

**REVIEW ON EFFECT OF NATURAL MEMORY ENHANCING DRUGS ON DEMENTIA*****K.Yalla Reddy, ¹S. Mohana Lakshmi, ¹A. Saravana Kumar****^{*1}Sree Vidyanikethan College of Pharmacy, Tirupati, Andhra Pradesh, India-517102.****ABSTRACT**

Dementia is a syndrome usually occur Alzheimer's disease (AD) and vascular dementia (VD) due to disease in brain. It associate's the impairment of memory, thinking, learning disability, orientation and judgement. These changes effects on cognition functions to decline earlier function of learning and memory. Since, the drugs and natural remedies have been prescribed to enhance the memory and protects the memory functioning in dementia people. Which are today popular all over the world due to their proven effective qualities. The drugs acting on the brain are called as nootropic drugs. The natural memory enhancing drugs controlled the activity of acetylcholinesterase (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 inhibit's the excessive AChE activity and protects the people suffering with dementia. This review focuses on natural herbal drugs as memory enhancing agents on curing the dementia.

KEYWORDS: Memory, Enhancers, Dementia, Herbs, AChE activity.

INTRODUCTION

Dementia is syndrome or set of symptoms and signs occur at the same time is due to a disease in the brain. It is progressive impairment of memory, thinking, orientation, learning capacity, language and judgments. Changes in cognition occurs deterioration in the person's emotional control, social behaviors or motivation and other cognitive changes often include apraxia, 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) developed by Berg and published in 1988. Dementia occurs three stages characterized by severe memory loss, disorientation time and place and inability to make judgements.

Dementia occur due to the cerebral ischemia ,energy failure, calcium over load, glutamate mediated exitotoxicity, oxidative stress and structural and functional changes (Juan Wang *et al.*, 2009). The herbs that promote intelligence and memory enhancing are called Medhya. These memories enhancing agents action 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 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 refered as smart drugs. Memory enhancer herbs enhance the memory and increase the blood circulation in the brain. The drugs acting on cholinergic dysfunction mainly neurotransmitter (ACh) related to memory and learning. It will degraded by acetylcholinestrace (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 dementia. Current neuroprotective treatment options cover all of the molecular targets of

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dementia cascades. Protective effects of cholinergic agents especially AChE inhibitors (Juan wang *et al.*, 2009) on multiple mechanisms energy failure, glutamate mediated excitotoxicity, intracellular death pathway, oxidative stress, calcium overload.

The following list of the most effective herbs used in memory enhancement activity on dementia are evaluated by the researchers.

ILEX PARAGUARIENSIS (AQUIFOLIACEAE)

Ilex Paraguariensis Yebra mate tea (mate) leaves (Aquifoliaceae). It is an ingredient in the food and dietary supplement industries (Heck and De Meja, 2007), *Ilex Paraguariensis* having memory enhancement properties to treat dementia. It inducing social recognition ability on facilitation of adenosine receptors. The scientific literature has reported that mate tea is hypocholesteremic, hepatoprotective (Filip and Ferraro, 2003) and stimulant of central nervous system (Mazzafera, 1997). 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 (Pomilio *et al.*, 2002). The ilex leaves are reported memory enhancing activity on dementia on different models are spontaneous locomotor activity, social recognition task and inhibitory avoidance task methods (Rui Prediger *et al.*, 2002). The use of mate tea for improvement of cognition modulates short and long term learning and memory in animals on antagonistic action on adenosine receptors.

COMMIPHORA WHIGHITTI (BURSERACEAE)

Commiphora whighitti (Burseraceae) plant resin contain major constituent of guggulipid is goguuisterone. The guggulipid shows potential cognitive enhancer for improvement memory in scopolamine induced memory deficits (Gunjan saxena *et al.*, 2007). The gum resin exudates of commiphora whighitti tree used in ayurvedic medicine for more than 2000 years to treat a variety of ailments like obesity, lipid disorders, rheumatoid arthritis (Dev, 1987). Experimental studies with extracts and fractions of guggulu demonstrated anti-inflammatory activity (Gujral *et al.*, 1960). 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 (Raja *et al.*, 2004). However commiphora whighitti shows maximum effects on memory functions and potential for dementia disorder. The commiphora whighitti acting on impairment in learning and memory and decreased choline acetyl transferase levels in hippocampus (Lannert and Hoyer, 1998). The effect of guggulipid on learning and memory function on different models passive avoidance and

morris water maze was studied. (Gunjan saxena *et al.*, 2007).

GLYCYRRHIZA GLABRA (FABACEAE)

The roots and rhizomes of *Glycyrrhiza Glabra* (Fabaceae) is an efficient brain tonic it increases the circulation into the CNS system and balance the sugar levels in the blood (permender rathee *et al.*, 2008) significant action an memory enhancing activity as dementia disorder (Dinesh Dhingra *et al.*, 2004) Liquorice shows significantly improved learning and memory on scopolamine induced dementia. The main constituent of *Glycyrrhiza Glabra* is glycyrrhizin. The roots have anti ulcer, expectorant, diuretic, laxative, sedative, antipyretic (Lata *et al.*, 1999), anti microbial and anxiolytic activities (Ambawade *et al.*, 1998). Oxygen free radicals and other products of oxidative metabolism have been shown to neurotoxic (Sayre *et al.*, 1997). 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 there by enhancing the memory (Dinesh Dhingra *et al.*, 2004).

HUPERZIA SQURURUS (LYCOPODIACEAE)

Huperzia Scururus is a fern family (Lycopodiaceae) reported in Argentinean popular medicine as a memory enhancing agent *Huperzia squururus* mainly contain two major constituents hyperzine A and B are lycopodium alkaloids among the compounds with known activity an memory and learning (Zhu and Tang, 1988). It is used mainly as an aphrodisiac. *Huperzia Scururus* mainly acting an intra hippocampal administration an memory retention using step down test. (Vallejo *et al.*, 2007). Many studies have demonstrated the participation of the hippocampus in learning and memory processes. (Bliss and Colin Gridge, 1993).

LEPIDIUM MEYENII (BRASSICACEAE)

Lepidium Meyenii Walp (Brassicaceae), known as Maca. Maca showed to beneficial improves an memory and learning. It shows memory enhancing property on memory impairment is dementia patients. (Julio Rubio *et al.*, 2007) *Lepidium Meyanii* 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. (Wang *et al.*, 2006). Bleck Maca an male mice with memory impairment induced by scopolamine using water morris maze (Morris, 1984) and step-down avoidance test.

PANAX GINSENG (ARALIACEAE)

Panax Ginseng (Araliaceae) saponins having memory enhancing action the learning impairment induced by scopolamine. *Panax Ginseng* contain seponins

protopanaxadiol, protopantriol and oleanolic acid saponins improves the scopolamine induced learning disability and spatial working (Sung-Ha Jin *et al.*, 1998), ginseng root has been used as an East Asian medical herb for treatment of various diseases (Hu, 1977). Ginseng root improves learning ability in animals (Park *et al.*, 1994). A component of ginseng saponin, improves the cyproheptadine-induced recognition deficits in rats (Me and Yu, 1993).

GINKGO BILOBA (GINKGOACEAE)

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 there by improving memory (Permender Rathee *et al.*, 2008). These constituents include terpenoids bilobolide, ginkgolides, flavanoids (Kaemferal, quercetin, isorhamneting, steroids (sitosterol and stigmasterol) and organic acids (ascorbic, benzoic shikimic and vanillic acid. *Ginkgo biloba* shows prevention action on corticosterone produce neuronal atrophy and cell death in the hippocampus (Anna Walesiuk *et al.*, 2007). The Hippocampus corticosterone impairs GABA-mediated inhibitory neurotransmission and causes neurodegeneration, these can be prevention by *Ginkgo Biloba*. (Welzman *et al.*, 1997). *Ginkgo Biloba* also used is antioxidant, free radicals converging antiplatelet (Smith *et al.*, 1996) and neuroprotective effects and enhances long term potentiation. Beneficial actions of the plant against ischemia injury, hypoxia, cerebrovascular and cardiovascular diseases, cognitive deficits and dementia (Kanowski *et al.*, 1996).

EMBLICA OFFICINALIS (EUPHORBIACEAE)

Embllica Officinalis (*Euphorbiaceae*) posses memory enhancing action on improvement in memory in scopolamine and diazepam induced memory deficits. *Embllica Officinalis* inhibits the AChE activity. Amla contains major active constituents of vit-C, phyllembin, Due to vit-C the amla posses the beneficial effects such as, memory improving property, cholesterol lowering property and anti cholinesterase activity. (Mani Vasudevan and Milinol Perle, 2007).

SESAMUM INDICUM (PEDALIACEAE)

Sesamum Indicum in annual herb family (Pedaliaceae). It shows significant memory enhancing property to treat dementia. A method of preparing a synergistic herbal formulation of *Sesamum Indicum* as a brain tonic, cognition, recalling of thoughts and as an antioxidant capable of treating amnesia and having

property for improving memory (Pushpangadan *et al.*, 2004), *Sesamum Indicum* contains major active constituents protein, carbohydrates, vitamins, (Thiamine, Niacin), riboflavin, nicotinic acid, pantothenic acid and ascorbic acid. Sesame oil is rich in oleic and linolic acids. Main two constituents, sesamin and sesamol, sesame oil having the antioxidant activity, sesame seeds are considered emollient, diuretic, lactagogue and nourishing tonic, emmenagogue and cough. Powdered seeds are used in amenorrhoea and dysmenorrhoea (Kirtikar & Basu *et al.*, 1992).

Sesemin and Sesemolin exhibit little antioxidant activity (Wealth of India, 1994). *Sesamum Indicum* acting on hypoxia induces a reduction of memory and judgment that is associated with a decrease in acetylcholine synthesis (Gibson and Duffy, 1981).

MAGNOLIA OFFICINALIS (MAGNOLIACEAE)

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-O-methyl honokiol, honokiol and magnolol (Yong Kyung Lee *et al.*, 2009). Magnolol and honokiol shows anti inflammatory, anti bacterial, anti allergic activities, and treatment of neurosis, anxiety, stroke, fever and headache (Song *et al.*, 2005) Honokiol was promote a potassium-induced release of acetylcholine in a rat hippocampus slice (Tsai *et al.*, 1995), magnolol and honokiol exhibited an AChE inhibitory property, in rat spleen microsomes and human polymorpho nuclear leukocytes (Fukuyama *et al.*, 1992). *Magnolia Officinalis* shows memory enhancing property on memory and learning using water maze and step down avoidance methods (Yong Kyung Lee *et al.*, 2009).

CENTELLA ASIATICA (UMBELLIFERAE)

Centella Asiatica (*Umbelliferae*) commonly known as Mandookaparni is widely available Indian herb has been used for centuries in Indian system of medicine. It shows memory enhancing property on treating dementia. *Centella Asiatica* inhibit the memory impairment induced by scopolamine through the inhibition (Russo *et al.*, 2005) of AChE. *Centella Asiatica* contain 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 posses anti protozoal activity against *E. Histolytica*, (Indian medicinal plant, 2001) (Wealth of India, 1992) *Centella Asiatica* herbal formulation as a brain tonic, cognition, recalling of thoughts and as an antioxidant capable of treating amnesia

and having property for improving memory (Pushpangadam *et al.*, 2004).

ZINGIBER OFFICINALE (ZINGIBERACCAE)

Zingiber Officinale (Zingiberaccae) rhizomes possess potent memory enhance in scopolamine inducing memory impairment by significantly increased whole brain acetyl cholinesterase inhibition activity. *Zingiber Officinale* significantly improved learning and memory (Hanumanthacar Joshi and Milind Parlie, 2006) *Zingiber Officinale* contains major active constituents are gingerin, gingerol, shogaol and zingerone. *Zingiber officinale* rhizomes implicated in the treatment of cardiac diseases, piles, colic, asthma, diseases of kapha, vata and pitta (Yoganarsimhan, 2000). It is reported to possess antioxidant (Masuda *et al.*, 2004), anti hypertensive (Ghayur *et al.*, 2005), analgesic, anti-inflammatory (Young *et al.*, 2005). It also reported to possess anti-obesity enhances learning an morrison water maze (Topic *et al.*, 2002) and inhibits the β -amyloid peptide-accumulation, thus useful delaying the onset and progression of neurodegenerative disorders.

TINOSPORA CORDIFOLIA (MENISPERMACEAE)

Tinospora Cordifolia (GULVEL) (Menispermaceae) possess 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, these supplementation of choline enhances the cognitive function (Ashutosh Agarwal *et al.*, 2002). *Tinospora Cordifolia* also reported to possess anti arthritic, bitter tonic and anti bacterial activity (Bisset Nwai, 1983), diuretic, aphrodisiac activity (Kokate *et al.*, 2004). *Tinospora Cordifolia* enhanced the cognition in normal and cognition deficits animals in behavioural test Hebb William maze and the passive avoidance task.

SALVIA LAVANDULAEOFOLIA (LAMINACEAE)

Salvia Lavandulaefolia (Spansih sage) (Laminaceae) and other salvia special are prominent for their reputed beneficial effects an memory disorders, depression and cerebral ischemia, anti cholinesterase activity (Nicolette Perry *et al.*, 1996) helps the supplementation of ACh. It enhances the memory power *Salvia Lavandulaefolia* produced significant effects on cognition (Nicolette *et al.*, 2003). *Salvia* majorly contains essential oils, 1, 8-cineole, linalool, α - and β -pinene, carvacrol, luteolin. *Salvia Lavandulaefolia* have been reported to be antioxidant (Adam *et al.*, 1998). Anti inflammatory activity can be demonstrated isolated

essential constituents (Bingol and Sener, 1995) *S. Lavandulaefolia* possess oestrogenic activity (Perry *et al.*, 2001) by monoterpenoid geraniol, *Salvia Lavandulaefolia* inhibit the acetylcholinesterase and improvement of memory in dementia (Nicolette Perry *et al.*, 1996).

ACORUS CALAMUS (ARACEAE)

Acorus Calamus (Sweet flag) (*Araceae*) possess beneficial memory enhancing property on memory impairment, learning performance, behaviour modifying. *Acorus Calamus* 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 Serpentina*. (Permender Rathea *et al.*, 2008).

Acorus Calamus also shows anti inflammatory anti oxidant, anti spasmodic, cardiovascular hypolipidemic, immuno suppressive, cytoprotective anti diarrheal, anti microbial anthelmintic activities (Pulok Kumar Mukherjee *et al.*, 2007).

EVOLVULUS ALSINOIDES L (CONVOLVULACEAE)

Evolvulus Alsinoides L (Convolvulaceae) is used as nootropic or brain tonic in traditional systems of medicines. *Evolvulus Alsinoides L* potential memory enhancing agent used in treating dementia (Amritpal Singh, 2008), (Alok Nahate *et al.*, 2009) *Evolvulus Alsinoides L* contains alkaloids betaine, sankhapushpine and evolvine, scopoletin, scopolin, umbelliferone, 6-methoxy-7-O- β -glucopyranoside coumarin queretone-3-O- β -glucopyrenoside are reported (Gupta *et al.*, 2007). *Evolvulus Alsinoides L* possess anti bacterial and anthel mintic (Dash *et al.*, 2002) anti ulcer and anti catatonic activity (Purohit *et al.*, 1996), immunomodulatory activity (Ganju *et al.*, 2003).

ROSA ALBA (ROSACEAE)

Rosa Alba (Rosaceae) possess memory enhancing property *Rosa alba* produces symptomatic improvement in learning and memory *Rosa Alba* might proven to be a useful memory restorative agent in the treatment of cognitive disorders. *Rosa alba* reported the effects on cognitive functions learning and memory by using elevated plus-maze and passive-avoidance test. *Rosa alba* inhibits cholinesterase and improves the memory power (Nilofar Naikwade *et al.*, 2009) *Rosa Alba* also used in leprosy, biliousness burning sensation, appetite, cold, headache, bronchitis, ophthalmia, rheumatism and its perfume is a tonic for the brain and the heart (Zimmerman, 1983).

Conclusion

The review focuses on several natural memory enhancing agents acting on dementia. Dementia is syndrome usually occurs impairment on memory, thinking, 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 *Centella Asiatica*, *Tinospora Cordata*, *Glycyrrhiza Glabra*, *Rosa*

Album, *Zingiber Officinalis*, *Ginkgo Biloba*, *Panax Ginseng* etc. Which are today popular all over the world due to their proven effective qualities for treating dementia. Several medicinal plants used in ayurvedic polyherbal formulations for curing the dementia. And so many medicinal plants showing the memory enhancing property under several researcher studies in the current trend.

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