CHAPTER I

1.0 INTRODUCTION

In well developed countries and also in developing countries including India, herbs having medicinal properties are widely accepted for their therapeutical use with a higher population for remedies in health ailments without side effects, since allopathic medicines have side effects which are highly used by majority of population directly as a food in diet or in form of medicine in the treatment of diseases. India is one of country with highest population and a major part of the population are suffering with various disease and still even rapid growth in the medical as well as pharmaceutical areas, there are no satisfactory drugs in the management of many diseases, especially with the elder population many are suffering with major central nervous system related diseases in their last decades of life. Which making their life with lots of suffering and entirely the quality of life also decreasing day by day.

Now-a-days India is recognized as one of the botanical garden of the world because India has a wide variety of herbal plants which were clearly with practical usage in very ancient days were documented for its high medicinal values in traditional history periods, Ayurveda, Sidha and Unani are medicinal based on traditional background depends on herbs in their formulation. India is a fastest growing country in terms of population and documented to have highest population of elder people who crossed their sixtees. India is rich in bio diversity, viz species, genetic and habitat diversity.

Recently, the modern pharmaceutical industries are focused on plants for medicine development. One by fourth of the modern drugs formulations which are purchased on request/ prescription. Currently pharmaceutical industries are dependent on herbal source but their requirments are form their origin of raw material to higher medicinal plants which are widely available in the tropical regions of forests in India and also thorouhg out the world.

1.1. INTRODUCTION

INDIAN HERBS IN GLOBAL OPPORTUNITES
1. Availability of Strong traditional documents which supports the medicinal claim is mainly from Ayurveda. From very ancient times the herbs were used as folk medicine, but many of used herbs were started documenting, today those documented in earlier days become as a source of knowledge there by the traditional knowledge of drug utilization become as a main source even today in the treatment of many complicated diseases.

2. Plants were used as the source of medicine form the days which are immorable but even today the herbs hold main role in the fulfillment of many medicine and become as a chief source. Even Plants which were used for centuries very high safety margin even on chronic usage but almost all allopathic drugs from chemical sources are having high side effects and created chemophobia in the users. To over come this other alternatives for the chemicals are only the herbal souce even day by day the consumers are increasing, which made development of the herbal industries all across India.

3. Encoragement is given for the cultivators, for cultivating herbal based medicines to meet the requirement and also to maintain qualities in the cultivated crop, many herbal based pharmaceutical industries are developing their own land for the cultivation of herbal plants and also adopting the land which is suitable for the cultivation givng royalty or by direct involvement in the financial matters and other than this in India there is a friendly government policies (in growth culitivation and harvesting, buying of medicinal raw substances form the cultivators not only form India and also form other countries form where the socources are found and also encourgment in the expoert of resources for the other countries by giving lot of relaxation in the selling policies, in the herbal sector.

4. Due to increase in the utilization of medicine derivved from herbal source, day by day demand for the herbal medicines are increasing inorder to meet the demand and to face the challenge in the treatment of new diseases occurring and also for effective treatment of the disease which are already exist form decades, many herbal industries in India are changing and established as a research based industries along with production (Why Indian drugs).
FASTER EXPANSION OF PLANT DRUG MARKET

➢ Uptodate information on current practice and knowledge of harmful side effects, adverse effect on prolong usage and also toxic effect upon chronic usage from synthetic drugs in most of the human population.

➢ Inefficiency of the synthetic drugs and can also shows only an symptomatic relief of allopathic drugs against certain diseases which can become dangerous if not treated completely.

➢ Even economical consideration will also be given before selection of the raw materials in the processing of a formulation, because the ultimate price of the formulation depends on the cost of the raw materials used in the preparation of that formulation. Plant based drugs are comparatively less expensive, due to many reasons like they are available naturally and can be cultivated, with less expensive.

➢ Among Western population major proportion of population are demanding for herbal formulations in the treatment of many acute and chronic diseases, due to its advantages when comparing with the allopathic medicines usage history, for either actue or chronic usage.

➢ Pharmaceutical industries are now highlighting the importance for plant drugs in their research for the search of new drugs or molecules in treatment of many emerging new diseases.

DEGENERATIVE DISEASES

The term degenerate means to change from higher to lower form in any organ system. In central nervous system degenerative diseases are diseases of gray matter which is around two to four millimeter in thickness which constitutes cerebral cortex which consisting of billions of nerve tissues in it with un-known reasons, mechanism of occurrence and progression. Advancement in the age and genetic manipulation are mainly considered as the one of the major factor in occurrence and progression of these dreadful diseases, still the reason behind are multifactorial in origin.
The diseases can be classified based on clinical aspects and anatomic distribution of the lesions/presence of biomarkers of degenerative diseases into individual syndromes examples includes Alzheimer’s disease. In average the life span of patients who are suffering form this kind of disease may be around eight years may also extend upto twenty years during these period of progression in disease its symptoms leads to disturb or decrease the quality of the life in patient such that they cannot lead a normal healthier life.

**REGION OF THE BRAIN AFFECTED AND THE COMMON DEGENERATIVE DISEASES .**

1. **CEREBRAL CORTEX:** it can be considered as a major region in the brain because it plays a major role in the regulation of other higher centers of the brain. the cerebral cortex region is filled with gray matter which play a primary role in the processing of the sensoray information and processing of the sensory information which are obtained form the sensory nerves and storage. The chief function of this cerebral cortex is storage of information. This information may be received to the brain by sensory nerves by learning process. Abnormities in this region of the brain leads to impairment in the memory of the person diseases includes eg AD, Pick’s disease

2. **BASAL GANGLIA AND BRAINSTEM-** this is the region is the brain which is responsible for the secretion of the dopamine. Different pathways have been identified in the secretion of dopamine. Dopamine is a neurotransmitter which regulates movement in the person ie muscle coredation. Motor and sensory nerves are equally held responsible in the regulation of these pathway. Defeciences of these dopamine secretion either increase or decrease leads to neuronal diseasese examples: Huntington’s disease and Parkinson’s disease

3. **SPINAL CORD AND CEREBELLM,** which are considered as the major part of central nervous system in the transmission of messages helps in the communication between the higher centre with the stimulus generated from the external or internal stimuli which are essential for survival, spinal cord even relay sensory nerve information to the brain region containing innervations of sensory
and motor nerves eg: Cerebellar cortical degeneration, Olivopontocerebellar atrophy, Spinocerebellar atrophy

4. **MOTOR NEURONS** they are efferent nerve that carry nerve impulses towards motor nerves to elicit the response, these motor nerves are innervated abudantly in the skeletal muscle rhythmic contraction and relaxation of these muscles will make us to move. In diseases like motor neuron disease it makes unable to show locomotory responses as the nerve terminal brining efferent impulses will be blocked or some time get distructed and it makes unable to do any task. The locomotion is very much essential for the living organism, in human a very well developed motor areas can be seen in the brain, which are highly innverated with the nerve terminals, they are many etiological factors can be enlisted here which can cause distrubence in the transmission of the nerve impulses disturbing the locomotion in the person. eg. Motor neuron disease, Werdnig-Hoffmann’s disease

In an average those who got affected with alzheimers disease starting from the day of diagnosis to death quiet flacuation in the duration of life span has been reported sometimes fluctuations can be reasoned as the intrest and responsibility taken by family people or care taken by the care providers, but in majority of documented cases with disease it may be in average of four to eight years.

In some cases it can also crosses more than twenty years, from many reports it identified very less propotion of death were recorded only if proper care was taken to the victim by their care givers and in some cases it was also occurred with less death cases if diagnosised earlier and treated with the available facilities or by using some drugs called as nootropic agents.

**1.02. PROBLEM ON HAND**

Indian epidemiological studies reveals dementia as a largely a hidden problem of our country (Ashutosh A etal )^{10}. Around the world approximately over 10 million cases of alzheimers disease were reported and the advancement in age may the risk factor.
Several population censuses which was conducted in different regions of the world which was basically focused on helath of elders population in the society predicts that during the year 2020 all round the world there will be seventy percent of people in the age 60 in India contributes around 14.5%. increase in population day by day is a greater challenge in prevention or control of many disease. Dementia may occur due to many reasons. Worlds elders population are also increasing day to day as population increase, the number of alzhemiers suffers are also increasing. So documenting the suffers by conducting survey plays a major role in the regulation of the suffers with disease. The report also highlights when world reaches 2030, 2050 it may get doubled or tripled. Today in world 24.3 millions are suffering from dementia many are from developed countries.

Some reports also highlights that in the world, it was considered such that it may be from any part of the world, it was recorded and even have a strong evidence, which was obtained from the yearly census on the epideplogy department of each country which released a shocking data suggesting that some one in each seventy seconds of every twenty four hour of the day develops Alzheimer’s disease and based on its severity of complication it is considered as fifth main reason for death in the elder population who are leading their late decades in their life.

Alzheimer’s affects anyone at anytime of their whole life concerned without having any warning indicators or any type of early symptoms due to confusion in the diagnosis of particular type of dementia and it may be linger in many cases until it takes the final stage due to disease progression. Alzheimer’s in India also quickly becoming often more and more common due to the globalization, as the society is also trying in expanding into one of the world’s largest and fastest running industrial giants among the entire world.

Globalization in every region or part of the world cultivates a new and fully artificial life style and stressed life style which is becoming a very common and also considered as one of the major reason which can give a major contribution for the development and also progression of forgetfulness and poor memory. Forgetfulness and poor memory now a day which is becoming an unanswerable question of the present world (Parle M etal). 53
Alzheimer's affected population are expected to increase year by year this is also strongly supported by the recent epidemiological studies carried out by various parts of the world. The detailed picture of epidemiological survey is denoted as in the year 2050 it will be around 14.32 million in 2045 around 12.47 million people, in 2040 10.68 million people in the year 2035 around 9.07 million people, in the year 2030 7.61 millions, in the year 2025 6.35 million people, in the year 2020 5.29 million people, in the year 4.41 million people, in the year 2010 3.69 million of people, in the year 2005 3.09 million of people and in the year 2000 it was 2.58 million of people. It is the data suggesting Indian dementia progression during 2000 to 2050.

The genetic factor and also the advancement in age even stress life style which can cause change in the gene sequence are considered as the great risk factor for the precipitation and also progression of AD in humans. Alteration in the gene ie the mutation is also considers very strong major risk factor among the suffers. Generation to generation the disease can be transmitted and causing a burden to a sufferer. Now due to the advancement in the recombinant technology it is becoming to understand better and can also able to correct the mutated gene by using gene therapy but hundred percentage successes has not been achieved but researchers all over the world are working on this gene. in recent years; attempts have been made to develop drugs for treatment of dementia and attention deficit disorders to improve memory and learning. These agents which are used in treatment of this deficit diseases are generally called as nootropic agents or cognition enhancers.

**PREVALENCE OF DEMENTIA BY AGE AND GENDER.**

Alzheimer’s disease is a neurological disease which can be seen most maximum in the old people those who are in their late sixty. Here is a pictogram of alzheimer’s disease in major cities of south india and it is compared with some cities of Europe.
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![Graph showing prevalence of dementia in India compared with Europe.](image)

Figure 01: Prevalence of dementia in India compared with Europe.
Aged women are compared with men in pictogram: 4. It suggests that aged women are very much prone to disease when comparing to adult male. The study highlights to show importance in the female aged by prophylactic or by early diagnosing. Begin women is considered as a risk factor the occurrence of disease, especially in the menopause age some studies suggests that decrease in the estrogen level may be considered as a hormonal risk factor in the occurrence of the disease. If proper care taken than the disease severity can be ruled.

EPIDEMIOLOGY GENDER BASED

Females are more prone to dementia when compared to males. Various epidemiologies studies carried out in different parts of countries gives the common conclusion that womens are more prone to different type of dementia than comparing to men. The exact reason behind this is not known it may be considered due to the body physiology and mental make up of the persons and hormonal change that occurs in the women in their different stages of life may held important role in the occurrence and not only in occurrence of the disease but also having a prominent role in the progression of the disease. One of the epidemiological studies carried out in the year 2010 also suggests this; the main reason for the epidemiological studies was to generate a data which clearly suggests about the clear risk factors in the disease. As gender wise comparison the data suggests that womens are prone to the dementia than the percentage suffers from men. Year in age as considered as one of the risk factor and accordingly the datas were collected. From the study it suggests that population in the range of sixty to sixty four
about two percentage of males were affected by dementia where as with female it is around three percentage high. Age is considered as one of the major risk factor in dementia as advancement in the age it also increases the occurrence and severity and progress of the disease. Little advanced population studies suggest among the age category of sixty five to sixty nine only three percentage of male population with this age got affected with dementia whereas with female population with this age was found to be quite high around four percentage.

The aged population of seventy to seventy four only around four percentage of male population was got affected with dementia where as it was high in womens around five percentage in average. In the little advanced aged population which included the age group of seventy five to seventy nine around five percentage of mens got affected with dementia the vale is too less when comparing with that of women population which is of around seven percentage which is too high. Still the studies in the advanced age population which group consists of senior citizens with eighty to eighty four even the womens are more effected when comparing with the men around fifteen percentage of men got effected in this category where as ten percentage of womens affected with dementia problems.

The category of population consist of aged people of eighty five to eighty nine it was recorded highest percentage of women suffers comparing to that of male aged populain, a recorded rate of twenty percentage was observed with womens with around fifteen percentage of male suffers. In the very advanced stage of life which consists of population having age ninty and above there prevalence rate was found that female suffers are more than male about fourty percentage of female suffers were recorded to a value of thirty percentage of male sufferers. So form the data it evidence that females are more prone to disease.

**COGNITION:**

The term cognition is the process of information processing which can be the operation of the mind. The cognition deficient problem is the major health problems which is affecting with major group of the population it is a global suffering. Age is considered one of the major risk factor in the progression of this, other than age, individual
life style, food habits exposure to stress will also have a major contribution in the precipitation of the disease.

COGNITION DEFICIT DISORDER

Cognition deficit disorder is common among the aged people which make them suffer a lot. Congition disorders disturb the daily routine work and also makes impossible to remember the ongoing events and the people suffering with this problems will be unable to identify their close personalities, such that it makes the life very miserable. Complete the persons who got diseased should depend upon the care giver and the care giver should take proper care for the patient because the disease always affects the normal routine tasks of the persons.

The persons who are prone to this disease are affected with cognition i.e self awareness of the surrounding and the daily routine tasks, almost all the developed countries and in the developing countries many elder population is affected by this cognition disorders and year by year the ratio of suffers are increasing. There is no proper treatment for the deficient such that the person once susceptible to the disease throughout his life has to suffer a lot and he becomes burden to the family. Every part of the world we can find the people having the problem in the cognition, Among sufferers of thirty million around world population nearly three million patients were Indians.

THE NERVOUS SYSTEM:

In human body among all the organ system nervous system is a complex structure among organ system which primarily consists of brain and spinal cord, which is having all the regulatory actions over other organ system and also involves in the personal skill and behavior of the individual, the regulation is carried by the help of the chemical substance which called as the neurotransmitter which is having a prominent role in the well being of the person. Very important functions of the nervous system is learning, and storage i.e memory.

LEARNING AND MEMORY
Learning is defined as the change in behavior to a given situation brought about by repeated experiences in that situation, which is acquired when a stimulus or a sequence of stimuli are transmitted to the brain which is encoded into a memory trace, possibly by formation of new synaptic connections in brain areas involved in forming and storing the acquired information. Which include the hippocampus, cortex and cerebellum. At a later date memory can be recalled in acquired learning. Some of this acquired information is lost due to spontaneous decay or by interference by other stimuli. Registration (acquirement of learning), retention (memory storage) and retrieval (recall) constitute the memory process.

LEARNING.

Learning may be defined as the ability to alter behaviour on the basis of experience. Human brain is subjected for lot of new experiences even day by day, or by hour by hour, minute by minute or every second by second every information may be consider as a stimulus which get carried by the sensory neurons and ultimately encoded in the terms of neurotransmitter by electrical changes in the brain and ultimately the information will reach to hippocampus and cerebral corex region of the brain. Where depending upon the nature of stimulus it may be stored as a memory which can be recollected whenever required.

FORMS OF LEARNING:

Learning in human is a complex phenomenon which involve several complicated steps; learing may start with the senory stimulation by vison or by hearing, even learning is an never ending phenomenon, throughout the life human beings are exposed to learn many days. Learnig is thought to be a never ending phenomenon, because in day to day life human will be subjected for a new tasks which from the knowledge of the older experience and recalling it he learns the new, but learning becomes complete only when the learned things become stored and when it get recalled and utilized upon the requirements to tackle many daily works safety and effectively. There are different types of learning some of them are summerised as follows.

NON-ASSOCIATIVE LEARNING:
Non associative learning obtained by recalling the memory which is obtained by practice or by the personal earlier exposed novel environmental stress or by repeated learning the new things with interest or sudden unknown things learning in an unknown time or in unknown place or sometimes in the known place also. i.e, earlier experience in completion of work or which exposed the individual person to stimulation and many a times helps to ignore the stimulus which became a habituation in the person.

ASSOCIATIVE LEARNING:

In associative type of learning the stimulus which helped him to learn will also creates an stimulus which helps him to create an behavioral changes in him or it can also helps him to improve the learned memory which was already present in him by his earlier experience, which may become permanent for his long term assessments.

MEMORY:

It is the phenomenon of storage of information obtained through practice i.e by learning either it form non-assosiate or associate learning. Memory is must for learning and to correct mistakes and similarly one would not be able to repeat successes or accomplishments without memory, except by chance.

Some type of memories last for a time of few seconds, where as other type of memories can last for hours or days or months or some times even upto years. The common classification of memories is as follows:

IMMEDIATE TYPE OF MEMORY:

Immediate type of memory is a type of short term memory but, which involves the normal steps includes acquiring information and latter it will be transmitted throughout the nerve, the information will be flotted and transmitted in the form of nerve impulses called as electrical impulses but it can be stored in the gray matter of the cerebral cortex in the brain. Short term memory lasts in few days or weeks but immediate type of memory which lasts for short time it may in seconds and minutes. Immediate type of memory gets usually disturbed in the old age.
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SENSORY INFORMATION STORAGE:

It is also called as SIS where the information is stored for very shorter period around one by tenth of the second, where the information will be transmitted within the nerve they are transmitting it. This type of memory is difficult to recollect when ever required because it stay only for a fraction of seconds.

SHORT-TERM MEMORY:

Short term memory or also called as STM which includes memories that last for days or at most a week , some of them will have strong short term memory but with many it may be weak such that it helps in learning of the activates it may take time in such individuals unless they are, converted into long term memories.

INTERMEDIATE LONG-TERM MEMORY:

Intermediate LTM is a type of memory which last for days or sometimes upto several weeks but eventually fading away if not the memory traces which are repeatedly activated which may be sufficient to become more permanent. i.e can be converted or stored into long term if repeatedly recalled and by practicing.

LONG-TERM MEMORY:

Memory which acquired by practice can be stored , once stored, can be recollected up to many years or even entire lifetime, which some time recalled with sense organs activation like sound heard by ear or odour felt by oflection in nose, taste felt by taste buds in tounge and many more recollects very old memory or person behind that memory.

THE FUNCTIONS OF MEMORY:

Memory having a big role in routine functioning of aperson. But memory is not a simple task but it is a complicated phenomenon which consists of several steps. Memory is having a major prominent work in prediction of future possible threat and plans to
overcome. Here are some of the very important steps which are involved in the memory process of a person.

A. Registration
B. Retention
C. Retrieval

THE STAGES OF MEMORY:

1. Sensory memory
2. Immediate memory
3. Recent memory
4. Remote memory

SENSORY MEMORY:

This is a major type of memory which is a Shortest of all memory travels and get terminated in visual and auditory centers located in the brain region. Visual memory lasts for a very shorter period which is always less than one second. Eg: Sound which are generated when a person cough sound of the persons, dogs barking sound. With this it becomes a easier task to know the identity of the person. Sensory system of the body called as the sense organs which play a very prominent role in the transmission and perception of different learning object either by sound, or in the form of vision or some time even in the form of smell or even in the form of taste. Once it get perceived then immediately it will be transmitted to the cortex region in the brain.

IMMEDIATE MEMORY:

Many a time it is not essential that the learned or any type of sensory information is not required always to be stored and it is not the mean that only with help of the stored memory only the person can do the work but even though some times the memory formation not occur in the cortex of the cerebrum even the recalling becomes possible this type of information which is not permanently stored like long term memory is called immediate memory. It is referred to amount of information a subject can keep in conscious awareness without active memorization. It has time frame of only thirty
secounds. And the information processed through this route is usually buffered around perisyluian cortex and frontal lobes of the brain.

**RECENT MEMORY:**

It has time interval of minutes to months and is stored in Hippocampus, Mamillothalamtric tract or Dorsomedial thalamus. It is of two types:

1. Declarative Memory.
2. Procedural Memory.

Declearative and procedural memories are the type of long term memories. Declarative memory works in the control of the person when he requires he can recall the events by his experience it is a fact and knowledge. But the procedural memories are the different type it is not under the control of a person i.e many a time many type of skills on repeated learning or practicing it become a part of the life some time it is called as a acquired reflex unknowing it will be exhibited for example riding a car playing a peano. etc. they can be stored for long time and can be recalled.

**REMOTE MEMORY:**

This is the oldest of all memory and refers to all past experiences. The time frame of this type is from months to lifetime and is stored in association cortex. It can be retrieved with the use of hippocampal system.

**FORMS OF MEMORY:**

I. Declarative may be Episodic or Semantic is the one which can be recalled as a picture whenever needed.

II. Non-declarative: may be Motor skills, cognitive skills or Priming is the one obtained by regular practice it is nothing but collection of all experiences.

**MAJOR AREAS IN BRAIN:**

Principal parts of brain are
1. The brain stem
2. The cerebellum
3. The diencephalon
4. The cerebrum

Cerebrum has four lobes

1. The frontal lobe has
   I. Motor area
   II. Supplemental motor area
   III. Premotor area
   IV. Brocas area
   V. Prefrontal lobe
   VI. Voluntary eye field
   VII. Area of hand skills

2. The parietal lobe
   I. Primary sensory area
   II. Sensory association area

3. The temporal lobe
   I. Parieto occipitotemporal association area
   II. Preprontal association area
   III. Limbic association area

4. The occipital lobe
   I. Vison related area the prominent area which involves in
      the vison of the person though both sensory and motor
      neurons.

NEUROPHYSIOLOGY OF LEARNING AND MEMORY PROCESSES:

The classical circuit of Papez (hippocampus, fornix, mammillary bodies of the
hypothalamus, cingulate gyrus, parahippocampal gyrus and hippocampus) having a major
role in the neural substrate of emotional aspects of behaviour.

A second pathway leading from the cortical association areas, via the cingulated
gyrus to the hippocampus, through the septal nucleus via the forsomedial thalamic
nucleus to the prefrontal cortex, enables the information to be stored, presumably
allowing it to reverberate for some time. Memory comprises of registration, consolidation
and retrieval. Cholinergic neurons in forebrain and brainstem send diffused projections to hippocampus and cortex.

Fig. 2: Diagrammatic representation of major pathways involved in the information processing pertaining to learning and memory mechanism

METHODS IN LEARNING.

There are different ways and methods for learning among them generally it can be summarized as follows, the skill of learning can be improved by repeated involvement in the learning it’s a natural phenomenon. The effective learning process in almost all cases can follow the order which got described below.

- **CONDITIONAL LEARNING** –
  This type of learning involves learning of new things in the human beings by their earlier exposures or by mistakes which caused alter about the threat which is going to occur while doing the work.

- **CONCEPTIONAL LEARNING** -
This type of learning involves learning which can occur with the information which is already known to him or which he had already exposure to him which the information got stored in the cerebral cortex which may be in the form of short term memory or long term memory. Conceptual learning is possible only with the memory which is already existing in the person and also done by the stored memory in the DNA ie it rely on genetical.

- **CONTEMPLATION LEARNING**-
  This type of learning involves expanding the memory already which is present in the present which he learned form different daily tasks.

**NEUROTRANSMITTERS IN LEARNING AND MEMORY**: (Chiyomi Taga etal)\(^2\)

**NEUROTRANSMITTER & RECEPTOR SYSTEM**

Various neurotransmitters and receptor systems which are engaged in the memory purpose can be summarized as below. Neurotransmitters are the chemical substances that secreted upon nerve stimulation, it is the answer given by the brain for a particular stimulation. All nerves upon stimulation secrete a chemical substances depending; upon their secretions even some time the nerves are named here a list of neurotransmitter enlisted are focused on their role in the memory.

The neurotransmitter should posses many qualities to meet their ideal requirements then only they are considered as neurotransmitters. The neurotransmitters should be secreted in high concentration when the nerve undergoes stimulation. The neurotransmitter synthesis should take place in the nerve terminals for their synthesis the precursors which are essential for their synthesis should be present in the same nerve terminals where it is synthesizing should present with the required enzyme which helps in the synthesis of neurotransmitters. They should be always released in the quanta’s (very small fractions which are essential for the normal physiological function of the system). In the nerve terminals inside the vesicles where neurotransmitter get synthesized not the synthesizing enzyme should preset but also the terminating enzyme should present which can terminate the action of neuro transmitter. Other than this for regulating the secretion
of neurotransmitter there are a set of receptors at the presynaptic nerve terminals which are called as auto receptors they always regulate the level of secretion of neurotransmitter by their feed back method.

The major neurotransmitter includes, nor-adrenaline (sympathetic nerves), serotonin or also called as five hydroxyl tryptamine (serotogenic nerves), aspartate (amino acids acts through NMDA receptors), histamine (mast cells, autacoids), acetyl choline (cholinergic nerves) (Chiyomi Taka etal)\textsuperscript{21}.

Nerve is of the two type’s afferent nerves and the efferent nerves. These afferent nerves carry information from sensory organs to the brain any type of stimulation that can stimulate the afferent nerve fibres in the terminals of the nerve which can be connected with the organs, it immediately sends the impulses to the brain. As a respond to this stimulus brain sends impulses through efferent nerves, this type of communication is only possible through the involvement of secretion of some chemical substances they are called as the neurotransmitters. It is the answer given by the brain to the questions given the sensory afferent nerve fibres through efferent nerve. This is called as communication.

Memory is one consider as a complicated phenomenon which involves many inter-neuron secretion for the completion of these complicated phenomenon. Imbalance in the neurotransmitter can leads to neurodegenerative disorders. Some examples can be considered to explain in the neurotransmitter level in the brain increase in dopamine leads to schizophrenia. Dopamine is an amine neurotransmitter gets secreted from dopamnergic nerves, which are secreted from five different path way which is having different physiological role.

Dopamine shows its actions by binding to dopamnergic receptors which are once again five in numbers. Dopamine is responsible for regulating the personality of the person, like behavior of the persons, posture, locomotion, eating pattern of the person. There is a direct relation ship between dopamine and memory. Many of the drugs which are claimed for Nootropic action and are already used in the current medical practice are having a property to inhibit dopamine action, which is a quiet common side effect with the treatment. Where decrease is the motor action which can be seen in the patient s who are all treated with Piracetam.
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Neuro transmitters of memory includes acetyl choline, upon cholinergic nerve stimulation the nerve terminals secretes acetyl choline which can show its actions by binding to cholinergic muscaranic receptors. Many hypothesis are focused on the cholinergic transmission and their deficits and their major role in the memory. Based on this consideration cholinergic hypothesis generated suggests that acetyl choline is the major neurotransmitter of all cranial nerve which are having a direct link with the brain and having a major role in the memory. And even it have been suggested that the patients suffering from amnesia are having common problem with the acetyl choline level. Many of the drugs in the treatment are targeted on the metabolism of acetyl choline. It is metabolized by two enzymes called as pseudo cholinesterase and butyl choline esterase, decrease in the level of acetyl choline causes deficit in the memory.

Learning and the Memory is a very complicated process which requires involvement of many neurotransmitters with the proper conduction of the nerve impulses. Many type of learning can be enlisted according to the exposure of the person to the daily events, even though for success full learning there should be proper secretion of neurotransmitters.

Histamine is an amine neurotransmitter secreted from the inflammatory packets are called as autocoids are also called as local hormones. Histamine can also show its central action by binding on the histamanergic receptors located centrally; here histamine is acting as a neurotransmitter in the communication of the nerve. Even for learning histaminergic nerve stimulation is thought to be essential. They are considered as a minor pathway but even though they are having a prominent role in the learning behavior of the persons. This action cannot be neglected as they can cause stimulation of various areas of the brain which are concend with the learning and storage of the learned phenomenon.

Other neurotransmitter having role in learning is aspartate. Aspartate is a amino acid which is categories as a excitatory neurotransmitter which mediates its action through binding to NMDA receptor (n- methy d aspartate receptor) they are considered as excitatory stimulus shown through the stimulation.

Serotonin is another neuro-transmitters which is produced and secreted upon the response to the stimulation that arised in the neverve, which can travel the entire nerve
which secrete a chemical substance which is commonly called as a neurotransmitter form the serotogenic nerve fibers which upon secretion can show its physiological response upon binding through different types of 5-HT receptors which are widely distributed in the body and even the regions of central nervous system and even they can engage with the learning and storage phenomenon in the human and in the higher vertebral animals.

Neuropeptides are also a transmitter in the nerve terminals which elicits their effect through G protein coupled receptors, which includes endorphins, dynorphins, enkaphalins, they mediate in the transmission of sensory information towards the brain. During their sensory information transmission they, relay on many neurotransmitters which get secreted in the pre synaptic nerve terminals which includes nor-adrenaline, acetyl choline, GABA, aspartate and many more. The neuro peptides are also called as happy hormones, which can mediate many response through sensory afferent and they can elicit their response through motor nerves, which are efferent in nature.

GABA is an inhibitory neuro transmitter which can elicit their response through binding receptor of GABA. GABA receptors are of two types one is G-protein linked receptors and the others is ligand gated ion Chanel receptors. Neurobehaviour processing in the brain are mediated through chlorine Chanel receptor mediated. They helps in the relay of information form the sensory nerves in the junctional areas of the brain.

Some studies also suggests that the involvement of cholinergic nicotinic receptors in the learning and its storage. Nicotine is a alkaloid which can stimulate some category of receptors depending on this the name nicotinic receptors have been given. Even for the transmission of sensory information their processing the involvement of nicotine can been observed. Acetyl cholines which are considered as a primary neurotransmitter in the processing of information through sensory nerves can also bind on the same binding site of the nicotine. This nicotine is considered as a agonist of the cholinergic nicotinic receptors. They can also potentiate the action of cognitive process by stimulation action.

1. Glutamate (NMDA, AMPA receptors)
2. Acetylcholine (Muscarinic, Nicotinic)
3. Dopamine (D1, D2 receptors)
4. 5-HT (serotonin) (5-HT$_3$, 5-HT$_{1A}$ receptors)
5. Nor-adrenalin (α, β-receptors)
6. Neuropeptides (G-protein coupled peptidergic receptors)
7. GABA-β-carbolines (GABA-A / Benzodiazepine receptors)
8. Neuro steroids (NMDA / GABA-A receptors).
9. Histamine (H1)

Memory, learning and behavior also relay on neurotransmitters, Acetylcholine found to be the main neurotransmitter in learning and memory. The reduced AChE activity (hippocampus and cortex) is reported in Alzheimer’s disease which leads to the loss of memory to lead normal life tasks.

Cholinergic agonists and anti-cholinesterase inhibitors works synigergically if this combinations are used or some time if used alone in the management of dementia works by showing improvement in memory and releated learning. It has been suggested from many research that the major receptors involved in the learning and also storage of memory are several types of nicotinic receptors and they are directly linked in the process of memory.

1.03. IMPORTANCE AND SCOPE OF THE PROJECT

Alzheimer’s disease (AD) is one of the major health and socio economical burden with the aged population of the country in many parts of world and the documented rated 14.2% in India.

Neuro degenerative diseases are many in types among them major problems with dementia is one of the major mental health issues in both developed and industrialized countries across the world. Population census predicts many developed countries elderly (crossed sixties) are going to increase seventy percentage in the year 2020 among it India contributes 14.2 percentage.

Alzheimer disease is a type of neurodegenerative disease where a nerve death leads to an imbalance and missed communication between nerves such that sensory and
motor information transmission will be get disturbed, sometimes it may be temperoral but many a times it becomes permanant changes in the individual.

There are many reasons for nerve death and changes in the nerve architecture making it unable to involve in the normal physiological roles. Degeneration of cholingeric nerve holds a direct and prominent role in alzheimers disease

Some studies in India revels that Persons above 40 years of age show 0.43% prevalence where as those aged above 65 years show 2.44% prevalence. The causes for dementia may be due to AD (50 to 70%), blood vessel disease (20 to 30%) or by other nervous disorders. Approximately over 10 million people around the world are affected by Alzheimer’s disease and the severity increases with increase in age.

Allopathic psychoactive drugs have been the mainstay of treating mental illness in India and worldwide. Some nootropic agents (Piracetam) are widely used but the resulting chemophobia associated with them and other similar agents has made their use limited.

During last few years there has been increase in usage of alternative medicines by the patients for such ailments, many herbal medicines have been accepted in our country for treating anxiety disorders and cognitive dysfunctions’ Anticholinesterase are best used in alzheimer’s disease shown effective action in CNS but lack of information about it and predictivity of effect is a unsolved matter.

Limited information about AD is further expanding, prediction of treatment with ChEI but not having complete solvation. So we need an ideal drug in cognitive symptoms.

According to the literature review essential oils of *Cymbopogon Citratus or Andropogon Citratus* and *catnip (Nepea Cataria)* claimed for different pharmacological activities like, anti oxidant activity, anti inflammatory activity, anti microbial activity, anxiolytic, enhancement of brain neurotransmitters, anti-depressant activity. The plants are native herb from India and are cultivated in other tropical and subtropical countries. Establishing whether or not therapeutic effects of both herbs are beneficial to patients requires research and generation of scientific evidence. So in the current study is an
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attempt to establish the scientific data of these plants as common alternative for treat AD which affects neurotransmission related to behaviour and memory dysfunction.

2.0. ORGANIZATION:

2.01. WORK PLACE:

The present work entitled studies on therapeutic potential of two herbal drugs in treatment of alzheimer’s disease was carried out under the supervision of Dr. Raja Raheshwari N. Asst professor, in Karavali College of Pharmacy which is located in the southern part of Karnataka state in the city Mangalore city area known as vamanjoor. The work was monitored in the department of pharmacology in the laboratories and the necessary documents which generated during studies were also stored in the departmental documentation department.

The present work utilizes animals for the screening and the animals were scancened after presenting the work in front of the institutional animal ethical committee (IAEC) and the approval letter given by the committee also affixed in the annexure of the main thesis and the two herbs used in the study were also identified by the botanist Dr. Kempe gowda HOD of department of botany Bangalore university Tumkur. And the same document also enclosed in the final thesis in the annexure part.

2.02. PRODUCTS

In the present study two herbs were used for the screening of their activity against the treatment of alzheimers disease which is a type of dementia.

In traditional practicles in India, plants were used as the source of medicine form the days which are immorable but even today the herbs hold main role in the fulfillment of many medicine and become as a chief source. Even Plants which were used for centuries very high safety margin even on chronic usage but almost all allopathic drugs from chemical sources are having high side effects and created chemophobia in the users. To over come this other alternatives for the chemicals are only the herbal souce even day
by day the consumers are increasing, which made development of the herbal industries all across India.

Aromatic oils are used in the treatment of many major diseases form the date unknown. Since from olden days plants having aroma were used for therapeutic purpose even Hippocrates was prescribing it. An aromatic property of the plants is due to the presence of essential oil which consists of traces of active principle which are volatile in nature and which can be seen in it. It consists of terpenes as a active constituets but their therapeutic potentials have been lately evaluated.

Recent reports have showed that neuro-behavior effects of essential oils. *Cymbopogon citratus* & *Nepeta Cataria*, are aromatic medicinal plants popularly known as “Lemon grass” and “catnip” used in the folk medicine as anxiolytic, dementia and anti-hypertensive. Several pharmacological studies suggest herb posses strong analgesic, sedative/hypnotic, anxiolytic, anticonvulsant. Considering the lack of studies on *Cymbopogon citratus* & *Nepeta Cataria* on the Nervous system and its use in the folk medicine, the objective behind present work was to highlight the Nootropic effects of this essential oils in various Alzheimer induced animal models.

2.03. PROCESSES:

*Cymbopogon Citratus* & *Nepeta cataria* were collected in the month of November, from local suppliers in Udupi & Mangalore, Karnataka, and were authenticated by renowned botanist (Dr. Kempe Gowda department of botany from Bangalore university and the authentication letter issued form the department is stored in the departmental library for documentation purpose and the same copy is enclosed. The authenticated plant material were cleaned well with the help of clean plain water and was dried naturally and the air-dried samples were used for the extraction of essential oil. Size reduction was done by using cutter blade, the cutting was continued until getting a fine pieces which are suitable for subjecting in to the round bottom flask for best packing as particle size of the substance is having a very important role in the extraction process for better yield the herbs were subjected for size reduction. The finely size reduced plant materials were then submitted for steam distillation for extraction and the essential oils
were collected very carefully and are stored in the department to carry out screening activity in various selected animal models.

C. SAMPLE PREPARATION

Fifty grams of clean and dried plant materials of *cytisus capitatus* and *Nepeta cataria* were separately used for the distillation process and the plant materials were freshly cut with a cutter blade machine and the materials from each batch were taken separately and they were subjected for hydro distillation process and the process is carried out for a period not less than 3 hours in a cleaned 250ml steam distillation sets.

i. HYDRO-DISTILLATION:

The following procedures were followed to carry out hydrodistillation for crude herbs of whole plants of *cytisus capitatus* and *Nepeta cataria*. Before starting of the distillation process, samples were taken in the flask and mixed with hot water for a duration of fifteen minutes such that the samples in the flask was made completely wetted with hot water. For cooling purpose the water was kept circulating through out the extraction process and the heating started. The extraction was performed for a maximum of three hours. The cooling was turned off at the end of the extraction.

ii. EXTRACTION OF THE ESSENTIAL OIL:

The distillate was then transferred to a clean separating funnel and 50ml of methylene chloride added to extract the distillate was than transferred to Erlenmeyer flask extraction procedure repeated with fresh 30 ml portion of the reagent. The methylene chloride solution was dried by adding 20 gm of anhydrous sodium sulfate to the flask and left to stand for 15 minutes. As the organic solution was drying, a clean, dry, beaker was weighed and the solution transferred to it, leaving the drying agent behind. The methylene chloride was evaporated from the solution in a water bath at 40°C.

DEMENTIA:
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Dementia is usually chronic and progressive in nature not a disease, but rather a group of symptoms caused by the impact of multiple diseased brain is generally defined as the “destruction of personal skills in knowing what is happening which is going to interfere with the social well being. In dementia, performance of learned motor skills; social skills and control of emotions are primarily affected but not the events from long-term memory.

Dementia not only causes a terrible reduction in the quality of life of the sufferer but also causes difficulty to the care giver because the persons who are suffering with dementia require a complete care and it will be a burden to the care giver which makes the life struggling.

The causes of dementia are many among them primary importance is given to the free radicals. Human body is exposed to different types of environmental toxins daily in one or the other forms due to his routine works. And also due to the exposure of the body to some chemical substances, which may also introduce through food, or through inhalation due to pollution, or as a side effect of a drug or some time due to exposure to the sunlight can generate oxygen free radicals. Drug after administration undergoes metabolism even these metabolic products generation due to metabolism also generates free radicals which can cause neuronal damage along with some tissues in the body which cannot be controlled, but the fact which is severe is once the nerve cells dies there is not regeneration of the cell such that permanently it will be get lost which may serve as a chief cause for the neurodegenerative diseases.

Neuronal metabololism is considered as the second most reason for the dementia because, nerve cells need more supply of ATPs it will get supplied continuously by its own metabolism if the metabolism occurs under anerobic conditions then there will occumaliton of lactic acid may occurs in the nerve cells which alters ther PH. It may get decreased or the cells will be get exposed to the acidic envornment in this acidic envornment many of the enzymes will be inactive or protein degradation may occurs, chromatin condensation may occurs and alos it will leads to the generation of oxygen free radicals overall all defined mechanism becomes a possibilities for the degeneration of the nerve cells which ultimately causes dementia.
Aging is considered a major complication in dementia because majority of the dementia cases are seen in the elders. Age is considered a risk factor in the occurrence of the disease as well as in the progression of the disease too. During aging many physiological changes which arise due to dysfunctions of various organ systems which will not favour normal homeostasis in the body which can slowly precipitate dementia. Other major problem faced during ageing is apoptosis it is nothing but programmed cell death it is quiet common in the aged people, neuronal death occurred during aging will become as a precipitating factor for the dementia.

The above mentioned factor can increase DNA damage it may due to the release of oxygen free radicals, which can also causes genetic manipulation and causes the major reason for the neuronal death. The damaged DNAs will be not in the condition to produce the precursor for the transcriptions and there by new protein supposed to be produced for the normal survival of the cell may be effected. Even the free radicals causes damage to the proteins in the cell wall and the major reason for this is thought to be the ageing as it increases the physiological response in the body.

**SYMPTOMS OF DEMENTIA:**

- Memory loss
- Inability to concentrate
- Reduced in personal skills
- Reduced performance in decision making
- Mental confusion
- Changes in the sense organs functions
- Cannot identify any objects or persons
- Sleeplessness
- Disorientation (place, people, time, vision)
- Absent or impaired language ability (aphasia)

**DIFFERENT STAGES IN THE DISEASE** (Balaraman R et al) 12
1. Stage of Pre-Dementia: this stage can be seen quite before the occurrence of the symptoms of the dementia very early it can been seen in this period the person may develop some symptoms or some times it may be devoid of the symptoms, if care taken during this period the disease can be postponed for some years. Stage of pre dementia is normally seen within two months of the progenessis of the disease.

2. Stage of Early-Dementia: this stage is seen very late period of life when primarily symptoms started with the begning of the dementia. It is considered to occur after a long duriation of an average of twenty years. This stage is seen for a longer time or the person who started suffering form the disease stays back in this stage for the long time.

3. Stage of Moderate-Dementia: this stage is an intermediate stage and can be seen for a moderate duration of years of one to five years in the dementia stage.

4. Stage of Advanced-Dementia: in this period the severity of the disease will be more the person stays in the stage for the duration of more than ten years in average. in this stage all the symtoms, which can be enlisted in the AD can be seen in the patient who is suffering form the disease and who had already crossed the other three statges of dementia. Treating the person who is in the last ie advanced stage is difficult, also the persons life becomes messerable because he have to completely depend on the care giver for his remaning lifespan.

**PATHOLOGICAL CHANGES IN THE AD**

The below explination are about the changes in the brain during AD. Memory storge occurs basically in two region of the brain the hippocampus and cerebral cortex. The hippocampus stands second in the storage of the information; primary preference can be given to the cerebral cortex. Even though hippocampus is having a major prominent work in the processing of the sesory signals of the memory. In alzheimers disease patients brain atopsy shown that a sever shrinkage in the hippocampus region, which is the main pathological changes that occurs in the AD. Due to the shrinkage in the hippocampus region reduced in the blood circulation around the region and leads to
nutrition defency which leads to neuro degeneration which occur in the majority of the cases due to the irreversible type of cell injury.

In the irreversible type of cell injury occurs here due to the shrinkage of the hippocampus generates an anerobic environment in the brain which causes changes in the normal physiology of the cells which causes acidic environment , the pH of the cell reaches to the acidic due to formation of lactic acid the entire internal environment turns to acidic which causes functional changes in the cell some time it can cause permenant damage to the cell become irreversible in their normal functions which can leads to slow death of the cells surrounding the hippocampus which will becomes the chief cause in the progression and occurrence of disease in the sufferers.

Cerebral ischemia is the major reasons for many type of neuronal disorders because lack of oxygen can causes immediate type of metabolic changes in the cell which can cause permanent and non repair able changes in the cell.

CAUSES OF DEMENTIA:

Dementia-like symptoms may temporary develops with under listed reasons .

1. Drugs (almost all the drug which can generate free radicals and can cause changes in the internal envernoment of the cell by change in the pH )
2. Alcohol caused Dementia in chronic and mild drunkers: chronic usage of the alcohol in the young age also in the elders can precipitate the disease and it is considered as a major risk factor.
3. Substance Abuse many centrally acting drug which are having hallucination effect which are abused by many peoples called as drug adicts for its pleasurable effect in the brain can cause a texture change in the formation and release of the neurotransmitter which may become a greater risk factor in the occurrence and also in the advancement of the disease.
4. Cigerate smoking and usage of tobacco : people those who are having a habit of smoking more number of cigeratte in a day who are called as Chain smokers are having a high risk of occurrence of the disease and the ratio is too higher, when it is compared with smokers than that of non- smoker
5. Vitamin Deficiency: vitamins are the micro nutrients which are essential for maintainence of normal physiology of the body and proper functioning of the nervous system. Vitamins are the major source of protection in the body they can counteract the free radicals generated in ongoing events. They act as anti oxidants. It is consider that the generation of free radicals are having a pathogentic role in the occurrence of the disease.

   Vitamins in normal concentration in the blood can over come or act as a prophylactic substance either it can prevent this type of cell injury process which occurs due to the exposure of the cell to the oxygen free radicals. Vitamins are having neuro protective action due to the property of neutralization of the oxygen free radicals. So the diet should consists of vitamins suplimesnts regularly. The vitamins defeciency may occur to vitamin deficiency diet consumption or due to distrubtion in the absorption in the vitamin from the diet consumed due to failure in the transport mechanism.

6. Infectious Diseases: infection if not treated completely, or even after treating if resistance developed due to immonlogical defecencies are due to development of the resistance in the host or may due to occurrence of new infectious disease when the treatment is in progress and even some time failure of the drug in the treatment of the infections it may cause permanant damage to the nerve structure which is the major reasons for the cause of dementia and some examples for the uncurable disease which occur due to infections includes Whipple's disease, Syphilis, Creutzfeldt-Jakob disease, HIV infection they can increase the risk of dementia.

7. Metabolic Disorders like hyperglycemis include diabetis mellitus. Insulin deficiency is the major reason for diabetis mellitus but the complications are shown due to hyperglycemia which increases polyl formation in the body which changes the internal environment of the cell there by it can cause neuropathy in the sufferers. The best possible way to control dementia is only possible by maintaining normal blood glucose level this can be possible by regular medication and regular excersice and monetering of blood glucose level.

8. Pseudodementia: a mixture of reasons may stimulate the disease pathogensis like stress and food habit, disease triggering factor is cell damage it may be due reactive
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oxygen free radical or anxiety stress, this is considered as a major risk factor in occurrence of the disease. Still advance in age around in the late life of a person at age sixty the disease occurs mainly due to the inflammatory reply to many physiological and pathological reasons.

9. Brain Tumors: cancer is considered to be the major burden in the occurrence of dementia. Many of neurodegenerative diseases are due to the lack in the maintainence and nourishment in the cancerous growth due to disturb in the normal feed back mechanism it disturb the normal well being in the tissue due to imbalance in the regeneration and degeneration which may become one of the major reasons for the neurodegeneration.

10. Toxins: exogeneously administred toxins which may arise due to increase in the dosage of drug used in the treatment of the diseases. Some times due to the invasion of pathogens into the body as the metabolic waste they can release the metabolite which are toxic in nature which can cause damage to the celllular strucrute in the nerve some time it turn to be irreversible in nature, which may become one of the chief reasons for the dementia and other type of neurodegenerative diseases in human. Exposure to the industrial hazards and chemicals and consuming of artificial and packed food and preservative used in the packed food are also acts as the chemical mediators in the development of dementia.

11. Normal-pressure hydrocephalus: the cerbro spinal fluid has a major role in the regulation of the pressure in the brain and its surrounding tissues by a very well known phenomenon called as bovensic action. The cerebrospinal fluid distributes the weight of the brain uniformly. The pressure which occurred in the cerebro spinal fluid can also helps in the exchange of the required nutrients form the fluid to the brain tissues and also the liberated waste products of the metabolism form the brain tissue to the cerebro spinal fluid. Any factors which can cause increase in the pressure of cerebro spinal fluid or which causes decrease in the quantity of cerebro spinal fluid causes a tension in the nerves surrounding the brain which can be damaged some time the damage become permanent can cannot be repaired and even cannot be re synthesized so permanently causes dementia.
12. Subdural hematoma: even the internal bleeding called as haemorrhage in the blood vessels like emboli can obstruct the active blood circulation which can slowly causes cellular changes in the brain. Which may be the permanent changes and which cannot be rapirable.

13. Head injuries such as trauma due to accidents

Dementia may occur in different persons due to different reasons and even there are several types dementia are seen but some dementia which occur due to sudden exposure of some stimuli are reversible (drugs, alcohol, hormone, vitamin imbalances or depression) & some dementia which occur due to sudden exposure of some stimuli can become irreversible type (disease which may occurred due to infection which causes weakening of the blood brain barrier and also can effects the nerves in the nervous system can become a major reason for the occurrence of the disease or head injury) and it become a permanent type of demntia.

2.04. PROFILE:

I. CYMBOPOGON CITRATUS

Locally called lemongrass, is a tropical perennial herb. It had wider application in therapeutics in olen days in many countries including India. Itis a Greek word “kymbes” (boats) and “pogons” (beards), resembling to the spikes seen in the flower.

TAXONOMICAL CLASSIFICATION

Kingdom : Plantae
Order : Poales
Family : Poaceae
Species : citrates

COMMON NAMES

English : Lemongrass, Citronella, Squinant

Hindi : Sera, Verveine

PARTS USED: aerial part and entire grass can be used.
SYNONYM(S)

- Lemon grass stalk,
- *Andropogon citratus*.

PHYTOCHEMISTRY (Akhila A etal)†

Main active principle of the grass is the essential oils some times it is also called as the volatile oils. These oils are having the property of evaporation on exposure to high temperature and to the natural environment. Lemongrass has a very similar resemblance smell of fresh lemon, but lemon grass is not having the sour taste but lemon lemon is sour in taste. The phytoChemical investigations conducted with the essential oils of lemon grass commonly called as lemon grass oil,

In the 19th century paracelceus had revealed that many of the compounds responsible for the pleasant odors is due to the presence of the chemical substance which are having exactly ten carbon atoms which are called as terpenes, which smells like lemon, if they were hydrocarbons and terpenoids if they contained oxygen and were alcohols, ketones, or aldehydes. It was found that there are also minor and less volatile plant constituents with 8, 20, 30, and 40 carbon atoms.

Lemongrass oil consists mainly of citral and some terpenes. borneol 0.1-0.4%, alpha-cardinene 1.0%, delta-cardinene 0.3%, delta-3-carene 0.03% beta- 0.18% beta caryophyllene 0.18%, βcaryophyllene oxide tr. 0.61% 1,8-cineole . citral a 41% citral b , 20-30% citronellal 0.1-5%, citronellol 0.1%, citronellyl acetate 2.2% 0.96% 0.72%, p-cubebene 0.5%, 3-cuminyi oxide, a-curcumene, p-cymene 6.6% p-cymene 0.20, p-cymene-8-ol, decanal 2%, n-decylaldehyde, 3,7-dimethyl-7- octen-1-ol, dipentene 0.23% P-elemene 0.42-1.33%, elemicin S, elemol 1.20%, geraniol 0.5-40.2%, geranyl acetate 1.95-3.0% 1.0-3.0% 3.58%, ec-humulene, limonene 1.9-2.42%. tr, linalool 0.8-3.4% .

linalyl acetate, transip-menth-2-en-1-ol tr.-0.1%, methyl heptenone 2.62%, 6-methyl hept-0.5-2.3%, myrcene 0.1-19.2%, nerol 0.3-4.5%, nonanal 0.2-0.7%, 2-
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nonanone 0.07%, 4-nonanone 0.3%, cis-p-ocimene 0.06% 0.2%, trans-P-ocimene 0.1-0.2%, p-phellandrene 0.07%, oc-pinene 0.19-3.5%, p-pinene 0.19%, terpinen 0.41%, oc-terpineol 0.2–2%, p-terpineol 0.17-0.40%, terpinolene 0.1%, oc-thujene tr.-.01%, x-thujone 0.1%, undecan-2-one 0.4-0.6%.

The major terpenes in C citratus include citral-α or geranial (10%–48%) and citral-β or neral (3%–43%), borneol (5%), geraniol (2.6%–40%), geranyl acetate (0.1%–3.0%), linalool (1.2%–3.4%), and nerol (0.8%–4.5%). (Paula Melarirî et al) There are traces of camphene, camphor, α-camphorene, fenchone, α-pinene, β-pinene, terpineol, terpinolene. (Akhila A et al)4

THERAPEUTIC USES: (Arhogho E. M., etal)9

*Cymbopogon citratus* used in tropical and subtropical countries and in producing a pleasant aroma in their herbal teas. It’s also used in the treatment of fever, jaundice, hypertension, as analgesic, in soap making and as an insect repellant, ameliorates nervous and gastrointestinal abnormalities. Their essential oil have antibacterial and antifungal, activity. Its sedative and anticonvulsant properties as well as its use as an anxiolytic agent has been documented.

Analgesic externally applied fresh juice of the aerial part of the herb can show best pain relieving property, Anti Pyretic which is having property to increase perspiration due to its cutaneous vasodilation increase in blood cirucalition in the superficial skin which are exposed to the environment. & Anti Septic: It can reduce pain and inflammation .Anti Depressant, Anti Microbial and Anti Bacterial: internally or externally it can inhibit microbial and bacterial growth, Astringent: this property is helful in stoppage of bleeding in gums or any external wound they can cause sudden sedimentation of skin proteins in the applied areas there by they can form a plug which can prevent the oozing of blood, there by act as a barrier and also consider this as an life saving properties .Carminative: It can efficiently handle gas trouble. ,

Deodorant: it can reduced bad odur in the mouth and also in sweat it may be acumuludated to its strong potent antibacterial property which helps to show the activity and long lasting cooling action made it popular in usage in the olden days and in some
rural population but due to processing and storage problem they are not marketed for this purpose even though they are economical naturally available and long time effectiveness, no irritations on skin and allergies they are consider as a safest upon oral administration not only orally but even applied topically does not shown any allergic response.

Diuretic carbohydrates present in the herb may be responsible for this activity, it increase the urine formation and the frequency of excretion also increases this property are helpful in the treatment of edema due to unkown reasons and also combine the property which can aid as an antihypertensive agent Febrifuge, Fungicidal, Galactogogue, Insecticidal, Nerve, nervousness, vertigo, Alzheimer’s disease, Parkinson’s epilepsy & aTonic: (Arhogho E. M., etal)  

![Image of Cymbopogon citratus and Catnip](image)

**Fig: 4. Cymbopogon citratus, CATNIP (NEPETA CATARIA)**

**II. CATNIP (NEPETA CATARIA)**

The name Nepeta (Nepete in Italy; Cataria means cat in Latin). The genus Nepeta (Lamiaceae) is represented by approximately in Asia, and also Europe and Africa and 33 species are present, 17 of which are endemic in Turkey

**Name :**Catnip
Latin: *Nepeta cataria* L.

**TAXONOMICAL CLASSIFICATION**

- Kingdom: Plantae
- Division: Angiosperms
- Order: Lamiales
- Family: Lamiaceae
- Genus: Nepeta
- Species: *N. cataria*

**COMMON NAMES:**

- Cataria,
- Catmint.

**Parts Used:**

- Leaves,
  - fresh or dried

**Synonyms:**

- Catmint,
- Catnep,
- Catnip.

*Nepeta cataria* (appr two hundred and fifty species of Catnip).

**PHYTOCHEMICALS**

Most conducted studies on Nepeta species are done to check the potential activity of EO & it is found to be 1,8-cineole, and it has been reported that 1,8-cineole has remarkable antioxidant activity.

Nepeta species contain monoterpenes, sesquiterpenes and cyclopentanoid iridoid derivatives, as well as nepetalactone. EONC possesses greater amount of monoterpenes
(95%), mainly 1,8-cineole. However, the major component of essential oil of N. ciliaria has been found to be β-caryophyllene oxide (% 40.7), a sesquiterpene.

Nepetalactone, Acetic Acid, α & β-nepetalactone, , nerol, geraniol, and citral. The same monoterpenes Also ursolic acid, beta-sitosterol, campesterol, α-amyrin, betaamyrin and sitosterol β-glucopyranoside.

The chemical ratios seen in the essential oils varied depending upon the place the plants are grown and climatic condition of the place depending upon that it adopts its composition. Similar to the previous reports, nepetalactone isomers is the major constituent of the Catnip EOs in all stages of growth, which reached its maximum level at the floral budding stage. and alpha-citral as the most abundant compounds of the catnip oil. α Pinene β Pinene are considered very rich in the chemical composition but the proportion get increased upon the growth and development.

TRADITIONAL USES: (Ashutosh A etal)\textsuperscript{10}

In traditional system, this plant was used in the management of various smooth muscles pain occurs due to spastic pain and also used in the treatment of various allergic conditions, and to treat infection due to its cidal actions of the bacteria it also posses strong free radicals scavenging activity upon usage it can act similar to some vitamins. EOs, especially with known antibacterial effects (Ashutosh A etal)\textsuperscript{10}.

50% nepetalactone, 33% nepetolic acid, and 14% viscous yellow neutral in N. cataria essential oil. Ursolic acid, flavonoids and phenolic acids were also detected in N. cataria essential oil. Nepeta species are widely used by the reason of their antiseptic, diuretic antitussive, and antiasthmatic activities in folk medicine.

Cat sniffed, catnip can stimulate it, but when eaten it acts as a sedative. Nepetalactone causes a hallucinogenic effect. May be similar to LSD, marijuana. catnip acts as an aphrodisiac, not found in humans the cat is reacting to similar "feel good" pheromones can also be observed. The response shown by activation of olfactory system. Essential oils having a very pleasant flavor which make it to appreciation form the consumer and even having many therapeutic applications. As a flavouring agent the herb was widely used in the preparation of tea which produces a good aroma especially in
the cold region the people widely depends on these type of herbal teas to combat the cold condition

Therapeutic uses of Catnip Essential Oil due to its properties like antispasmodic (it can be used in the treatment of the sudden spasmodic condition occurred in the stomach due to the constriction of the smooth muscles of the stomach as its is having muscle relaxing property), carminative (it can expels the gases in the digestive system, providing comfort feeling the person after regurgitation), diaphoretic (this property made it to use widely in the management of fever, by excessive sweating it can cause relief from fever, it is having conditioning action in the body, emenagogue, nerve, stomachic, stimulant even seen in central nervous system and also in the respiratory system, urinary system, skin and cardiovascular system, astringent,astringent property make it to be useful in the healing of wound and especially healing of ulcer, on nervous system it is having wide role especially dose dependent it is having sedative action upon inhalation it can decrease anxiety in the animals modles etc. it is having sexual stimulant property which is widely seen with some speices in animals especially with cat it can cause constriction of the blood vessels in the skin and can cause hair rising experience in cats.

*Nepeta cataria*, can control fever which is having property to treat even some time of viral and flu fever, Stimulates the appetite it can also increase gastric hydrochloric acid secretion which can cause appetite in the person who consumed the essential oil and also other reason why it is used popularly because it is having good flavouring and little of counter irritant property of the drug also made it to use as a appetizer in the people those who have bad or less eating habbit.

3.0. THE PROBLEM / HYPOTHESIS

3.01. INTRODUCTION:

Alzheimers disease can occur in all caterogires of age it was also noticed at the very early age of birth (age zero) the reason for occurrence of disease was considered as genetic factors which carries certain genes which are involved in the formation of
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disturbed neuronal plaques which can precipitate alzheimers the only possible treatment is to treating the genes.

During adult age also disease can be observed during the age twenty the reson behind many cases included as deposit of amyloid proteins.as advancement in age around age fourty the disease triggering factor is cell damage it may be due reactive oxygen free radical or anxiety stress, this is considered as a major risk factor in occurrence of the disease. Still advance in age around in the late life of a person at age sixty the disease occurs mainly due to the inflammatory reply to many physiological and pathological reasons. In very late stage of life at age eighty and above the reason for disease was considered as loss of synapse, which disturbs neuro humanal transmission, neutritic plaques which causes destruction of functional areas in the brain.

➢ Progressive deterioration of short term memory or the in ability to learn and retain small amounts of information;
➢ Language disfunction (aphasia) such as difficulty finding words and loss of auditory comprehension leading to inability to understand questions and follow directions; and
➢ Inability to draw and recognise two and three dimensional figures (Brain.KR etal)\(^\text{17}\).

3.02. DESCRIPTION:
The development and also the progession of the disease is regulated form many of the factors which are exposed form the surroundings may be in the form of inhalational chemicals or in the form of adverse effects of the drugs or in inborn metabolic and genetic makeup of the individual body the descriptions are given below in each sections

INCREASE RISKS FACTORS: FEMALE :

Detailed studies on literature review on current neuro sciences, revealed that females are more prone to alzheimers disease when compared to males, so gender is consider as a major risk foctor for the progenesis and progression of this dread ful
disease. Even hormonal changes during amenuria like decrease in estrogen level also evidence for the disease

HIGH BLOOD PRESSURE FORM LONG TIME:

Blood pressure is defiend as the lateral pressure exerted by the blood on the vessels while flowing which govern the perfusion rate in the person as human brain is always supplied with high perfusion for its large requirements of glucose and oxygen when exposed for high pressure may lead to breakdown and leakage of minor cappliers can some time leads to internal hamerrohage, this thrombus may leads to necrosis of the surrounding tissues may leads to permenant damage, the special feature with the brain is once neuronal death occur it becomes a permanent loss in the neuronal count as it cannot be regenerated, may leads to deficiency in its actual functions

EXPOSURE TO HEAD TRAUMA:

Repeatdly exposing head to trauma or some time unintentional accidents leading head injury may be a risk factor and other type like professional sports personalities who enage in sports like boxing may also very easily prone to the disease. Not only the head trauma but also the size of the head alzheimers disease is most common in people with small head size. Even the advancement in the age with small head size or repeated trauma or head injury may also precipitate this disease

ADVANCEMENT IN AGE:

It is one of the natural factor which can induce disease in the person which cannot be control but progesion of the disease can be identified by sutable diagnosis test and precautions can be taken.

Percentage impaired age wise suggest that in the age sixty five to sixty nine ten percentage of impairement was recorded. In the age range fromm seventy to seventy four it was found to be fifteen percent and in between seventy five to seventy nine it was documented of nineteen percent and in age from eighty to eighty four it was twenty percent and age from eighty five to ninty nine it was around fourty percent and age hundered and older it was documented a highest impaired rate above ninety percent with
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this document it is suggesting that advancement of age is a major risk factor in the Alzheimer disease.

Among all the hypothesis which are put forward in understanding the pathogenesis and progression of alzheimer disease it proves a common information that the changes in the brain is mainly due to the advancement in the age. It is a major factor which can leads to worsen the disease due to its distractive action on neurodegeneration which can disturb neurohumorol transmission in the brain.

GENETIC FACTORS:

Gentical studied carried in mapping and cloning in 1987 found that the gene located in chromosomal sequence of 21 can code for APP a protein which have a major role in signaling in transport in the membranes of endoplasmic reticulum and even the building blocks proteins which makes amyloid protein which is having a close relation with the receptor proteins.

Alteration in the gene ie the mutation is also considers a major risk factor. Generation to generation the disease can be transmitted and causing a burden to a sufferer. Now due to the advancement in the recombinant technology it is becoming to understand better and can also able to correct the mutated gene by using gene theraphy but hundred percentage successes has not been achieved but researchers all over the world are working on this gene.

3.03. DETAILS:

Alzheimer disease is a general type of dementia, the dementia can be classified by different ways depending on their clinical presentation, major type of classification uses symptoms as the major parameter in the classification, because by observing the symptom it become easy to diagnosis the disease in the primary condition. But the symptoms of all dementia is almost same only by proper diagnosis and thorow detail examination makes it easier to identify the disease. Depending on the appearance of the disease or appreance of disease symptoms alzheimers disease can be classified in two types they are
1. Early onset alzheimers disease
2. Late onset alzheimers disease.

The first type of alzheimers disease ie early onset is seen before sixty years of age and the second type i.e, late onset is seen when person crosses sixty years of age.

SYMPTOMS OF ALZHEIMER'S DISEASE:

The pathophysiology of AD may begin long before clinical symptoms are apparent. There is an extended time course, with risk factors from genetic predisposition and environment in the clinical expression of the disease.

Symptoms like decreased concentration is the major symptom which destroy persons life style and make him to dependent to care takers for doing their routine works due to demensia which make the condition worsen than the normal.

Some research also suggests that Atrial Fibrillation can also causes blood coagulation casuing stroke leads to Alzheimer's Disease. The clotted blood inside the capillaries in the major blood vessels are called as emboli, once this emboli formation occurs it obstruct the passage of blood in the respective blood vessels, especially brain tissue which requires more blood circulation is affected a lot. It may leads to the shrinkage of the region which is supplied with affected blood vessels. The only possible ways to over come this typ of complications is to rule out the emboli and the normal circulation should be achieved in the blood vessels.

Alzheimer’s disease pathogenesis and progression of the disease can be given schematically by using the following flow chart. Which explains the overall the involments of many mechanisms in the precipitation and elevation of alzheimers disease in the victim (Achliya G etal.)

AMYLOID HYPOTHESIS

In the extra ceullular space upon the stimulation of the secondary messangers in favoured environment it leads to the deposition of plaques of beta amyloid proteins. in the same way In the intra ceullular space upon the stimulation of the secondary
messangers in favoured environment it leads to the deposition of NFT. Due to the change in the internal environment of the cell it will leads to disturb the homeostasis mechanism of the cell. Homeostasis is the maintainence of the internal environment of the cell even there is slight fluctuation in the internal environment by utilizing body componentary mechanism. Due to this disruption it leads to disturb calcium ion concentration in the cell.

Calcium ion act as secondary messanger in the cell communication. Alteration in the calcium ion concentration leads to interfere in cell communication so fails to exhibit homeostasis. It leads to generation of oxygen free radicals, the generated oxygen free radicals causes some irreversible changes in the cells in the nerves making it permanently damaged and function less. This may be the major pathogenesis step involved in the progression of the disease. Because the nerve tissue once get damaged and it is difficult to get repair and also the regeration is not possible. It may leads to deficient in the number of the nerve tissue there by the release of the neurotransmitter by the nervous system will be affected a lot there by leads to the abnormality in the normal physiological function of the body. When cholinergic nerve concerned this can lead to disturb in the both learning and memory tasks in the humans.

Various substances stimulates formation of plaques and tangles, inflammatory reaction includes Microglia, Astrocytes, Free radicals.

**NEUROCHEMISTRY**

The neurochemical imbalances occurs with AD. Researchers reported that neurotransmitter level in cerebral cortex is directly propotional to the neuronal number. Degradation of neurons causes reduced neurotransmitter level a new hypothesis called cholinergic hypothesis bases on this factor.

It not only occurs with destrucution of neuron but also due to elevated levels of two enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) which hydrolyses acetyl choline, which causes a drastic decrease in the level of acetyl choline a primary neurotransmitter of cholinergic nervous system which helps in consolidation of
memory. The current available therapy also depends on targeting this enzyme by inhibiting it for protecting acetyl choline from degradation.

SYNAPTIC AND NEURONAL DEATH (NEURODEGENERATION)

Synapse is the effective junction in between the nerve terminals where the essential informations are transferred between the nerve through a chemical mediators called as neurotransmitters, here we can find two nerves connected through a chemical connection rather than anatomical connections. They are very much essential for a nerve to communicate. Depending on nerve secretion at the terminal neurotransmitter the nerves are named like acetyl choline form cholinergic nerve.

Alzheimer disease is a type of neurodegenerative disease where a nerve death leads to an imbalance and missed communication between nerves such that sensory and motor information transmission will be get disturbed, sometimes it may be temporal but many a times it becomes permanent changes in the individual.

There are many reasons for nerve death and changes in the nerve architecture making it unable to involve in the normal physiological roles. Degeneration of cholinergic nerve holds a direct and prominent role in alzheimers disease.

Granulovacuolar degeneration are more commonly found in Alzheimer’s disease.(Achliya G wtal)¹

Change of nerve cells during Alzheimer’s disease it can cause disintegration of microtubules leading to the degeneration of the nerve and nerve structure get change making it functionless and also death of the group of the nerve the main reason for this the deposition of beta amyloid plaques, upon precipitation it generates an oxygen lack environment there by causes cell injury the neuronal injury once occur it become permanent and irreversible. So the dementia once occurs in the person in any of his/her life span will be permanent and irreversible. But if care taken in the primary stage it can be controlled and even we can prevent of occurrence of the disease

HYPOTHESIS OF ALZHEIMER’S DISEASE :
Alzheimer disease is one of the major serious complication among the central nervous disorders caused primarily due to neuro degeneration, upto many years the pathogenesis of AD was not known and it was neglected with the confusion of age induced disease but recently a great importance have been given in this area and lot of research works are in progress in theis area. As in the world total population the major propotion of the population is form elders who is living in their fourties and above. Even some epidemiological studies also suggests that by the year 2020 the worlds elders population will be get double there the complication occurs with this disease also get double off, so this area of research is having lot of pressure in development of the new drug to manage the needy. Years together in the research on this area concludes with Various hypothesis which are put forward in order to understand the possible pathogenesis of alzheimer’s disease and very important among them are summersied here very briefly. Even many hypothesis are becoming very strong in the treatment of the disease with relevant scientific documentation of the disease throughout the world.

**TAU HYPOTHESIS:**

Among all hypothesis put forward to understand the possible pathogenesis of alzheimers disease tau hypothesis is having a major role in the precipitation of the disease. Tau proteins are the micro filamentary proteins upon exess gene expression the production of this tau proteins get increases which then slowly starts to deposits on the nerve surface causing it to diseased by interfere with its neuronal communication mechanisms leading to death of the nerve cells. The nerve cells once under go degeneration then they donot have the protpery to degenerate so it causes permantent damage in the suffers. This occurs mainly due to the Presence of neurofibrillary tangles which appear like a paired helical filament –PHF arises, it occurs due to accmuilation of tau proteins a microtubule-associated protein (MAP),
Fig 4: Disease progression in tau hypothesis

STEPS INVOLVED IN THE PATHOGENESIS OF AD

TAU HYPOTHESIS

- Accumulation of phosphate in the surface of tau protein will causes it to develop a filament which is paired by its nature. The first step phosphorlation is the activation step which then stimulates the other steps in the progression of the disease.
- Now on the free surface of the neurons the paired helical structural filaments starts to deposit very slowly.
- The paired helical structure form some kind of non functional proteins which are called as non functional tau proteins which got deposited on the surface of the neurons then starts to interfere with the normal function of the neurons. some time even it can cause irreversible nerve damage.
- The other possible mode of action of tau protein in the pathogenesis of alzhiemers disease is that it can stimulate the formation of neutric plaque. Once the formation of neutric plaque started in the nerve it is the indication of the approach of nerve towards its end. When plaques are deposited in high number slowly the nerves start dying, so it causes a permanent dementia in the person.
Amyloid Hypothesis:

Accumulation of beta-amyloid plaques which is made up of beta-amyloid proteins and apoE, is the main pathogenesis behind the hypothesis.

APP is a amyloids precursors proteins which can be seen in between the cell membrane. Different enzymes can seen in this region which includes alpha, beta and gamma secretases, among this alpha secreatase plays a major role in the precipitation of AD. These alpha secretases causes break down of APP into small fragments, they will be more soluble fragments when comparing with the source from where they got generated. The small pieces are having the property of aggregation they starts grouping together, they can also disturb in the synaptic transmission after getting precipitated on the synaptic region they can cause impairment in the memory.

The aggregated parts of amyloid proteins then strats to deposit on the nerve fibrils, but during prolong exposure it causes toxicity in the nerves. They can cause inflammation in the nerve due to this the deth of the nerve cells may occur. Even apoptosis may also be affected.

INFLAMMATION:

Serum amyloid P and alpha1 antichymotrypsin are inflammatory proteins causes inflammation in brain areas which has a chief major prominent in AD. In the current allopathic treatment many of the anti-inflammatory agents are used in the combination while treating alzheimers disease, as alone anti-inflammatory agents are not having any role in the treatment of the disease. But it can act synergistically by preventing neuro inflammation. Relief form inflammation by using this category agents hasten the drug theraphy. Even the neuro inflammation causes permeant damage to the nerve structure and even also causes necrosis in the blood vessels which can generate hypoxia conditions in the surrounding tissues which can cause a permanent non repairable damage.

FREE RADICALS:
Role of oxygen-free radicals in promoting amyloid aggregation, accumulation of this proteins was identified as a hallmark in the patients of Alzheimer's disease (AD) especially in lack of oxygen environment like ischemic and tissue-hypoxia.

CHOLINERGIC HYPOTHESIS:

The neurochemical imbalances occurs with AD. Researchers reported that neurotransmitter level in cerebral cortex is directly proportional to the neuronal number. Degradation of neurons causes reduced neurotransmitter level a new hypothesis called cholinergic hypothesis bases on this factor. It not only occurs with destruction of neuron but also due to elevated levels of two enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) which hydrolyses acetyl choline.

ACETY CHOLINE PATHWAYS

The acetyl choline secreted form the para-sympathetic nerves. Upon stimulation it will be get synthesized from precursors which can be seen the vescicles in the parasymathetic nerve terminals along with the enzyme synthesizing it. The areas involved in the synthesis of acetyl choline are Neocortex, Frontal ,Amygdale, Hippocampus, Nucleus basalis of meynert. Acetyl choline synthesis is a simple esterification reaction ie is called acetate activating step with the help of the enzyme choline synthetase.

CHOLINERGIC IMPARIMENT

Turn over of acetyl choline is the natural feed back mechanism to regulate its concentration in the nerve terminals. It will be regulated by auto receptors situated in the nerve terminals and already secreted neurotransmitter it will be balanced by some metabolizing enzyme present in the nerve terminals they inclue acetyl choline esterase and butyryl choline esterase. Due to over activation some time it causes complete metabolism of the released acetyl choline it leads to the deficiency of the neurotransmitter, which leads to abnormalities when disturbed to the normal
physiological role. SDAT disease affects 3 major areas in the brain, Cerebral cortex, Basal forebrain, hippocampus

**BRAIN AREAS IN ALZHEIMER’S DISEASE:**

![Alzheimer's disease brain areas](image)

**Fig5: Alzheimer’s disease (areas in brain)**

**ALZHEIMER'S DISEASE OVER VIEW** (Brunton L etal)\(^{18}\)

A highlight on some of the pathophysiological properties which are involved in the alzheimers disease (Patil S etal)\(^{123}\).

1. Formation and deposition of amyloid plaques in the nerve tangles
2. formation of neuro fibrilllary tangles
3. neuronal dengenaration
4. beta amyloid is a proteinous substance can precipitate in the nerve terminals leading to cause impairment in the transmission and neuronal death. These amyloid plaques upon depositon can cause neuro toxicity which becomes the chief cause for the progression of the AD.
5. APP gene gamma secretase increase in A beta formation
6. tangles having aggregation of highly phosphorylated tau protein neuronal protein
7. Cholinergic system dysfunction or abnormalities in the formation and secretion of acetyl choline form the parasympathetic nerve terminals, making it to secrete less
amount of acetyl choline which does not match the requirement or degradation of the secreted acetyl choline by choline esterase enzymes.

8.04. HISTORY:

ALZHEIMER’S DISEASE A HIGH LIGHT:

In the year 1907 a German psychiatrist Alois Alzheimer was the very first person who was working on the aged person dementia problem which were not known properly during that time studied on dementia occurring in the aged suffers coined the term Alzheimer disease. On investigation on the patient he noticed senile plaque and neurofibrillary tangles (cerebral cortex) while doing autopsy in a memory lost 50 year female patient named Auguste D. it is recognized by cognitive impairment and psychiatric complications.

The possible treatment were available in the treatment of this disease includes in the current and past history includes Pharmacodynamics, Possible mode of action of drugs, which are claimed to treat dementia can be enlisted as follows. The drug can follow any one of the below enlisted mechanism to elicit their response.

1. Increasing global / regional cerebral blood flow (CBF)

2. Direct support of neuronal metabolism.

3. Improving the level of neurotransmission.

4. Improvement of discrete cerebral functions, e.g. memory

All cerebroactive drugs, basic assumption has been that improvement in cerebral circulation is possible, real and therapeutically useful.

DRUGS ACTIVE IN CEREBRAL

a. Cholinergic activators:

- Tacrine,
- Rivastigmine,
- Donepezil,
b. Glutamate (NMDA) antagonist:
   - Memantine

c. Miscellaneous cerebroactive drugs:
   - Piracetam,
   - Pyritinol,
   - Dihydroergotoxine,
   - Piribedil,
   - Ginkgo biloba.

Tacrine is the first centrally acting anti-cholinesterase to be introduced for AD can work to compensate the level of acetyl choline in the nerve terminals of brain by preventing it degradation by blocking the hydrolyzing enzyme (Joshi H etal)\(^\text{36}\) but due to presence of muscaranic blocking side effects had made it limited use. (Vasudevan M etal)\(^\text{62}\) many other natural and semisynthetic cholinesterase inhibitors are widely used in the mangament of the disease symptoms in the treatment. It has mild side effects.

NEW DRUGS UNDER RESEARCH WHICH ARE HOPED FOR THE TREATMENTS:

- Cholesterol-lowering drugs.
  - Atorvastatin
  - Simavastatin.

- ANTI-OXIDANTS.
  - Vitamin E,
  - Ginkgobilba,
  - Melatonin,
  - Idebenone and
  - folic acid

- ANTI-INFLAMMATORY DRUGS.
  - Aspirin,
  - Ibuprofen,
  - Indomethacin,
DICLOFENAC

- Metal chelator (Desferrioxamine, Clioquinol),
- Vaccines (AB-42 can-1792),
- Monoclonal antibody (m266)

NERVE GROWTH FACTOR TO KEEP NEURONS HEALTHY (Avadhesh C. et al)\textsuperscript{11}

Also there is a predominant role of cholinergic muscarinic receptor system in learning and memory deficits but also speculated multiple neurotransmitter receptor interplay. these nerve growth factor are having direct role in the stimulation of the growth of nerve which are having specific role the possible mode in the treatment of the AD is to improve the cholinergic transmission across the brain. These growth stimulating factors are having a key role in promoting the growth of the nerve when the new nerve get generated or damaged nerve got repaired they can release the synthesized neurotransmitter both synthesis and release become active and also it can be treated by pharmacological intervention to increase cholinergic transmission.

NOOTROPIC AGENTS:

Nootropics (psychotherapeutic agents/ “smart drugs”), act as a booster in brain which facilitate the acquisition of memory and enhance memory retention (LaddeShivakumar)\textsuperscript{99}. They can overcome or retard cognitive decline occurring in old age and in some diseased condition. These drugs should possess the following properties:

- Facilitate learning acquisition and memory consolidation, and prevent or mitigate impairment of memory induced by aging, amnesic agents and other averse factors.
- Facilitate interhemispheric transfer of information.
- Improve tonic corticle control over subcorticle centres.
- Not to induce any overt behavioral or autonomic effects even on long term administration.
CLASSIFICATION OF NOOTROPIC AGENTS WITH MECHANISM OF ACTION:

A number of drugs, belonging to different chemical families or groups are claimed to show nootropic activity. These are

1. **Nootropic (Cognition Enhancers):**

Piracetam and its congeners aniracetam and oxiracetam, (effective in energy metabolism). This category of drug are widely used in almost all part of the world not only with the aged population but also with the young and children those who are having difficulty in remembering or poor memory or children with attention deficient disorder. They are widely used in different formulation. Especially with children it is used in the form of syrups. Even it is well documented and used widely due to having a promising role in the improvement of memory with poor learners and widely marketed in India under different names also the global market of the drug was found to be high it covers a major instrest in the economical sector of the countries, but the exact mechanism behind this is not clear but it is thought to be due to increase in the relase of the ATPs in the nerve terminals which can boost up the neuro humerol transmission across the synapse region.

2. **Metabolic Enhancers:**

Dihydroergotoxin (Codergocrine), Nicergoline, Piribedil, Pentoxyfylline. The main acton of this metabolic imporving drug is that it can increase the activity of the cardio vascular system by their direct role on the blood circulation by having a influence on blood vessels in the cranial system. These act by increasing global or regional cerebral blood flow (CBF)/ it can also due to the stimulating propry in the central nervous system is considered as a psycho stimulations in the regions of higher centers in the brain.

3. **Cholinergic activators or Cholinesterase inhibitors:**
Tacrine, Rivastigmine, Donepezil, Gelantamine, Alicept, Exelon. AChE prevent the break down of the neurotransmitter ACh (label B). Thus ACh is given extra time to transmit messages. Acetyl choline is the major neuro transmitter in the transmission of the nerve impulses in the formation of the memory in the nervous system and it was thought that the reduction in the level of acetyl choline is the major reason behind the pathogenesis of the alzheimers diases and a hypothesis is also put forward which explains the role of acetyl choline the formation of the memory and it is called as cholinergic hypothes. The current allopathic treatment of alzheimers disease uses anticholine esterase inhibitors which can block the enzyme reversibly there by it can prevent neuronal degradation of acetyl choline.

4. **Vasoactive cerebral protectors:**

    Pyritinol (Pyrithioxine). They protects the brain and other nevers by its property of nourishment it can increase the nourishment in the tissue this can be achieved by constant supply of brain the regions like brain which depens on high amount of oxygen and glucose and also causes vasodilation which can increase the cerebral blood circulation and provide a constant supply of nutrients which are required for the synthesis of the essential substances which can nourish the brain or they can also have an influence on the sympathetic overflow by having a modulatory role on the synthesis of sympathetic nervous system neurotransimenter like nor adrenaline which can show its effects on monoamine receptors. Vasodilation is considered to be an important phenomenon in the reagulation of the circulation which required since increase in blood supply in the brain regions can keep it highly active and can supply rich nutrients and also help in the activation of some nerve which are engaged in the regulation of the normal physiological functions in the body.

5. **Anti-inflammatory drugs:**

    Steroids and NSAIDs. They can reduce various secondary mediators of inflammation which can be seen the vesicles or on the packet where get filled
with the fluids, which can elevate the signs of inflammation their by leading to stress on the cell some times leading to permanent loss of cellular structure and also normal function leading to necrosis. But neurons once destructed cannot be regenerated.

Neuro inflammation is considered as one of the major risk factors in occurrence of many nervous diseases. The released secondary mediaters for the inflammatory packet plays a crucial role in the progression of the disease, even they are also prone to number of infection caused by bacteria. Nerve cells with inflammation causes degeneration of the original structure of the nerve cells such that it makes it function less. The only possible way to combat this is by using NSAIDs which can prevent the formation and release of the secondary mediators of the inflammation.

Mono therapy with non steroidal anti inflammatory agents shown a promising role in the improvement of the disease system by unknown mechanism, still it is unclear.

Many drugs under this category are available in the market which posses strong anti inflammatory action. Prevention of neuro inflammation by using these catogery of drugs some time can improve cognition by its neuro protective function but individually drug cannot be used in treatment of alzheimers disease but in combination it can be used but how drugs engaged in workd is still remains unclear.

6. Antioxidants:

Many naturally available sources are rich in vitamins which includes fruits and vegetables which pocess a storng free radical scavengering action in the their by it can prevent neuronal degeneration and also effective as neuropro-tective agents Vit E& C, Ginkgo biloba, Flavanoid. Lycopin which is obtained form the tomato is also claimed for the anti-oxidant activity. Even lycoping is used in the topical applications to prevent the age induced wrinkiling of the skin which causes due
to the death of the cells due to generated free radicals which shows promising role in the management of the alzheimers disease.

MISCELLANEOUS DRUGS:

The below mention categories of drugs do not influence the major pathway concerned with the alzheimers disease but it can show betterment or improvement in the alzheimers disease by acting on some of the compensortry pathway. That is the reason they are not mention under the category of nootropic agents. Different categories of drug can be used in treatment of alzheimer disease available in combination with the nootropics in market they includes :

ANGIOTENSIN CONVERTING ENZYME INHIBITOR:

It belongs to a class of antihypertensive and also very widely drugs under this category used in the management of various cardiac complications mediate their action by preventing the formatin of active angiotensin II. ACE inhibitors like captopril, enalapril a trandilapril has comparable effects of nootropic drug oxiracetam. Further ramipril and losartan have shown significant improvement in basal as well as scopolamine-impaired performance in experimental animals.

SILDENAFIL (VIAGRA):

Sildenafil has been introduced to manage the male impotency and which can increase the dilation of the blood vessels also to serve the purpose and nowadays they are a high economy for many of the pharmaceutical manifesteer across the world, was shown to improve memory in experimental mice when injected intraperitonially. The possible mechanism is thought to be improving in the cerebral circulation due to its dilation action in the arteries. They mediate their action by inhibiting enzymatic action (phosphodiesterase) there by increasing free nitric oxide in the nerve terminals. They are considered as endothelial rexalation factors.

5HT₃ ANTAGONIST:
Serotonin is a amine neurotransmitter which elicts its action by binding on its specific receptor they are many in number they can show site dependent actions. many of antagonist of serotonin receptors are widely used for their different pharmacological actions. Among that one drug is Ondansetron, a selective 5HT₃ antagonist which is widely used as an anti-emetic agent some experimental studies on animals shown that ondesetron shown significantly improvement in the learning and memory.

ESTROGEN:

Estrogen is a sex hormone of females which regulate the puberty and adult hood in the womens. studies suggests that improvement in memory was observed in some postmenopausal women. Estrogen is having a negative impact in the memory due its rapid feed back mechanism by auto regulating mechanism.

L-ARGININE:

Arginine is a aminoacid they are categorized under excitatory neuro transmitter they mediate their action via binding with N-methyl D aspartate receptors which are found on the terminals. It is also suggests to posses antio oxidant activity. This property of the drug made it usage in the combination of the anti-oxidant prepration and generally it is used in the aged population as a preventive drug in the management of the alzheimers disease also it can be used.

Animal studies suggest that Nitric oxide (NO) enhance memory, also NO precursor, L-arginine administration increases the NO concentration in brain . nitric oxide can increase in the cerebral blood flow by dilating the artiries. This property of gases can helps in the supply of proper glucose

SSRIS:

Serotonin is also called as five hydroxyl trypatmine or 5-HT is a amine neuro transmitter plays a pivotal role in the transmission of sensory nerve impulses. It is synthesized and secreted from serotogenic nerves terminals its secretion is auto regulated by reuptake mechanism which hinders its concentration in the nerve terminals as memory is a complex process which involves a multi neurotransmitter enganged with it
many studies suggests that decrease in amine transmitter can also cause dementia in persons, now already in the market these reuptake inhibitors are widely used Selective serotonergic antidepressant drugs fluoxetine, sertraline and tianeptine have influence on cognitive behavior in both depressive and non-depressive animals. The drugs attenuated the cognitive deficits observed in depressive rats and produced retention deficits in non-depressive rats.

8.05. CRITICALITY:

India stands for world’s second largest populated country, and major portion of the elder population and a very less percentage of young population and very small population of children (attention deficient syndrome) also affected by very miserable and highly care dependence nerve degenerative disease of Alzheimer’s affects anyone at anytime of their whole life concerned without having any warning indicators or any type of early symptoms due to confusion in the diagnosis of particular type of dementia and it may be linger in many cases until it takes the final stage due to disease progression. Alzheimer’s in India also quickly becoming often more and more common due to the globalization, as the society is also trying in expanding into one of the world’s largest and fastest running industrial giants among the entire world.

Herbal industries in India are expanding due to the attraction and understanding of the population for the beneficial and less harm of the utility of herbal products in the management of the diseases. The essential oils are extensively used in many preparations in the Ayurvedic formulation, for example in the form of orally used soft gelatin capsules and in the form of inhalation therapy. Even essential oils are familiar among the people as aroma therapy which is having a wider application in the management of many chronic ill conditions affected by the human in any stages of their life. Major part of the economy in the market and also has proven their capacity to withstand in the global market by competing with the widely used and highly branded allopathic medications.

Essential oils of *cymbopogon citrates* and *nepeta cataria* are being extensively used by majority of the population in the diet. The very important benificitaory use of these essential oils is in making herbal tea. The teas are consumed by all age population,
in India the herbal tea is consumed form major proportion of population commonly called as lemon tea for their cool and tension relieving property and even caffeine present in the tea can also cause little stimulation of the central nervous system and also improves the mood of the person who have a habit of consuming it regularly, in routine daily practice the day may not start without a cup of tea in many homes.

The severity of occurrence of the disease in the aged people are increasing very fast rate the research work are not meeting the demand in the field because for many years the disease was considered as one of the very common neglected disease due to the lack of information of the disease about its pathogenesis and also with the possible common reasons for the occurrence of the disease. Research and epidemiological studies suggests that not only the aged peoples are affected by the disease but also the young and adults are also suffering with the disease the reason is very quiet commonly the anxiety and stress very commonly seen in the present generation which is making the population to face many dangerous disease among them dementia is one of the serious and stands for the second position in the death and reduced life of the person the first cardio vasucular disease stands which causing majority of the death incidences in the adult and young population.