Role of Ayurvedic plants in prevention and management of Senile Dementia of Alzheimer's type: A Review

Padmini Mishra[1], Aruna Agrawal[2], Suresh Purohit[3], G.P. Dubey[4]
[1,2]*Research fellow collaborative program, Faculty of Ayurveda, Institute of Medical Sciences, B.H.U. Varanasi (U.P) 221005, India*
[3]*Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, 221 005, India*

Abstract **- Senile dementia is one of the age associated, irreversible, mental problem characteristic symptoms of various neurodegenerative diseases. It is considered as the most common form of dementia and it is observed that people over the age of 70 years suffers from a significant memory loss. It includes forgetfulness, difficulty in performing routine task, acetylcholine deficiency and inflammation of brain tissue. Although there is no cure for Alzheimer's disease but drugs are designed to delay the progression of disease. Various biomarkers has been well established which diagnose the Alzheimer's disease. Medicinal plants have been used for the development of drugs, almost 100 new products are already in clinical development. This review gathers various medicinal plants and their constituents, have been used in traditional system of medicine for treatment of cognitive impairment. Plants such as curcuma longa, bacopa monneri, hippophae rhamnoides, centella asiatica and ginkgo biloba are used in the prevention and treatment of Alzheimer's disease and various biomarkers are also discussed.**

Index Terms **- Alzheimer's disease, senile dementia, amyloid peptide, antioxidant activity, anti-inflammatory, loss of memory.**

INTRODUCTION

Alzheimer's disease (AD) which is considered as one of the most important neuro-degenerative diseases is also characterized by progressive cognitive deterioration along with decline in the activities of routine life leading to neurophysicatric symptoms or abnormal behaviour [1]. The principle cause of dementia is the degenerative condition of neuronal cells known as Alzheimer's disease. When it affects people under 65 years it is termed as pre –senile dementia. The second most common cause of vascular disease of brain is termed as multi-infract dementia. In the past, it was termed as arteriosclerotic dementia. However, AD is the most common type of pre-senile and senile dementia [2]. It is the major cause of dementia in later life and is characterized by severe, progressive problems in moving newly learned information into long term memory [3-4]. It also includes a pattern of forgetfulness, short attention span difficulty in performing routine task, language the problems, disorientation, poor judgement problem with thinking, misplacing things, depression, irritability, paranoia, hostility and lack of initiative. Various studies suggests that persons with mild cognitive impairment are at increased risk for progressing to AD [5]. The disease result in progressive loss of memory and gradually patients lose the ability to function and to take care of themselves [6-7] because of ageing brain cells become in efficient for glucose intake and mitochondrial energy production. This allows for the buildup of cellular debris, eventually destroying neuronal cells and causing age related cognitive decline. Nutrients that restore energy and their production may therefore, help to prevent or control brain ageing.

SENILE DEMENTIA

Senile dementia is the mental deterioration (loss of intellectual ability) that is associated with old age. Two major types of senile dementia are identified: those due to generalized "atrophy" (Alzheimer's –type dementia) and those due to vascular problems (mainly, strokes). Senile dementia is often used when referring to Alzheimer's disease.

In senile dementia there is the loss of neurons in the locus coeruleus. White matter changes in brains from

patients with dementia. There is reduction in the level of acetylcholine due to increase in the activity of acetyl cholinesterase (AChE). The activity of dopamine (DA), noradrenalin (NA) and 5-hydroxytryptamine (5-HT) system also reduces. The active amines decreases while the end metabolites decreases to lesser extent or normal. The level of active amines reflects the number of neurons, while the levels of end metabolites shows the rate of turnover in the system. 3 –Methoxy-4-hydroxyphenylglycol (MHPG) increases above normal levels. This indicates an increase in the rate of turnover in the NA system. Monoamine oxidase increases in advanced age, which further increases in patients with AD and SD. This is assumed that enzyme localizes in extra neuronal tissue, and increase reflects gliosis. In brains from patients with AD and SD neuropeptides are studied. Only somatostatin and substance P however, seems to reduce, which indicates selective damage of neuropeptides.

STAGES OF ALZHEIMER'S DISEASES

Stage 1- No impairment- memory and cognitive abilities appear normal.

Stage 2- Minimal impairment/normal forgetfulness-memory lapses and changes in thinking are rarely detected by friends, family or medical personnel; about half of all people over 65 begin noticing problem in concentration and word recall.

Stage 3- Early confusional/mild cognitive impairment. While subtle difficulties begin to impact function, the person may consciously or subconsciously try to cover up his or her problems. Difficulty with reverting words, planning, organization, misplacing objects and forgetting recent learning, which can affect life at home and work. Depression and other changes in can also occur. Duration: 2 to 7 years.

Stage 4- Late confusional/mild Alzheimer's. Problems handling finances result from mathematical challenges. Recent events and conversations are increasingly forgotten, although most people in this stage still know themselves and their family. Problems carrying out sequential takes, including cooking, driving, ordering food at restaurants, and shopping. Often withdraw from social situations, becomes defensive, and deny problems. Accurate diagnosis of Alzheimer's disease is possible at this stage. Lasts roughly 2 years.

Stage 5- Early Dementia / Moderate Alzheimer's disease. Decline is more severe and requires assistance. No longer able to manage independently or recall personal history and contact information. Frequently disoriented regarding place Stage 5- Early Dementia / Moderate Alzheimer's disease. People in this stage experience a severe decline in numerical abilities and judgment skills, which can leave them vulnerable to scams and at risk from safety issues. Basic daily living tasks like eating and dressing require increased supervision. Duration: an average of 1.5 years.

Stage 6- Middle Dementia / moderately Severe Alzheimer's disease. Total lack of awareness of present events and inability to accurately remember the past. People in this stage progressively lose the ability to take care of daily living activities like dressing, toileting, and eating but are still able to respond to nonverbal stimuli and communicate pleasure and pain via behavior. Agitation and hallucinations often show up in the late afternoon or evening. Dramatic personality changes such as wandering or suspicion of family members are common. many cannot remember close family members, but know they are familiar. Lasts approximately 2.5 years.

Stage 7- Late or Severe Dementia and Failure to Thrive. In this final stage, speech becomes severely limited, as well as the ability to walk or sit. Total support around the clock is needed for all functions of daily living and care. Duration is impacted by quality of care and average length is 1 to 2.5 years.

At an anatomical level Alzheimer's disease is characterized by gross diffuse atrophy of brain and loss of neurons, neuronal processes and synopses in cerebral cortex and certain sub –cortical regions. This results in gross atrophy of affected regions, including degeneration in temporal lobe, parietal lobe, parts of frontal lobe and cingulated gyros [8]. Level of neurotransmitter such as acetylcholine, serotonin, nor-epinephrine, somatostatin are reduced in neurodegenerative disorder but glutamate levels remain usually elevated [9].The pathological changes and modification are observed in AD, brain tissue and increased levels of both the Amyloid-β (Aβ) peptide, deposited extracellular in diffuse and neuritis plaques, and hyperphosphorylated tau (p-tau), a microtubule assembly protein that accumulates intracellularly as neurofibrillary tangles (nFts) along with loss of neuron

cells and synapses. However, because of the numerous pathogenic factors are associated with progression of AD whereas the synthetic drugs have a low response rate and with limited effect. Frequently, drugs are associated with major side-effects and the chronic toxicity that affect almost every organ system and affect on cognition and behaviour [10].

Recently, the usage of medicinal herbs has supported new alternatives source of anti-Alzheimer's for the treatment of AD and these herbal medicines are potentially beneficial for treating certain neurodegenerative disorder. The use of herbal formulation finds the way of curing AD. Ayurveda declared, more than a few plants of herbal formulation, the so-called 'Madhya' plants, possess such antioxidant, and anxiolytic properties. In Ayurvedic, numerous medicinal plants have been used to treat neurodegenerative diseases such as AD and modify the progress and symptoms of AD. Recently, some ethno-pharmacological techniques have been discovered and used for identifying potential new anti-Alzheimer's drugs from herbal sources and these drugs involve in the improvement of cognitive decline and AD's symptoms [11].

This reviews article was reported the different plants and their active constituents that have been used in traditional Ayurvedic medicine for the management of AD.

Prevalence and incidence In United States more than 4.0 million people over the age of 60 are affected with AD whereas in India its total prevalence is per 1000 people and in future this number is increases four times by 2050. According to World Health Organization (WHO), females (6%) are more affects with AD than male (5%) and its frequency increases to 50% by the age of 80 years [12-13].

RISK FACTORS

The etiological factors of disease ranges from oxidative injures, autoimmune complexes, inflammatory factors platelet aggregations, syntheses and degradation of Amyloid proteins, deficiency neurotransmitters and cerebro-vascular pathology to neuronal degeneration. In population studies, higher dietary intake of fat and calories is found to be associated with increased risk for Alzheimer's disease, whereas high intake of fish oil, rich in omega -3 fatty acids, such as DHA (Docosahexanoic acid) is associated with a decreased risk [14-17]. Amyloid beta is a short peptide, that is an abnormal by product of the transmembrane protein Amyloid precursor protein (APP) whose function is unclear but thought to be involved in neuronal development [18]. The pre-senile are component of proteolytic complex involved in APP processing and degradation [19].

On the other hand, plaques which contain misfolded protein in beta amyloidal form in brain produce clinical signs of Alzheimer's disease and plaques together with neurofibrillary tangles are the prominent pathologic signs of the disease. These features can only be discovered as autopsy and help to confirm the clinical diagnosis. Medications can reduce the symptoms of disease, but they cannot change the course of underlying pathology [20]. Therefore, both Amyloid plaques and neurofibrillary tangles are clearly visible by microscopy in Alzheimer's disease's brain.

Nwmba et al (1991)., had reported the apolipoprotein E (Apo E) is found in brain plaques and neurofibrillary tangles [21], is not only characteristic of Alzheimer's disease, but is also present in healthy brain. The Apo-E gene is inherited as one of three alleles, e2, and e3 and e4 allele conferring increased risk of developing Alzheimer's disease in older adults [22]. A number of epidemiological studies have demonstrated that the frequency of e4 is markedly higher in AD [23-25] whereas the elevated high –density of lipoprotein cholesterol is associated with significantly decreased risk of dementia, independent of Apo-E status and other potential variables suggesting that cholesterol fractions could be involved in both Alzheimer's disease and vascular dementia. The prevalence of Alzheimer's disease increases with the degree of arthrosclerosis. The Rotterdam study has shown that indicators of atherosclerosis of the carotid arteries and presence of atherosclerosis of large vessels of the legs are associated with Alzheimer's disease [26]. A strong interaction between Apo-E, e4 allele and atherosclerosis was observed suggesting that at least one Apo-E, i.e. e4 allele and severe atherosclerosis had nearly 20 times increased risk for Alzheimer's disease [26-27].

Recently, some studies have revealed that mutation in pre-senile -1or pre-senile -2 have been documented in some families. Mutation of pre-senile -1 lead to most aggressive form of familial AD [28]. Evidence from rodent studies suggests that the familial AD mutation

of presenile-1 results in impaired hippocampus dependent learning which is correlated with adult neurogenesis [29)]. Sometimes environmental factors have claimed to increase risk of Alzheimer's including prior head injury, particularly repeated trauma, previous incidents of migraine headaches, exposure to defoliants and low activity adulthood [30-33].

Ageing or oxidative damages in brain, itself cannot be barred, but its senescence can be diminished. It is important to understand that interventions that reduce the risk of developing disease in the first phase but may not alter disease progression after symptoms become apparent. Adults with damaged blood vessels in the brain or atrophy in their temporal lobe are most likely to develop AD. It is known that blood vessel damage in the brain is more likely to occur in patients suffering with high blood pressure, high cholesterol or diabetes. Therefore, prevention of these conditions can lower risk of developing AD as well as heart attack and stroke. Therefore, cause factor of adult AD has not yet been well understood at molecular level. It has been identified as protein misfolding disease due to the accumulation of abnormally folded Amyloid beta protein in the brains of AD patients [34].

Some studies have declared that senile dementia Alzheimer's type was found associated with the decrease in the cerebral cortical levels of several proteins and neurotransmitters, particularly, acetylcholine its synthetic enzyme, choline acetyl transferase (ChAT) and nicotinic cholinergic receptors. Reduction of acetylcholine may be particularly related to degeneration of cholinergic neurons in the nucleus basal is of Meynert and also many areas of cortex as well as reduction in the non-adrenaline levels in brain stem. Early identification of AD provides an opportunity to enhance quality of life and long-term care.

BIOMARKERS

A biomarker is independently evaluated as an indicator of normal biological, pathogenic processes and pharmacological responses to a therapeutic intervention and can differentiate healthy person from diseased one. Therefore, epidemiological research discovering various biomarkers for identification of AD and biomarkers are also involved in the diagnosis of mild to moderate AD. Internationally, these biomarkers have been well-established to diagnose AD in cerebro spinal fluid with ELISAs: β-Amyloid, total tau and phospho-tau-181 [35-36].

Treatment, management and herbal medicine

The administration of medications and monitoring of their effects in the elderly peoples compromise one of the most important and complex aspects of health care. A broad range of modern non-tropic and physic tropic agents are being used to manage the age related cognitive impairment and associated functional disorders. But the long term interventions of such agents have their own limitations due to adverse effect of various biological systems [37]. Age related cognitive decline occur gradually but sudden cognitive decline is not a part of normal ageing. When people develop an illness such as AD mental deteoriation usually happens quickly. In contrast, cognitive performance in elderly normally remains stable over many years, with only slight decline in short-term memory and reaction times (38-40).By transporting fatty acid into mitochondria, the amino acid acetyl –L carnitine with the antioxidant lipoic acid helps reverse mitochondrial breakdown, oxidative damage and memory loss [41-42]. Several clinical trials suggest the acetyl-L carnitine and phosphotidylserine delays the onset of age related cognitive decline and improve overall cognitive function in the elderly subjects [43-44].

The studies have suggested that between antioxidant in-take and age related cognitive decline. Higher blood level of vitamin-c, beta carotene [45] and vitamin –e supplementations accelerated learning and prevent memory deficits associated with oxidative stress [46-48]. Similarly high intake of mono-unsaturated fatty acids and caffeine has been associated with protection against age related cognitive decline [49-50]. Intellectual stimulation, regular physical exercise ,social interaction ,diet with fruits and vegetables and low in saturated fat ,vitamin B ,folic acid ,omega -3,fatty acids, Docosahexaenoic acid, vitamin –E ,all reduce Alzheimer's risk[51-52].

Acetyl cholinesterase inhibitor is important to enhance the activity of cholinergic neurons. AChE inhibitors reduce the rate at which acetylcholine is broken down and hence increase the concentration of AChE in the brain. Acetyl cholinesterase –inhibitors seemed to modestly moderate symptoms but do not alter the course of the underlying process [53].

Currently available medications offer relatively small symptomatic benefit for some patients but do not slow disease progression. Tacrine, donepezil, galantamine and revastigmine drugs generally used for the treatment of Alzheimer's disease, all drugs have doubtful clinical utility, and many side effects [54-55]. The satin has been found to reduce the incidence of Alzheimer's disease and Parkinson's disease by almost 50 percent as reported by researchers from Boston University School of Medicine. Some currently approved drugs such as statins and thiazolidinediones have also been used for the treatment of and prevention of Alzheimer's disease [56].

Plant origin medicines are gaining popularity and are being investigated for a number of disorders, including neurodegenerative disorders like AD. A number of scientific researches have been carried out on medicinal herbs and investigated that possess anti-Alzheimer's activity. Numerous reports have been declared the plants possess anti-inflammatory and antioxidant activities that may be used in the treatment of AD because anti-inflammatory and antioxidant activities of plants reduced the inflammation and aging of neuronal cells of the brain in AD. Medicinal Plants contain natural COX-2 inhibitors that inhibit acetyl choline

Esterase (AChE) and enhances the cholinergic system in the brain may be useful in treating AD.

In Ayurveda, some herbs like Shankhpushpi, Amalaki, Gugguli, Guduchi, Yashtimadhuk, Padma (Nelumbo nucifera), Vacha, Convolvulus pluricaulis, Pancha-Tikta-Ghruta, Musta Arjun, Amalaki, Ashwagandha, Galo Satva, Kutaj etc, are splendid herbs for decline brain neurodegeneration caused by Alzheimer's and boost the brain's ability to function, and therefore, make available steadiness. We have highlighted some of the important plants for their anti-Alzheimer's properties, in our laboratory and elsewhere during the last few years (Table-1).

Table 1 List of medicinal plants used for treatment of senile dementia

Plant	Family	Reference
Bacopa monniera	*Scrophulariaceae*	59
Curcuma longa	*Zingiberaceae*	57,11,58
Ginkgo biloba	*Ginkgoaceae*	59,11
Salvia officinalis	*Lamiaceae*	60
Rosmarinus officinalis	*Lamiaceae*	61
Matricaria recutita	*Asteraceae*	62
Melissa officinalis	*Lamiaceae*	63
Glycyrrhiza glabra	*Fabaceae*	64
Galanthus nivalis L.	*Amaryllidaceae*	65-66
Huperzia serrata	*Lycopodiaceae*	67
Commiphora whighitti	*Burseraceae*	68-69
Lipidium Meyenii Walp	*Brassicaceae*	70
Panax Ginseng	*Araliaceae*	71,11
Acorus calamus	*Araceae*	72
Angelica archangelica	*Umbelliferae*	73
Tinospora cordifolia	*Menispermaceae*	74
Magnolia officinalis	*Magnoliaceae*	74
Collinsonia Canadensis	*Lamiaceae*	75
Bertholettia excelsa	*Lecythidaceae*	76
Urtica dioica	*Clusiaceae*	77,11
Withania somnifera	*Solanaceae*	78

Bacopa Monneri (Brahmi)

Taxonomical classification

Kingdom: plantae

Division: angiospermae

Class: dicotyledonae

Order:lamiales

Family:scrophulariaceae

Genus:bacopa

Species:monniera

In ayurvedic system, brahmi (bacopa monneri) act as a nerve tonic ,diuretic ,and cardiotonic and using in treatment of epilepsy,insomnia ,asthma ,and rheumatism. It contains some bioactive molecules such as saponins and triterpenoid bacosaponins that include bacopasides III to V ,bacosides A and B ,and bacosaponins A,B,C and glycosides include bacopasidesIII to V bacosides A and B ,and bacosaponins A,B,C and glycosides include the jujubogenin bisdesmosides bacosaponins D,E,F, alkaloids, plant sterols, betulic acid ,polyphenols ,and sulphahydryl compounds bacosides A and B, and

bacosaponins A, B,C and glycosides include the jujubogenin bisdesmosides bacopasaponins D, E,F,alkaloids, plant sterols, betulic acid, polyphenols, and sulphahydryl compounds that have antioxidant activity [57]. It inhibited cholinergic degeneration, reversed the depletion of acetylcholine, reduction in choline acetyltransferase activity, and decrease in muscarinic cholinergic receptor binding in the frontal cortex and hippocampus and protected neurons from beta-amyloid-induced cell death by suppressing cellular acetyl cholinesterase activity. Thus, BM improved memory and cognitive function and treat the AD [79].

Mechanism of action

Bacopa has been described as one of most popular medhya drug (noo-tropic agent).Several studies have revealed that this medicinal herb is advocated as a nervine and mental tonic and may be used for the treatment of neurological and mental disorders[80-83].In another recent study conducted in animal model , Bacopa has been shown to decrease whole brain AChE activity which reflects that Bacopa might prove to be useful memory restorative agent in the treatment of Alzheimer's and dementia.[84-85]. A clinical study on human subjects has demonstrated the potential of Bacopa monniera in the treatment of Neuritis.

Centella asiatica(Mandookparni/ Bramhi)

Taxonomical classification

Kingdom:Plantae

Division:Angiospermae

Class:Dicotyledonae

Order:Umbelliferae

Family:Apiaceae

Genus:Centella

Species:asiatica

C.Asiatica is a slender perennial creeper which grows throughout the tropical regions in the world. The leaf, known locally as Gotu Kola,has been used in AM for revitalizing and strengthening nervous function and memory. For example, an Ayurvedic formulation composed of 4 herbs, including C.asiatica is used as a restorative and for the prevention of dementia[86].In TCM ,it is also used to combat physical and mental exhaustion[87-88]. An alcoholic extract of the plant possessed tranquilising and potentially cholinomimetic activities in vivo, which may be due to the presence of the triterpenoid brahminoside[88].Aqueous extract of the whole plant enhanced cognitive function in rats, which was associated with the in vivo antioxidant activity of the extract [94]. An aqueous extracts modulated dopaminergic, serotonic and adrenergic systems in vivo and improved learning and memory[88].

Mechanism of action

Centella asiatica has been demonstrated to possess neuro protective property.[89] The studies have revealed that Centella asiatica has been demonstrated to possess neuro protective property.[89] The studies have revealed that Centella asiatica has ability to prevent cognitive deficits that occur following treatment with Streptozotocin and to protect cholinergic neurons from the toxic effects of aluminium indicating its role in reducing the Alzheimer's disease neuropathy.[89-90] Recent study conducted on transgenic animal model to evaluate the efficacy of Centella asiatica extract (CaE) in the management of A.D. It has shown that CaE can impact the amyloid cascade altering amyloid β pathology in the brains of PSAPP (presenilin 'Swedish' amyloid response that has been implicated in the neurodegenerative changes occurring in Alzheimer's disease.

Nardostachys jatamansi (Jatamansi)

Taxonomical classification

Kingdom: Plantae

(Unranked): Angiosperms

(Unranked): Eudicots

(Unranked):Asterids

Order: Dipsacales

Family:Caprifoliaceae

Genus:Nardostachys

Species: N.jatamansi

In the Ayurvedic system of medicine, the rhizomes and roots of the Jatamansi contain a variety of sesquiterpenes, coumarins and valerian including terpenoids, spirojatamol, nardostachysin, jatamols A and B, and calarenol [91]. Its extract have antioxidant property and significantly improved learning and memory and restoring memory in older individuals as well as in patients with age-associated dementia [92].

Mechanism of action

It is thought to be via MAPK inhibition [93] or preventing pancreatic stellate cell activation (noted with jatamansi in vitro [94]) Which is a common pancratitis treatment target.[95] An increase in heme-oxygenase 1(HO-1) has also been noted.[96]

Protective effects have been noted on the beta-cells of the pancreas, where oral ingestion of Jatamansi prior to stroptozotocin injections significantly protected from diabetes. [97] This was replicated in vitro in response to cytokine damage. Its mechanism is thought to preventing NF-kB downstream of pro-diabetic stressors. [98-99]

Hippophae rhamnoides(sea-buckthorn)

Taxonomical classification

Kingdom: Plantae
Subkingdom: Tracheobionta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Rosidae
Order: Rhamnales
Family: Elaeagnaceae
Genus: Hippophae
Species: rhamnoides

Leaves of Hippophae rhamnoides are equally important in medicinal properties, as they carry some unique flavonoides[100]. Hippophoae rhamnoides is also rich in flavonoid (vitamin P) and contains appreciable amounts of water 2-dimethylaminoethanol (DMAE) may increase the levels of brain neurotransmitter acetylcholine. In one preliminary trial, people with senile dementia were given DMAE supplement. It showed positive behavior changes (. Emerging evidence suggest a possible benefit of DHAE supplementation in people with Alzheimer's disease. Most studies have found people with Alzheimer's disease have lower blood DHEA levels than the normal control [101].

In a preliminary study, people who used antioxidant supplement (vitamin C or vitamin E) had a lower risk of Alzheimer's disease compared with people who did not take antioxidant. Large amount of supplement of vitamin E may slow the progression of Alzheimer's disease . Fruit of Hippophae rhamnoids is quite rich in vitamin C (300-600 mg/100 gm), which is 4-100 times higher than many fruits and vegetables [103-104]. Hippophae rhamnoides is a potent anti-oxidant . In experimental and clinical studies, the anti-oxidant effect of Hippophae rhamnoids is proven. The fruit, seed, and leaves of Hippophae rhamnoids contain an impressive array of antioxidant compound. The leaves are an equally rich source of important antioxidants including beta carotene. Vitamin E, flavonoids, catechins , elagic acid ,ferulic acid [103].

Mechanism of action

Antimicrobial and antitumoral effects, the phenolic compounds of Hippophae rhamnoides have the inhibitory effects against Gram-negative bacteria.[104] 70% Hippophae rhamnoides branches

extract has proven activity against TPA induced tumor . This activity is because of three phenolic compounds such as catechin, galloccatechin and epigallocatechin.[10] Antiulcerogenic effect Hexane extract of Hippophae rhamnoides has activity against indometacin; stress and ethanol induced gastric ulcer.[104] Liver diseases according to Zhao et al Hippophe rhamnoides could be used to protect liver from damage by calcium tetrachloride . Branches extract has proven activity against TPA induced tumor.[104] Liver diseases According tetrachloride. Combining Hippophae rhamnoides juice with antivirus can shorten the normalization time of serum ALT. [105]

Ginkgo Biloba(Ginkgo)

Kingdom: Plantae

Division: Ginkgophyta

Class: Ginkgoopsida

Order: Ginkgoales

Family: Ginkgoaceae

Genus: Ginkgo

Species: biloba

Ginkgo Biloba is a dioceous pernneial tree and is indigenous to East Asia and is used in TCM for improvement of memory loss and release hippocampus in vivo. For improvement of cognitive function, administration of plants extract AD to non AD patients in various randomized, double blind, placebo controlled and multi centre trials. [106]. Ginkgo biloba is a plant extract containing several compounds that may have positive effects on cells within brain and body. Ginkgo biloba is thought to have both anti inflammatory and anti oxidant properties to protect cell membrane and to regulate neurotransmitters function. Ginkgo has been used for centuries in traditional Chinese medicine and currently is being used in Europe to alleviate cognitive symptoms associated with number of neurological conditions.

Mechanism of action

The mechanism of action of ginkgo is believed to be produced by functions as a neuroprotective agent ,an antioxidant ,a free radical scavenger , a membrane stabilizer ,and an inhibitor of platelet –activating factor via the terpene ginkgolide B.[106,107] Other pharmacologic effects include the following : endothelium relaxation mediated by inhibition of 3`,5`-cyclic GMP(guanosine monophosphate) phosphodiesterase[108,109]; inhibition of age –related loss of moscarinergic cholinoceptors and alpha-adrenoreceptors ;and stimulation of choline uptake in hippocampus .[109,110] Ginkgo extract also have been shown to inhibit beta-amyloid deposition.[111]

Curcuma longa (Turmeric)

Taxonomical classification

Kingdom: plantae

Division: magnoliophyta

Class: liliopsida

Subclass: zingiberidae

Order : zingiberales

Family: zingiberaceae

Genus: curcuma

Species: c.longa

Curcuma longa is a rhizomatous herbaceous perennial plant of the ginger family, Zingiberaceae and derived from the rhizome and root. In Asia, it is used as a spice and coloring agent and in traditional medicine. Its active constituents are curcuminoids, including curcumin and it is the principal curcuminoid, responsible for the yellow colour of the turmeric root. Curcuma longa possess anti-inflammatory, anti allergy, antiseptic, antioxidant and antibacterial activity including detoxify the liver, balance cholesterol levels stimulate digestion, and boost immunity and due to their non-steroidal anti-

inflammatory property of turmeric is associated with a reduced risk of AD[112-113].

Mechanism of action

Curcumin appears to: increase the secretion of bile, promote the flow of bile to the intestine, it protect the liver(hepatoprotective effect) and support liver function, raise the level of glutathione in the liver ; stimulate the activity of glutathione S-transferase in the liver ; promote the detoxification of toxic substances ;inhibit blood platelet aggregation ; posses antibiotic properties ;lower the cholesterol level; possess antioxidative properties ;have a catabolic and metabolic effect on fat absorption ;have inflammation –inhibiting properties ; have a fungicidal effect on ,amongst others ,candida albicans.

CONCLUSION

The pharmaceutical company is facing serious challenges to find a lead molecule in neurodegenerative diseases and is becoming extremely expensive, riskier, and critically inefficient. With regard to diet and treatment option Indian system of medicine has gained increasing recognition in recent years. Early development of medicinal plant supplements required only epidemiologic information without an understanding mode of action. The natural product industry has came a long way from when it was considered unnecessary to test medicinal plants and their chemical component prior to use and to the introduction of good manufacturing practice guidelines for the industry. It might be worth pointing out that, while medicinal plants and their products has been prescribed for centuries for neurodegenerative diseases. It provides strong support for herbal therapy for AD. It is hoped that strong knowledge base of medicinal plant and natural product will improve the ease with which medicinal plant products and formulations can be used in drug discovery programme and development process, thereby providing new functional leads for AD and other age associated neurodegenerative diseases.

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