or may not specific symptom depending on the specific brain areas where blood flow is reduced. Vascular dementia starts the damage that starts in the brain areas that play a major role storing and retrieving information may cause memory loss that is very similar to AD. Multiple small strokes or other conditions that affect blood vessels and nerve fibres deep inside the brain may cause more gradual thinking changes as damage accumulates. Common early signs of widespread small vessel are impaired planning and judgment, uncontrolled laughing, crying, declining ability to pay attention, impaired function in social situations and difficulty finding the right words.

Causes of Dementia

Vascular dementia can have a number of less common causes, some of which are treatable. These include repeated injury to the head, Infections of the brain, such as meningitis or encephalitis, Huntington's disease, a rare genetic condition that causes progressive brain damage^[3] Creutzfeldt-Jakob disease (CJD), a rare and fatal condition that causes damage to the brain and nervous system, underactive thyroid gland, Dehydration, Lack of vitamin B in the diet, Poisoning, for example from lead or pesticides, Having a brain tumor, Certain lung and heart conditions that interrupt the supply of blood and oxygen to the brain. which may dementia^[4] cause vascular along with other features like Alexander disease, Cerebrotendinous xanthomatosis, Canavan disease, DRPLA, Fragile X-associated tremor/ataxia syndrome, Glutaric aciduria type 1, Krabbe's disease, Maple syrup urine disease, Niemann Pick disease type, C kuf's disease, Neuroacanthocytosis, Organic acidemias, Pelizaeus-Merzbacher disease, Urea cycle disorders, Sanfilippo syndrome type B, Spinocerebellar ataxia type-2.

Diagnosis

Proper diagnosis tests between the types of dementia cortical and sub cortical will help identification of disease state, however, there exist some brief tests (5–15 min) that have reasonable reliability and can be used in the office or other setting to screen cognitive status for deficits that are considered as pathological significance. Examples of such tests include the Abbreviated Mental Test Score (AMTS), the Mini Mental State Examination (MMSE),

Modified Mini-Mental State Examination (3MS), the Cognitive Abilities Screening Instrument (CASI), and the clock drawing test.

Other examinations

Many other tests have been studied including the clock-drawing test. However, another approach to screening for vascular dementia is to ask an informant (to fill out a questionnaire about the person's everyday cognitive functioning. And other laboratory tests are include vitamin B12, folic acid, thyroid-stimulating hormone (TSH), C-reactive protein, full blood count, electrolytes, calcium, renal function, and liver enzymes. Abnormalities may suggest vitamin deficiency, infection or other problems that commonly cause confusion or disorientation in the elderly.

Treatment Approches for Dementia

Treatment approaches for vascular dementia have included medical and non-medical interventions, however, there is currently no intervention that can halt or reverse the progression of vascular dementia. Nevertheless, a variety of treatment strategies are aimed at slowing the progression of the disease and maximizing the person's quality of life. Interventions often include a combination of medication, medical, psychological, environmental, behavioral, supportive counseling, and service provision.

Medical Treatment

Medical treatment of dementia involves the use of memory enhancing drugs that slow the onset of vascular dementia.

Acetylcholinestrase inhibitors

These AChE inhibitors include the active compound from the Chinese herb huperzine A, and FDA approved drugs are Tacrine (cognex), Donepezil (Aricept), Galantamine (razadyne), and Rivastigmine (Exelon) are for treatment of dementia induced by the Alzheimer disease.^[5] They may useful for other diseases causing dementia such as Parkinson's or vascular dementia.^[6]

Amyloid deposit inhibitors

Minocycline and Clioquinoline, antibiotics may help reduce amyloid deposits in the brains of persons with Alzheimer disease.^[7]

Antidepressant drugs

Depression is frequently associated with dementia and generally worsens the degree of cognitive and behavioral impairment. Antidepressants effectively treat the cognitive and behavioral symptoms of depression in patient with Alzheimer's disease, but evidence for their use in other forms of dementia is weak.^[8]

Anxiolytic drugs

Many patients with dementia experience anxiety symptoms. Although Benzodiazepines like Diazepam (Valium) have been used for treating anxiety in other situations, they are often avoided because they may increase agitation in persons with dementia and are likely to worsen cognitive problems or too sedating. Buspirone (Buspar) is often initially tried fort mild-to-moderate anxiety. There is little evidence for the effectiveness of benzodiazepines in vascular dementia, whereas there is evidence for the effectiveness of antipsychotics at low doses.^[9] Selegiline, a drug used primarily in the treatment of Parkinson's disease, appears to slow the development of dementia. Selegiline is thought to act as an antioxidant, preventing the free radical damage.^[10]

Antipsychotic drugs

Both typical antipsychotics (such as Haloperidol) and atypical antipsychotics such as (risperidone) increases the risk of death in dementia –associated psychosis.

Preventing vascular dementia

While it is not possible to prevent all cases of vascular dementia, there are some measures that can help prevent vascular dementia, as well as cardiovascular diseases, such as strokes and heart attacks. As experts in treating dementia often say, 'What is good for your heart is also good for your head'.^[11] The best ways to prevent vascular dementia are eat a healthy diet, maintain a healthy weight, Get sufficient and regular exercise, Drink alcohol in moderation and don't smoke.

In psychological treatments the individual with dementia is encouraged to take part with others in activities, for example, reminiscence, reality orientation. These interventions are believed to improve cognitive function, mood and behavior although the changes may be short term and may or may not prove to have any lasting consequences as the disease progresses. And supportive counseling, proper environmental conditions, physical supplements, orientation, exercise therapy these are help to reducing the dementia patients.

Herbal therapy

Despite of all the advances in modern and orthodox medicine, traditional medicine still plays a significant role in the lives of many people suffering with vascular dementia. A number of medicinal plants such as *Acorus calamus*, *Centella asiatica*, *Clitorea ternatea*, *Gingko bioloba*, *Curcuma longa*, *Withania somnifera*, *Terminalia chebula*, *Polygala tenulfolia*, *Rheum spp*, *Melissa officinalis*, *Angelica archangelica*, *Codonopsis piolosula*, *Salvia lavendulaefolia*, *Bacopa monniera*, *Biota orientalis*, *Celastrus paniculatus*, *Evodia rutaecarpa*, *Coptis chinensis*, *Crocus sativus*, *Hypericum perforatum*, *Magnolia officinalis*, *Piper methysticum and Convolulus pluricaulis*, *Rosa Alba*, *Tinospora Cordifolia*, *Zingiber Officinale*, *Sesamum Indicum*, *Emblica Officinalis*, *Panax Ginseng*, *Lipidium Meyenii*, *Commiphora whighitti and Ilex Paraguariensis*.

Acorus calamus

Acorus Calamus (Sweet flag) (Araceae) posses significant memory enhancing action on memory impairment, learning performance, behaviour modifying. It inhibits the acetylcholinesterase (AChE). Acorus Calamus contains majorly α -and β -asarone. The rhizomes of Acorus Calamus are used in loss of memory given in combination with other drugs like Centella Asiatica, Bacopa Monniera and Rauwolfia serpentine.^[12] Acorus Calamus also shows anti inflammatory anti oxidant, anti spasmodic, cardiovascular hypolipidemic, immuno suppressive, cytoprotective anti diarrheal, anti microbial anthelmintic activities.^[13]

Angelica archangelica

Angelica archangelica (Umbelliferae) it is a perennial herbaceous plant used to traditional Chinese medicine for the treatment of cerebral diseases. It shows significant memory enhancing property on various animal models.

Bacopa monniera

Bacopa monniera Linn. (Scrophulauraceae)(Brahmi) has been used as nerve tonic for Improvement of memory. The chemical constituent responsible for the effect of becoposides learning schedules was identified as a mixture of two saponins designated as bacosides A and B. They also enhanced protein kinase activity and produced an Increase in protein in hippocampus. Bacosides were also found to be safe in regulatory pharmacological and toxicological studies.^[14]

Biota orientalis

Biota orientalis belongs to family Coniferae is an evergreen tree that grows mainly in south East Asia. The seeds of the plant have been used in the treatment of vascular dementia, insomnia, and amnesia. The plant extract shows significant action against memory dysfunction.^[15]

Centella asiatica

Centella Asiatica (Umbelliferae) commonly known as Mandookaparni is widely available India. It shows memory enhancing property on treating vascular dementia. It inhibits the memory impairment induced by scopolamine through the inhibition^[16] of AChE. *Centella Asiatica* contains glycosides asiaticosides, centoic acid fatty oils, linolic, lignoceric, palmitic and stearic acid. Vellarine, pectic acids are present in the leaves and roots, and also contain as ascorbic acid. It is a brain tonic, and as an antioxidant capable of treating amnesia and having property for improving memory.^[17]

Clitorea ternatea

Clitorea ternatea (Leguminaceae) plant commonly known as butterfly–pea is a persistence herbaceous perennial legume. The rhizome has been used as a brain tonic and is reported to promote memory and intellect. The ethanolic extracts of the rhizome and aerial parts shows significant memory enhancing effects invivo. These effects were associated with increased levels of Acetyl cholinesterase invivo.^[18]

Curcuma longa

Curcuma longa belongs to family Zingiberaceae commonly known as turmeric have been used for the culinary properties in Indian curries and used as remeady against ageing. An aqueous extract of the rhizome demonstrated antidepressant activity in mice following oral administration which is associated with inhibition of brain MAO type A. Antidepressant activity is of significant importance in the management of AD.^[19]

Celastrus paniculatus

Celastrus paniculatus Willd. (Celastraceae) is used for learning and memory. In elevated plus maze model, Celastrus paniculatus extract has showed statistically significant improvement in memory process. The estimation of acetylcholinesterase enzyme in rat brain supports the plus maze and passive avoidance test by reducing acetylcholinesterase activity which helps in memory performance.

Crocus sativus

Crocus sativus belongs to family Iiridaceae commonly known as saffron crocus. Saffron is produced from the flowers. It contains carotenoids, xeazanthin, beta carotenes, and also cheif active constituent such as crocin, crocetin. The plant is used in the treatment of nervous disorders. An alcohol extract of crocus improved the ethanol induced impairment of learning and behaviour in mice. This may have been achieved by impairment of hippocampal synaptic plasticity^[20]

Commiphora whighitti

Commiphora whighitti (Burseraceae) shows potential cognitive enhancer for improvement memory in scopolamine induced memory deficits.^[21] Experimental studies have shown that cholesterol-fed wild type rabbits develop brain pathology similar to Alzheimer's disease, which is supported by human studies, showing that statin therapy reduces the risk of Alzheimer's disease.^[22] However it shows maximum effects on memory functions and potential for dementia disorder. The *Commiphora whighitti* acting on impairment in learning and memory and decreased choline actyl transferase levels in hippocampus.^[23]

Evodia rutaecarpa

Evodia rutaecarpa (Rutaceae) is a deciduous small tree that is used in treatment of vascular dementia due to the prevention of free radical formation by reducing the oxidative stress by antioxidant property. Dichloromethane extract of *Evodia rutaecarpa* strongly inhibited AchE in vitro and reversed scopolamine induced memory impairment in rats.^[24]

Emblica Officinalis

Emblica Officinalis (Euphorbiaceae) posses memory enhancing action on improvement in memory in scopolamine and diazepam induced memory deficits. *Emblica Officinalis* inhibits the AChE activity. Amla contains major active constituents of vit-C, phyllemblin, Due to vit-C the amla posses the beneficial effects such as, memory improving property, and cholesterol lowering property and anti cholinesterase activity.^[25]

Evolvulus alsinoidesl

Evolvulus Alsinoides L (Convolvulaceae) is used as noortopic or brain tonic in traditional systems of medicines. It is a potential memory enhancing agent used in treating vascular dementia.^{[26],[27]} It contains alkaloids such as betaine, sankhapushpine and evolvine,

scopoletis, scopolin, umbelliferone, 6-methory-7-0-β-glucophyranoside coumarin queretine-3-o-β-glucophyrenoside are reported It shows significant Immune-modulatory activity.^[28]

Ficus religiosa

Ficus religiosa Linn. (Moraceae) is a variety of fig tree. Its figs are known to contain a high serotonergic content, and modulation of serotonergic neurotransmission plays a crucial role in the pathogenesis of amnesia and also used in improvement of memory.^[29]

Gingko bioloba

Ginkgo Biloba (Ginkgoaceae) is also known as maiden hair tree, kew tree, ginkyo, yinhsing. The herb shows memory enhancing action by increase the supply of oxygen, and helps the body to eliminate free radicals thereby improving memory. These constituents include terpenoids bilobolide, ginkgolides, flavanoids (Kaemferal, quercetin, isorhamneting, steroids (sitosterol and stigmasterol) and organic acids (ascorbic, benzoic shikimic and vanillic acid. It shows prevention action a corticosterone produce neuronal atrophy and cell death in the hippocampus.^[30] The Hippocampus corticosterone impairs GABA-mediated inhibitory neurotransmission and causes neurodegeneration, these can be prevention by *Ginkgo Biloba*^[31], neuroprotective effects and enhances long term potentiation.

Glycyrrhiza glabra

The roots and rhizomes of *Glycyrrhiza Glabra* (Leguminaceae) is an efficient brain tonic it increases the circulation into the CNS system and balance the sugar levels in the blood significant action an memory enhancing activity as dementia disorder.^[32] Liquorice shows significantly improved learning and memory on scopolamine induced vascular dementia. The protective effect of liquorice extract may be attributed to its antioxidant property by virtue of which susceptible brain cells get exposed to less oxidative stress resulting in reduced brain damage and improved neuronal function thereby enhancing the memory.

Hypericum perforatum

Hypericum perforatum (Clusiaceae) St. John's wort extract is commonly used as a wound healing, anti-inflammatory, anxiolytic, diuretic, antibiotic, antiviral and cancer chemoprotective agent. It also has nootropic and antiamnestic effects that single administration of St. John's wort extract (500 mg/kg) caused PPI disruption in rats. The effect of antiamnestic doses of the extract on PPI has not been investigated despite the coexistence of impaired memory and PPI deficit in some neurological disorders.

Ilex Paraguariensis

Ilex Paraguariensis Yebra mate tea (mate) leaves (Aquifoliaceae). It is an ingredient in the food and dietary supplement industries^[33], *Ilex Paraguariensis* having memory enhancement properties to treat vascular dementia. It is inducing social recognition ability on facilitation of adenosine receptors. The scientific literature has reported that mate tea is hypocholestremic, hepatoprotective and stimulant of central nervous system.^[34] These mate tea leaves contain two active principles are polyphenols (chlorogenic acid) and xanthines (caffeine, theophylline, and theobromine) other flavanoids (quercetin, kaemferol) and vitamins C, B₁ and B₁₂.^[35] The leaves are reported memory enhancing activity on dementia on different models is spontaneous locomotor activity, social recognition task and inhibitory avoidance task methods.^[36]

Lipidium Meyenii

Lipidium Meyenii Walp (Brassicaceae), known as Maca. It shows beneficial improves an memory and learning. It shows memory enhancing property on memory impairment is vascular dementia patients.^[37] It is acting on cholinergic dysfunction mainly neurotransmitter (ACh) related to memory and learning. It will degraded by AChE and this inhibited by this memory enhancing agent.^[38] Bleck Maca a male mice with memory impairment induced by scopolamine using water morris maze^[39] and step-down avoidance test.

Melissa officinalis

Melissa officinalis is belongs to family Lamiaceae commonly known as lemon balm. It is a perennial herb native to West Asia. It has been used in the European system of medicine. The volatile oil has been reported to possess in vitro AChE inhibitory activity. A hydro alcoholic leaf extracts was effective in improving cognitive functions in mild to moderate AD patients.^[40]

Magnolia officinalis

The bark of *Magnolia Officinalis* (Magnoliaceae) used as a traditional memory enhancing agent in Chinese medicine for the treatment of neurosis, anxiety, stroke, dementia, *Magnolia Officinalis* inhibit the memory impairment induced by scopolamine through the inhibition of AChE. Magnolia officinalis contained 4-0-methyl honokiol, honokiol and magnolol.^[41] Magnolol and honokiol shows anti inflammatory, anti bacterial, anti allergic activities, and treatment of neurosis, anxiety, stroke, fever and headache.^[42] Honokiol was promote a potassium-induced release of acetylcholine in a rat hippocampus slice.^[43]

Polygala tenulfolia

The cognition-enhancing activity and underlying mechanisms of a triterpenoid saponin (polygalasaponin XXXII, PGS32) is isolated from the roots of *Polygala tenuifolia* Willd. The Morris water maze was used to evaluate the spatial learning and memory. It improves hippocampus-dependent learning and memory, possibly through improvement of synaptic transmission.

Panax Ginseng

Panax Ginseng (Araliaceae) saponins having memory enhancing action the learning impairment induced by scopolamine. *Panax Ginseng* contain saponins protopanaxdiol, protopantriol and oleanolic acid saponins improves the scopolamine induced learning disability and spatial working^[44], Ginseng root improves learning ability in animals.^[45] A component of ginseng saponin, improves the cyproheptadine-induced recognition deficits in rats.^[46]

Piper methysticum

Piper methysticum belongs to family Piperaceae, commonly known as kava is a perennial shrub that has been used in Polynesia, melanasia and Micronesia occupies in preparation of a drink to be consumed for the social purposes. The rhizome extract elevated the mood and enhanced cognition performance.

Rosa Alba

Rosa Alba (Rosaceae) shows significant memory enhancing property. It produces symptomatic improvement in learning and memory *Rosa Alba* might proven to be a useful memory restorative agent in the treatment of cognitive disorders. It is reported the effects on cognitive functions learning and memory by using elevated plus-maze and passive-avoidance test. It inhibits cholinesterase and improves the memory power.^[47]

Salvia lavendulaefolia

Salvia Lavandulaefolia (Spansih sage) (Laminaceae) is beneficial effects on memory disorders, depression and cerebral ischemia, anti cholinesterase activity^[48] (helps the supplementation of ACh. It enhances the memory power Salvia Lavandulaefolia produced significant effects on cognition.^[49] Salvia majorly contains essential oils, 1, 8-cineole, linalool, α -and β -pinene, carvacrol, luteolin. Salvia Lavandulaefolia has been reported to be

antioxidant.^[50] Salvia Lavandulaefolia inhibits the acetylcholinesterase and improvement of memory in dementia.

Sesamum Indicum

Sesamum Indicum (Pedaliaceae) is an herb. It shows significant memory enhancing property to treat vascular dementia. *Sesamum Indicum* as a brain tonic, cognition, recalling of thoughts and as an antioxidant capable of treating amnesia and having property for improving memory, It contains major active constituents protein, carbohydrates, vitamins, riboflavin, nicotinic acid, pantothenic acid and ascorbic acid. Sesame oil is rich in oleic and linolic acids. Mainly two constituents are sesamin and sesamolin, sesamum oil having the antioxidant activity.^[51] *Sesamum Indicum* acting on hypoxia induces a reduction of memory and judgement that is associated with a decrease in acetylcholine synthesis.^[52]

Terminalia chebula

Terminalia chebula (Combretaceae) is a ripe fruit which is used in the ayurvedic formulations for the treatment of various diseases. It is found throughout south East Asia countries. A number of glycosides have been isolated from haritaki including triterpenes arjunolic acid, arjunoglucoside, arjungenin. It is reported to enhance the memory and promote longevity.^[53]

Tinospora Cordifolia

Tinospora Cordifolia (GULVEL) (Menispermaceae) possesses memory enhancing property on learning and memory in normal and memory deficits animals. *Tinospora Cordifolia* mechanism of cognitive enhancement by immunostimulation and increasing the synthesis of acetylcholine, this supplementation of choline enhances the cognitive function.^[54]

Withania somnifera

Withania somnifera (Solanaceae), popularly known as Ashwagandha is widely considered as the Indian ginseng. In Ayurveda, it is used to promote physical and mental health, rejuvenate the body in debilitated conditions and increase longevity. The use of *Withania somnifera* in various central nervous system(CNS) disorder, neurodegenerative diseases such as Parkinson's and Alzheimer's disorders, cerebral ischemia, and even in the management of drug addiction.

Zingiber Officinale

Zingiber Officinale (Zingiberaccae) rhizomes posses potent memory enhance in scopolamine inducing memory impairment by significantly increased whole brain acetyl cholinesterase inhibition activity. Zingiber Officinale significantly improved learning and memory.^[55] Zingiber Officinale contains major active constituents are gingerin, gingerol, shogaol and zingerone. The rhizomes implicated in the treatment of cardiac diseases, piles, colic, asthma, diseases of kapha, vata and pitta.^[56] It also reported to posses anti-obesity enhances teach a morrison water maze.^[57] And inhibits the β -amyloid peptide-accumulation, thus useful delaying the onset and progression of neurodegenerative disorders.

CONCLUSION

The review focuses on several natural memory enhancing agents acting on vascular dementia. Vascular dementia is a syndrome usually occur Alzhemer's disease (AD) due to disease in brain, problems with blood circulation result in parts of the brain not receiving enough blood and oxygen. It associate's the impairment of memory, thinking, learning disability, orientation and judgement. These memory enhancing agents showed potential acting on cognitive functions by maintaining the Acetyl choline (Ach) level in the brain. In that *Acorus calamus, Centella asiatica, Clitorea ternatea, Gingko bioloba,* etc. Which is today popular all over the world due to their proven effective qualities for treating vascular dementia. Several medicinal plants used in ayurvedic polyherbal formulations for curing the vascular dementia, and so many medicinal plants showing the preventive role on memory deficits under several researcher studies in the current trend.

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