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AN OVERVIEW ON HERBAL MEDICAL ADVANCEMENT FOR DEMENTIA & ALZHEIMER'S DISEASE

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ABSTRACT:

In world of ever growing cognitive complexities and comorbidities the risk of Alzheimer's disease and dementia is on high rise since known. Basic reason behind the rise in the cases is due to greater survival of normal aging population and high level of chronic illness, head injuries and other effects affecting brain functions and working. With my efforts on this article I have tried to reflect a comprehensive yet efficient preview and insights on the matter in context of cognitive, complex, functional, behavioral, social, economic, clinical approaches and pharmacological aspects considering allopathy and herbal advancement as need of new approach for long term benefit against mentioned disease. The behavioral characterization and psychiatric disturbances are now very well explored and rigorous research to fill the gaps is currently going on and herbal advancement and research is currently needed to be more explored as it is a healthier and more preferable method to cure the disease showing long term effectiveness. Along with this more sophisticated diagnosis equipment like MRI, CT scan has somehow ease the process to diagnose the disease. We do have drugs like donzepil to counter this disease but it have side effects and also complete cure through allopathy is somehow not possible. To tackle this problem we have a very perfect option that is usage of herbal medicine like 'brahmi' which can reduce or even cancel out probability of having such disease if individual is consuming the medicine as prescribed the physician and have no side effects at all. Along with this herbal plants like *Eriodictyon californicum* also known as *California yerba santa* contains an active compound *flavanone sterubin* that could treat people with Alzheimer's disease one day.

Keywords: Dementia, Alzheimer's Disease, Yerba Santa, Donzepil, Eriodictyon Californicum

INTRODUCTION:

The primary question should arise while discussing the topic is that "why should we diagnose or treat memory loss diseases like dementia or Alzheimer's disease"[1] and the primary requisite answer is that we have a goal to improve the quality of life not quantity of life[2]. Current treatment can help to improve or maintain the patients's cognitive and functional status and neuropsychotic symptoms[3].

Although memory loss cannot be halted or reversed to where it was prior to their developing Alzheimer's disease, current treatments are able to improve patients' memory to where it was 6–12 months ago[4].

Important elements of the history to investigate the disease include:

- Characterization of onset or offset of the disease or disorder
- Memory loss or memory finding
- Word finding
- Fluctuations in attentions
- Getting lost or drown down in groups or family functions or gatherings
- Problems with reasoning and judgement
- Changes in behavior
- Depression or Anxiety
- Loss of insight
- Reviewing symptoms and past medical history [5]

[Tab .1]Comparison between medical evaluation and dementia evaluation: [6]

Medical Evaluation	Dementia Evaluation
Self-history important	Self-history can be unreliable
Family observations secondary	Family observations critical
Mental status examination can be deferred	Mental status examination critical
Laboratory studies often critical for diagnosis	Most laboratory studies are exclusionary, not diagnostic
Imaging studies may not be needed	Imaging studies critical

Epidemology

Global picture

As WHO suggests that by 2025, about 75% population of estimated 1.2 billion people aged 60 years or above will reside in developing countries. It is also estimated that people living with dementia will be almost double every 20 years to 42.3 million and about double to 82 million in 2045[7].

The rate of growth is highest in developing countries like INDIA, AFRICA, CHINA and various parts of SOUTH ASIA.

As per global burden of disease study of WHO and World Bank, Dementia contributes 4.1% of all (DALYs) I.e. diasability adjusted life years[8].

Prevalence of dementia and Alzheimer's disease in India:

Prevalence rates (PRs) from different regions of India differ widely. The rate may possibly be related to adoption of different methodology, screening instruments, defining criteria, multi ethnicity, and multicultural and environmental factors[9]. The prevalence of dementia of rural population in South India and that in North India showed a widely varying rate from 3.39 to 0.84%, respectively[10]. There are few urban studies from several regions of India showing similar varying rates: From 2.44 to 4.1% in West India, 1.83% in North India, 0.8-1.28% in East India, and 3.6% in South India[11].

[12] Prevalance of Dementia and Alzhimer's disease in India [Tab.2]

Region	Study	Age/gender	Number of subjects	Prevalence rates (%)		Instruments used	Remarks
				All dementia	AD		
South India	Shaji *et al.*, 1996[6]	≥60	2067	3.39	1.31	Screening: MMSE and CAMDEX Confirmation: Clinical and DSM IV	Rural South Indian population in Kerala
		Male	965	2.8	0.73		
		Female	1102	3.54	1.81		
	Rajkumar *et al.*, 1997[7]	≥60	750	3.5		Geriatric Mental State Examination	Rural South Indian population in Madras
	Shaji *et al.*, 2004[8]	>65		3.36			Urban South Indian population
North India	Chandra *et al.*, 1998[9]	≥55	5126	0.84		Screening: Hindi MMSE Confirmation: CDR and DSM IV	Rural North Indian population
		≥65		1.36			
		Male		1.8	0.77		
		Female		1.25	0.46		
	Raina *et al.*, 2010[10]	>60	1856	1.83		MMSE and EASI	Migrated population in Jammu region of J and K
West India	Vas *et al.*, 2001[11]	>40	24,488	0.43	0.25	Sandoz clinical assessment geriatric scale and MMSE for screening. CDR and DSM IV for diagnosis	Urban western Indian population in Mumbai
		≥65		2.44	1.5		
		Male	11,875		0.2		
		Female	12,613		0.3		
	Saldanha *et al.*, 2010[12]	>65	2145	4.1		Community screening instrument	Urban population in Pune
East India	Das *et al.*, 2008[13]	60	5430	0.8	0.38 VaD: 0.33	BMSE and KCB-Kolkata cognitive battery	Urban Kolkata
	Banerjee *et al.*, 2008[14]	≥50	6129	0.62		Screening questionnaire for cognitive dysfunction, KCB-Kolkata cognitive battery	Urban Kolkata
		≥60	2720	0.1.28	0.34		

Dementia sub types and Indian perspective:

From various studies occurred it was observed that percentage case for Alzheimer's disease is considerably high relative to other sub types of dementia[13].

The mean age at presentation in India is about 66.3 years, about one decade younger than in developed countries[14].

*Sub types and possible etiology of dementia from two different clinics from Indian origin. [Tab.3] [15]

	Central India[40]	Western India[12]
No. of cases evaluated	124	194
Age (years)	65.7±4.1	65.10±9.9
Gender (male) (%)	75.8	64.4
Type of dementia (%)		
AD	4.8	45.7
VaD	47.6	22.0
MID	-	15.0
FTD	-	11
Degenerative disease (HD, PD)	4.8	2.4
Alcohol	10.5	2.4
Nutritional including SACD (%)	7.2	1.6
Metabolic (DM-2, Hypo-2, thyrotoxicosis-2) (%)	4.8	-
NPH (%)	2.4	-
Head trauma (%)	-	1.6
Slow virus disease (%)	1.6	-

AD = Alzheimer disease; VaD = Vascular dementia; MID = Mixed dementia; FTD = Frontotemporal dementia; HD = Huntington disease; PD = Parkinson disease; SACD = Subacute combined degeneration; DM = Diabetes mellitus; Hypo = Hypothyroidism; NPH = Normal pressure hydrocephalus

Risk Factors considering dementia in India:

The considerable risk factors of dementia is advancing age, illiteracy, addiction, hypertension, diabetes, poor socioeconomic status, trauma, familial or genetic factors, nutritional factors, and stroke.

Study of elderly rural persons from North India, that the risk factors for cognitive dysfunction not amounting to dementia were nutritional deficiencies and certain common infectious diseases[16].

Nervous degeneration and Neurogenesis of brain in Alzheimer's disease:

Damage to either PNS or CNS leads to loss of neuronal flora of brain, whether from trauma or neuro degenerative disease like dementia or Alzheimer's disease that usually results in disability of nerve cells to transduce and transmit nervous signal and causing loss of function in affected person[17].

However in late late 90s scientists got the idea that not only mammalian body is capable of regenerating the neurons but also mammalian brain also capable of regenerating the brain neurons and the process is termed out to be 'Neurogenesis'[18].

The important aspects in neurogenesis of brain to dementia or Alzheimer's disease is the neurogensis in SGZ I.e. (sub granular zone) in brain lies between the dentate gyrus and the hilum of hippocampus which is associated with learning and memory[19].

It is observed that during adulthood , the development and formation of new neurons is started from neuronal stem cells thus stem cells can only turn into neurons in two regions of brain respectively which are *SVZ i.e.*

(sub ventricular zone) and SGZ i.e. (sub granular zone). Neural stem cells convert in neuroblast then mature with time in above specified zones[20].

The symptoms and course of dementia

In most of the cases, Dementia is a process that progresses with time and show evolving course of stages with span of time.

Symptoms, behavior, working, functionality evolves with course of time [21]. The course of dementia is generally a rough guide for disease because it is relatively based on Alzheimer's disease.

- ***Pre - dementia- mild cognitive impairment***

As early symptoms may subtle and attributable to many cases, there is slight problem to recognize early onset of dementia.

Currently, we have less knowledge to determine exactly how these early symptoms are and unable to differentiate between early symptoms and normal ageing[22].

- ***Early or mild dementia***

'Short term memory loss' is the most common early symptoms of Alzheimer's type dementia. Such persons forget about recent events like where they left keys an hour ago or what did they talked about on last night call or what they did on last weekend[23].

More primitive memories of childhood, adolescence, early adulthood remain unaffected in early stages of dementia but in case of probing some mild deficits will be revealed[23].

Generally memory disturbances are often neglected as age related issue but such cases only come to serious concern when these memory disturbances cause behavioral changes in patients with their family member[23].

Word finding difficulties (Aphasia) is common problem originate with affecting parietal and temporal cortical areas of brain.

Aphasia results in difficulty in finding the correct word for an object or a particular person. There is a general rule with dementia "last in , first out". Generally when dementia progresses the language skills and other acquired skills which are acquired later in life are lost first[24].

Personality and behavior changes are first put down to stress or anxiety or age related issue. Dementia involving frontal part of brain like ventricular, fronto parietal and Alzheimer's are some most prone to this effect or condition.[24]

Depression is also an early feature of dementia.

Acute confusion episodes including symptoms of hallucination, disorientation, hypnosis occurs variably. Walking in dream at night is also a state of this condition.

It is an extension of condition we also feel after awakening from sleep after dreaming and this is known as 'hypnogogic hallucination'[24].

- ***Moderate or middle stage dementia:***

The major feature which distinguish between mild dementia and moderate dementia is the need of a proper assistance and help and allow the person to enjoy the life and surroundings as they were before[25].
Paranoia developing hours to days is normal with case of any acute infection inside.

Language and calculation includes problem arising in naming familiar people and stuffs. "Speech Preservation" is commonly observed in patients in which giving same answer to different question or asking same question even after carer gave the before is seen. Comprehension is also severely affected. Complex commands are misunderstood. Unable to perform simple calculation without pen and paper.

Executive and Intellectual function includes progressive impairment of organisational skill and planning abilities.Judgement and insight about own capacity becomes poor, there is failure to recognise their own limitations.

Self care and functional capacity declines with this stage. Personal hygiene, looks, dressing, cooking, shopping and financial management and social skills become impaired and disturbed.

Activity disturbances includes 'wandering' of person and unable to find way back to home. In moderate dementia, wandering in patient is an absolute behavior.

Aggressive behavior is a complication of hallucination and paranoid delusions causes increased risk factor. This may lead to verbal abuse and irritability to actual violence.[

Sleep disturbances causes disturbances in sleep wake cycle. Sleep patterns progressively deteriorate as the dementia worsen causing poor sleep.

Misinterpretation, illusions and psychosis become prevalent with time and take many forms. It occurs in night when stimulus are less and in unfamiliar surroundings. There is usually a sense of persecution and suspicious feeling. A type of delusion known as "morbid jealousy" .[26]

- ***Severe or late stage dementia:***

This is the severe stage of dementia, there is no resemblance of independent function. Concentration becomes very poor with time and person is very distractible on most of task[27].

Language skills are rapidly lost. Speech becomes increasingly disturbed. Many suffers complete lost of speech (become aphasic)[28].

Executive and intellectual function become increasingly slow and disturbed. Insight to various condition becomes very poor. There is often no recognition of the extent of incapacity and the person may become very angry and distressed about being unable to do things when they want to[28].

Self care and functional capacity is most brutal to dementia patient as the person requiring a carer to do daily stuffs like toilet, bathing, dress or eat and become fully dependent on the carer. Swallowing becomes

problematic in later stage may result in recurrent bouts of pneumonia caused by inhalation of food and stomach acid[28].

Food refusal, uncooperative behavior of patient due to stubborn resistance is very tough to cope up with and leads to death.

What exactly happens in Alzheimer's Disease ?

It is said to be an age related neuro degenerative disorder involving clumping of abnormal beta-amyloid and tau proteins in the brain over many years. This eventually results in a gradually progressive dementia due to neuronal dysfunction and cell death, particularly in the hippo campus, medial, temporal and parietal lobes of the brain[29].

Clinical assessment of dementia and Alzheimer's disease

Neurological examination

In neurological examination the physician test following :-

* Eye speech
* Coordination
* Muscle tone and strength
* Speech
* Sensation [30]

Neurological exam also consists of brain imaging. If examination do not show dementia or Alzheimer but condition or symptoms get worsen by time then again person should have an appointment with doctor[31].

Mental cognitive status tests :

Mental cognitive status testing evaluates memory, thinking and simple problem solving abilities.

Such tests give overall over view of whether a person

* Is aware of symptoms
* Knows the date, time or where he/ she is
* Can remember a short list of words or phrases and have no basic linguistic problem.[32]

Mini-mental state exam (MMSE) and mini cog test-:

During the MMSE, a health professional asks a patient series of question designed to test range of mental skill. Max points are 30 points. A score of 20-24 indicates mild dementia, 13 to 20 suggests moderate dementia and less than 12 score indicates severe dementia.[33]

During Mini cog, a person is said to complete two task-:

- Remember and a few minutes later repeat the names of three common objects.

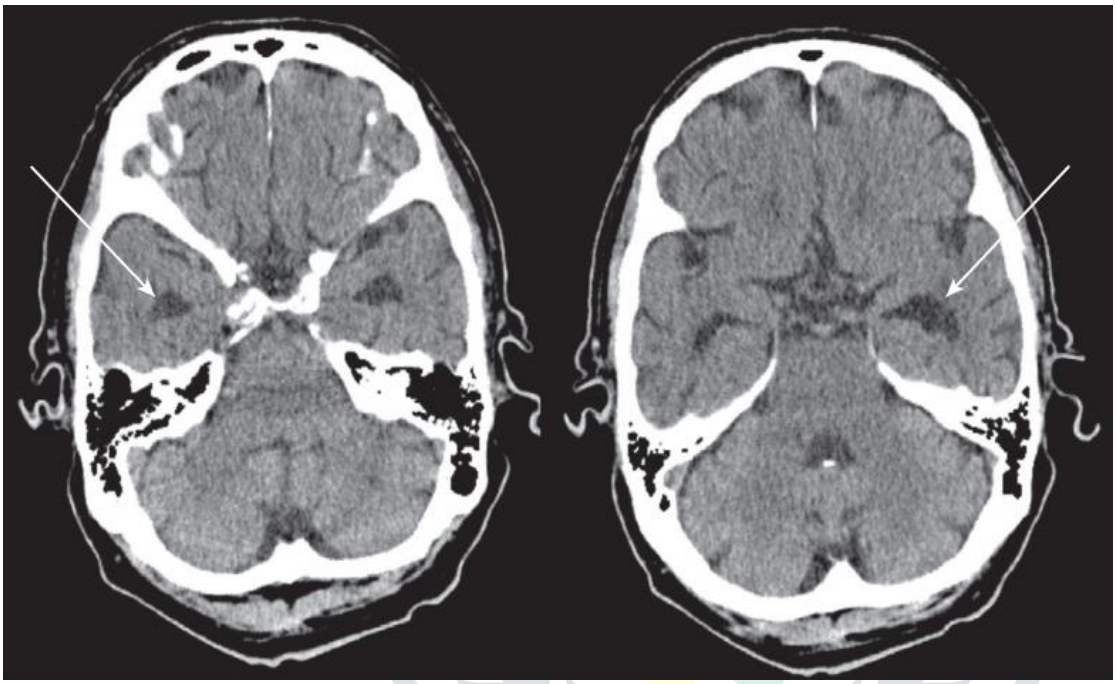
- Draw a face of a clock showing all 12 numbers in the right places and a time specified by the examiner.
- Score is measure to evaluate the test. [34]

Computerized tests cleared by FDA gives a clear sense of test combined with MMSE.[35]

BRAIN IMAGING:

Test includes structural scans of brain and require use MRI and CT scans to properly analyze the disease and rule out the possibility of confusing with groups of similar diseases.[36]

IN FIG [1]. *[37]



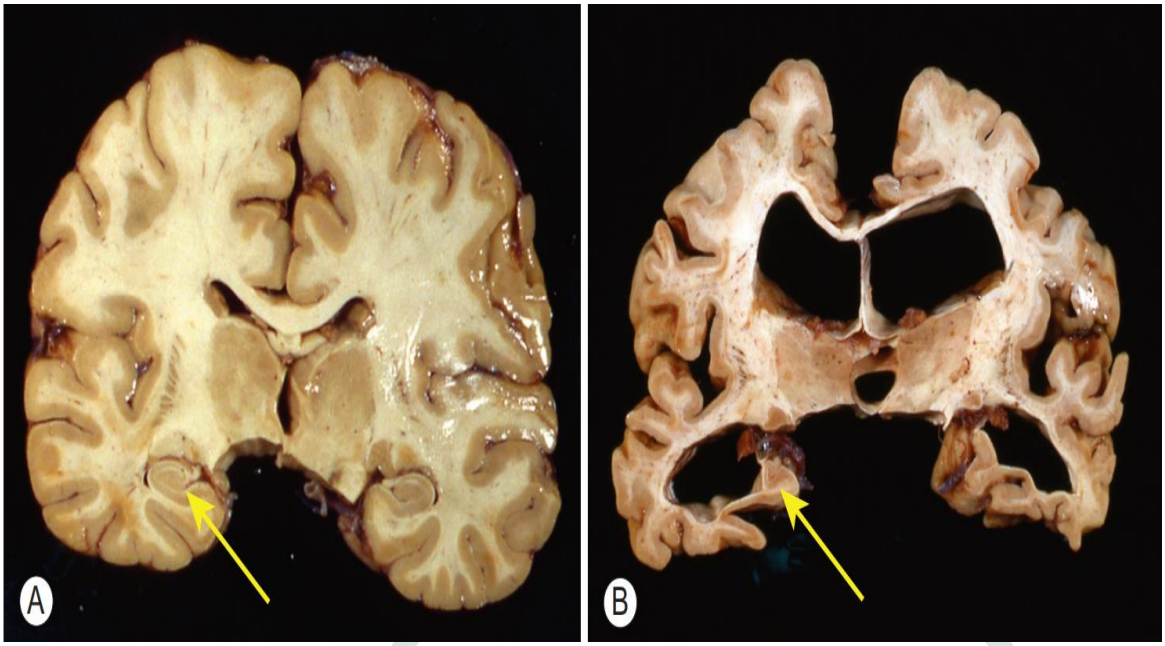
Selected slice of CT scan of a mild alzheimer's patients, we can note the prominent dilation of temporal horns of lateral ventricles, also known as 'ex vacuo dilation.

Cerebrospinal fluid test and blood test

Research suggests that Alzheimer's disease in early stages may cause changes in CSF levels of multiple markers such as tau and beta-amyloid, two markers that form abnormal brain deposits strongly connecting link to Alzheimer's. Thus testing CSF results in more accurate analysis of disease[38].

Likewise the currently available tests may predict the presence of amyloid changes in the brain or the presence of neuro degenerative disease or neuronal damage in brain. Blood tests cannot be used as a alone test to diagnose Alzheimer's disease or any other dementia, they will be used as part of a diagnostic with other analysis[39].

IN FIG [2]. [40]



Coronal view of gross pathology in Alzheimer's disease (A) compared with coronal view of brain with Alzheimer's disease showing atropic hippocampus and enlarged ventricles in affected brain.

Clinical treatment of dementia and Alzheimer's disease:

Clinical treatment includes drug therapy and psychosocial treatment for the disease.[41] Tremendous efforts, research and development has been made in case of dementia but what we have achieved is just the tip of the iceberg and still there is lot to be discovered and research process in various fields is going on.

So according to Indian pharmacopoeia 2011 4th edition, there are several listed anti-dementia and anti-Alzheimer's drugs. There are drugs that are prescribed according to schedule H.[42]

Donepezil :

- Indicated to use for treatment of mild to moderate Alzheimer's disease.[42]
- Contradicted for hypersensitivity, severe hepatic and renal impairment, pregnancy, lactation.[42]
- Adverse effects are Nausea, vomiting, diarrhoea, fatigue, insomnia, muscle cramps, bradycardia, convulsions, gastrointestinal, haemorrhage, hepatitis, urinary incontinence, influenza, pruritus, increased liver transaminases.[42]

Galantamine [41]

- Indicated for treatment of mild or moderate Alzheimer's disease and dementia syndrome. [42]
- Contradicted for hypersensitivity, severe kidney to liver problems, pregnancy and liver problems. [42]
- Adverse side effects include diarrhoea, nausea, anorexia, weight loss and chest pain.

Memantine :[41]

- Indicated for treatment of moderate to severe dementia of Alzheimer's disease. [42]
- Hypersensitivity to memantine. [42]
- Adverse side effects include fatigue, pain, hypertension, dizziness, headache, constipation, vomiting, back pain, hallucination, insomnia etc. [42]

Rivastigmine :

- Indicated for treatment of moderate to severe dementia [42]
- Hypersensitivity to carbamate derivatives, severe hepatic impairment.[42]
- Adverse side effects include mild cholinergic effect, nausea, vomiting, anorexia, dyspepsia, abdominal pain, depression.[42]

So we can analyse that side effects of these medicine exist in considerable amount. As the number of drugs prescribed increased, the risk of confusion increases.[43]

Traditional method of treatment prescribed according to Ayurveda and Chinese traditional medicine using medicinal herbs and plants

English medicine is preferred because of its targeted action altering body mechanism against disease and thus causing change in body owing to treat the disease, also they produce immediate effect and faster results. But in course of this action one thing which is left behind is the adverse effect or side effect caused by these drugs resulting to another complications develop in body.

Also Allopathic do not cure the disease completely, they help to control severity of disease but do not completely cure the disease and also they can not be consumed to avoid occurrence of such problem because they are not made for that. So, in such high time if we get our hands on practice of traditional medicine systems like Indian Ayurveda or Chinese traditional medicine system which is truly beneficial in long term approach as they do not cause any side effects and cure root cause of disease. The only drawback is that they take long time to show proper effect.

Here I have discussed some herbal crude drugs that can be used to provide relief in Alzheimer's disease and dementia, although some herbs for proper desired effect has been found but still there is lot of scope in finding out the more useful extract out of them and also various herbs are still there needed to be discovered and more study or research is needed to be found out on them. Meanwhile here I have discussed some of the medicines prescribed by Ayurveda and Chinese medicine system beneficial in case of Alzheimer's or dementia syndrome.

1. ***Centella asiatica :***

- It is a small annual herb belonging to family apiaceae is found throughout India and commonly known as 'mandukpurni' or 'jalbrahmi'. It is small fan shaped green leaves with white or light purple-to-pink or white flowers and it bears small oval fruit. Its use has also been described in the traditional Chinese medicine. It is used to delay ageing, prevent memory related disorders and is given with milk to enhance memory.[41]

Chemical constituents :

- Main constituents of this plants are asiaticosides, asiatic acid, madecassocide and madasiatic acid. [42]

Pharmacological activity

There is broad pharmacological activity such as anti inflammatory, anti oxidative , anti apoptotic, neuro protective, anticonvulsant, sedative, immuno stimulant. [43]

Pre clinical studies :

- Its benficial effects are showed decrease in malondialdehyde, increase in gluathione, Catalase and superoxide dismutase levels.
- It is also observed that there is an increase in dendritic arborization of hippocampal CA3 neurons, which may be one reason for improvement in brain function.[44]
- Triterpenoids are the major active component of ethanolic extract of *C. asiatica*, which consists of many chemical constituents such as asiatic acid, mecadessic acid, asiaticoside, scentellin, asiaticin and centellicin.
- Studies suggest that triterpene saponins present in the leaf show improved cognitive function by influencing central neurotransmitters.[45]

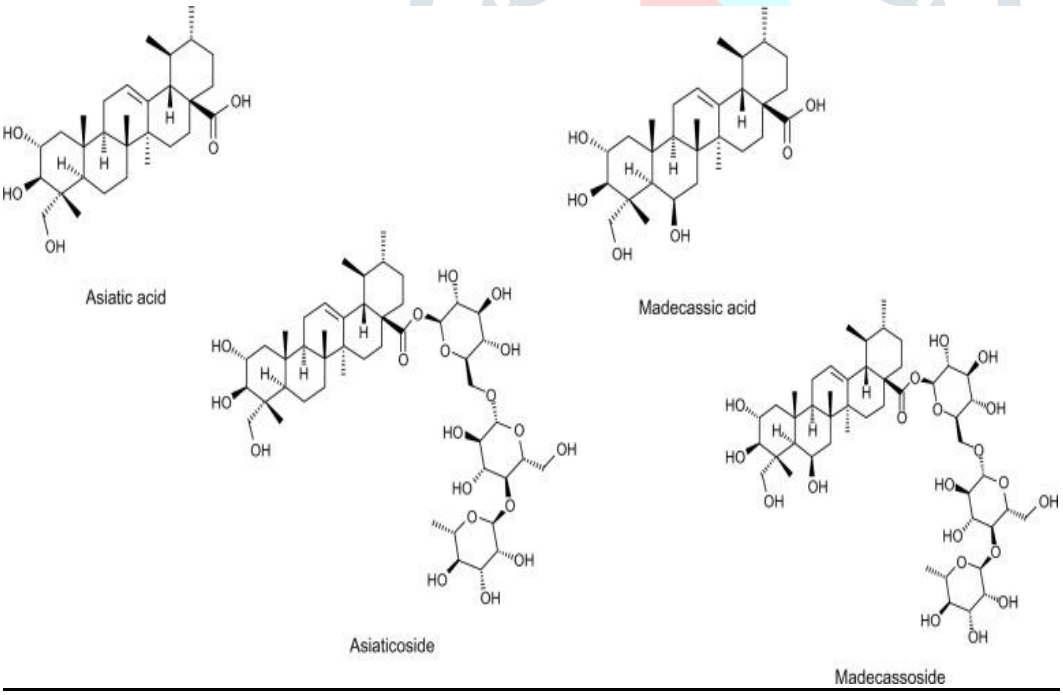
Clinical Evidence:

- The high dose enhanced working memory and improved self-rated mood . Thus, clinical and experimental studies support memory enhancing potential of C. asiatica. However, its use for treatment of AD remains to be evaluated.[46]

Marketed product: (mind focus with extract of jalbrahmi). [Fig. 3]

[47]

Active chemical: Constituents of centella asiatica [Fig. 4] [48]



2. *Bacopa monnieri* :

- This plant belongs to Scrophulariaceae family is a small perennial creeping herb with numerous branches having small oblong leaves and light purple or white flower. It is commonly known as Brahmi, is known for its revitalizing. "Medhya" is the property which strengths memory. [49]

Chemical constituents :

The main chemical content it consist of is triterpenoid saponins known as becosides. Alkaloids known as brahmine, nicotine and herpestine are also found. [50]

Pharmacological activity:

Herb shows various biological activity such as anticonvulsant, anti neoplastic, anti anxiety, brochodilator, immunostimulatory, hepato protective. [51]

Pre clinical studies:

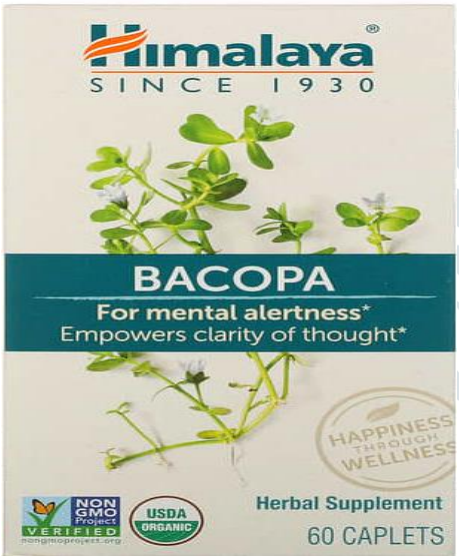
It contain several beneficial components such as alkaloids, flavonoids, glycoside, triterpenoids saponins and alcohols.

The alcoholic extract of the herb improved acquisition,consolidation and retention of memory in the foot shock motivated brightness discrimination test, active conditioned avoidance test. [52]

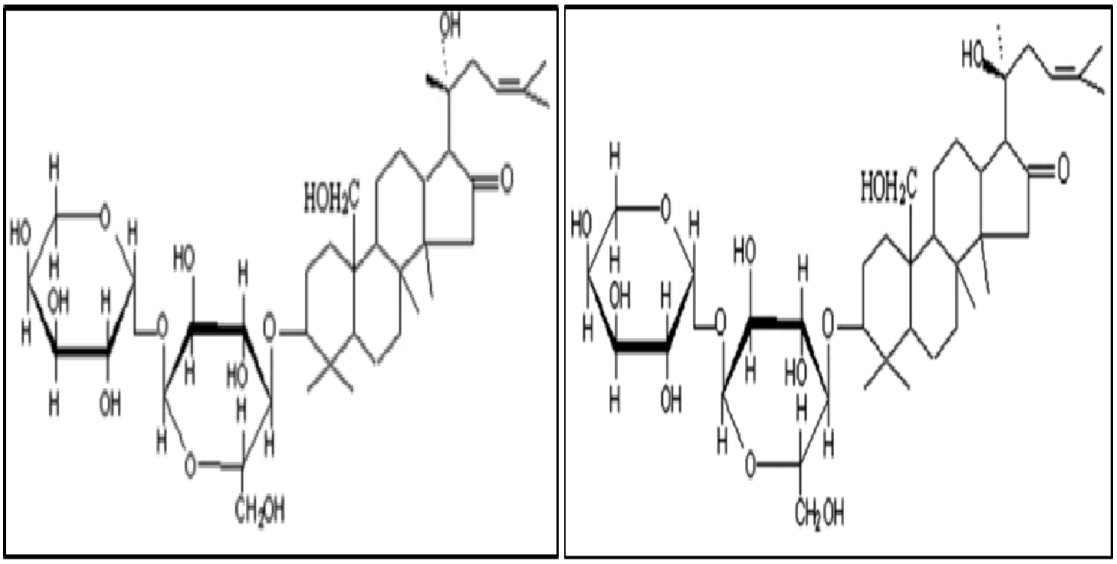
Clinical Evidence:-

There was reported significant improvement in verbal learning, memory consolidation and speed of early information processing after Bacopa administration for 12 weeks at a dose of 300 mg daily. [53]

Marketed product: Himalaya bacopa capsules [Fig. 5] [54]



Active constituents: Chemical constituents of Bacopa [Fig. 6][55]



Bacoside A (levorotatory); (b) Bacoside B (dextrorotatory)

3. ***Curcuma longa:***

It has perennial herb belonging to the family Zingiberaceae, also known as turmeric is obtained from rhizome of plant used commonly in India as flavoring agent and coloring agent. **[56]**

Chemical constituents :

Curcuminoids are main chemical component of curcuma, mainly including curcumin (difleuroyl methane), dimethoxycurcumin and bisdemethoxycurcumin. [57]

Pharmacological activity:

Pharmacological properties of curcuminoids such as neuroprotective, analgesic, antiproliferative, anti inflammatory, anti cancer, carminative, diuretic, anti tyrosine effective. [58]

Pre clinical studies:

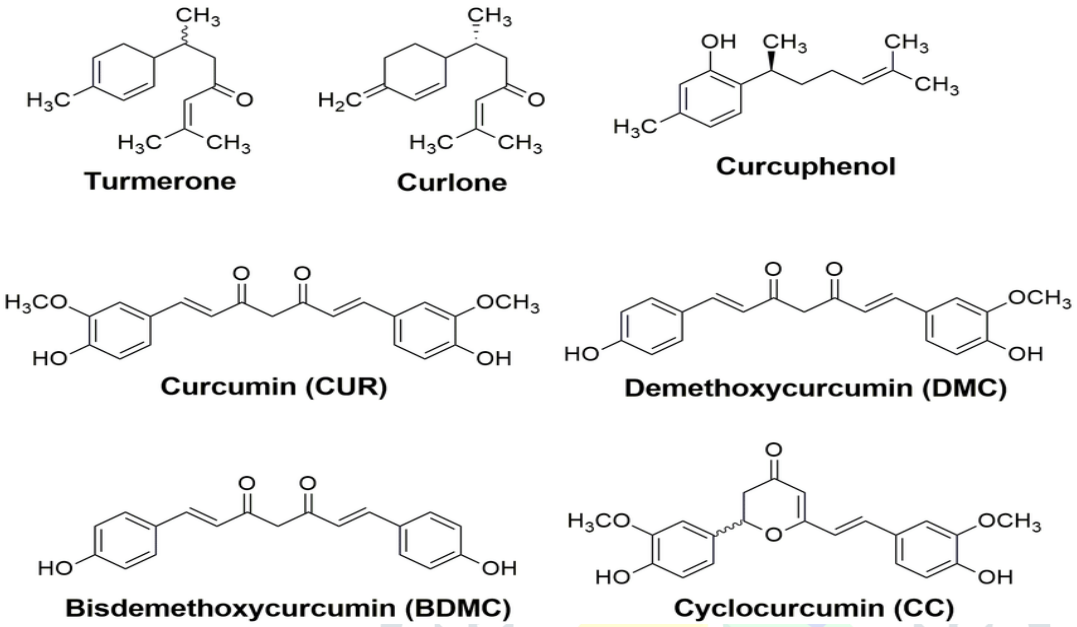
According to various experimental studies it is known that curcurmin possess wide variety activities like anti oxidant, anti inflammatory, anti cancer, cholesterol. [59]

Clinical Evidence:

Curcumin has shown to reduce both in vivo and in vitro Aβ plaque deposition. In-vivo, curcumin may protect cells from beta amyloid attack and subsequent oxidative stress-induced damage [60]. Curcumin can inhibit Aβ aggregation or promote its disaggregation at low concentrations . Another experimental study showed that curcumin treatment restored learning and memory functions in the STZ model of AD by reducing the oxidative stress. [61]

Marketed product: Biotoplevel with curcumin extract[Fig. 7] [62]

Active constituents:- Chemical constituents of Curcuma longa [Fig. 8] [63]



4. *Celastrus paniculatus:*

Celastrus paniculatus is large climber of family Celasteraceae. It is commonly known as 'jyotismati'. Traditionally, the bark and seeds have been used as brain tonic, to promote intellect and improve digestion, stimulant and expectorant. It is used to treat

many disease like depression, leprosy, paralysis and fever.[64]

Chemical constituents:

It shows the presence of various such as sesquiterpenoid polyalcohols and esters (malkanguniol, malkangunin, polyalcohol A–D and celapnin); alkaloids (paniculatine and celastrine); phenolic triterpenoids (celastrol and paniculatadiol); fatty acids (oleic, linoleic, linolenic, palmitic, stearic and lignoceric acid) and agarofuran derivatives.[65]

Pharmacological activity:

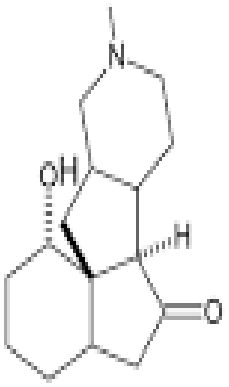
Pharmacological activities such as hypolipidemic, neuroprotective, anti-infertility, antiarthritic, wound healing, anti-inflammatory, antioxidant, analgesic, antimalarial, antibacterial and fungicidal action.[66]

Pre clinical studies:

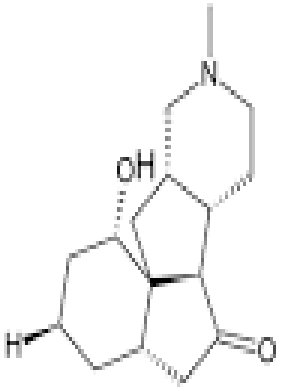
The antioxidant activity of *C. paniculatus* may be involved in improving the cognitive function. The aqueous seed extract improved memory performance in elevated plus maze and in sodium nitrite induced amnesia by reducing the AChE activity. [67]

Marketed product:- Qualia with exteact of jyotismati. [Fig. 9] [68]

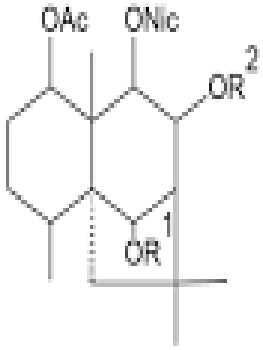
Active constituents: Chemical constituents of celastrus. [Fig. 10] [69]



Celastrine



Paniculatine



	R^1	R^2
Celapanin	Fur	Ac
Celapanigin	Bz	Ac
Celapagin	Bz	H

5. *Eriodictyon californicum:*

Eriodictyon californicum is a species of plant within the family Boraginaceae. It is also known as yerba santa (sacred herb), mountain balm, bear's weed, gum bush, gum plant, and consumptive weed.[70]

Chemical constituents:

Flavonols exhibit three C-ring substitution elements, namely 4-carbonyl, 3-hydroxyl, and 2,3-double bond. [71]

Pharmacological activity:

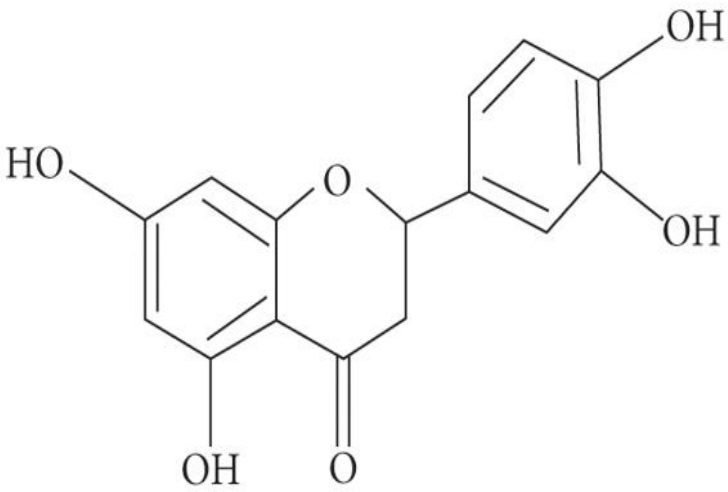
Amyloid-β (Aβ) 25-35-activated cell demise in primary cultured neurons is incompletely reduced by eriodicyton treatment by means of initiation of the Nrf2/ARE signaling pathway. In vivo and In vitro study exhibited that it eases LPS-modulated oxidative stress, neuro inflammation, and synaptic brokenness through the activation of MAPKs, NF-κB/Sirt1, and Nrf2/Keap1 pathways.[72]

Pre clinical studies:

Studies have shown that eriodicytol which is a flavonone extacted from plant shows removal of synaptic disfunction, removal of neuro inflammation, removal of LPS deviated oxidative stress and protect amyloid beta in 25-35 neurons. [73]

Marketed product:- Yerba santa extract syrup. [Fig. 11] [74]

Active constituents: Chemical constituents of Eriodicyton californicum [Fig. 12] [75]



Chemically active compound of *Eriodictyon californicum: (Eriodicytol)*

Research Gap:

Although a lot has been achieved in last 5-10 years but still what we know is just tip of an iceberg and there is scope of a lot to be discovered. Researches regarding more accurate assessment of the disease and better drug delivery system are in process. We are unaware of several aspects about disease which can lead to more proper evaluation of results and analysis.

There are still a lot of variety of medicinal herbs which need more attention and work as they are proven to be useful for brain enhancing property and have potential memory enhancing technique. Plants and herbs like *Acorus calamus* (vach), *Prunus amygdalus* (badam), *Orchis mascula* (salap), *Syzygium aromaticum* (lavang), *Mukta pishti* (pearl), *Tinospora cordifolia* (guduchi), *Picrorrhiza kurroa* (kutki), *Zingiber officinale* (sonth), *Boerhaavia diffusa* (punarnava), *Commiphora wightii (guggal)*, *Piper longum* (pippali), *Carum copticum* (ajwain), *Cyperus rotundus* (coco-grass), *Santalum album* (Indian sandalwood), *Elettaria cardamomum* (cardamom), *Foeniculum vulgare* (fennel), *Rosa damascene* (damask rose) and *Cinnamomum cassia* (cassia). [76]

CONCLUSION

In this article I have tried to compile every useful data relating to the topic which I thought of and also which was necessary to be mentioned to serve the purpose of review and make this article to create an impact on the topic.

Initially I have tried to cover introduction of disease and various concern related to it. Later on I have discussed Clinical stages, assessment, symptoms and versatility of the disease. I have discussed various methods of diagnosis as well as various method of treatment based on English medicine system ‘allopathy’ using synthetic drugs and Indian medicine system ‘ayurveda’ and Chinese medicine system using herbal crude drugs and medicinal plants and herbs.

Various methodology to examine the disease and rectify the problem, cure of disease has been discussed but still that is very less to cope up with the severity of disease and to properly handle the disease we need to work more aggressively on research and clinical trial of herbal drugs and medicine.

It is only possible by herbal medicine that we can control and cure the disease and even possibly reduce the chances of disease happening by strengthening our body to work against disease causing factors.

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