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Research/Review

Nutraceutical Management Of Alzheimer's Disease

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Abstract

The Alzheimer's disease is explains as paralysis agitans or shacking palsy, it is one of the neurodegerative disease produce the major symptom is damaging the memory power. Plaques and tangles block the communication between the nerve cells, prevents them from carrying out their signaling process. Mental status and neuropsycological testing may provide many details about mental function. In human brain contains over 100 billion nerve cells and other cells. The nerve cells work together to fulfill all communication needed to perform functions such as thinking and learning. This process is collapse with brain cell death forms the Alzheimer's disease. Early onset - family hereditary Alzheimer's disease (EO - FAD) are strongly linked to gene. Sudden changes in amyloid precursor protein causes the Alzheimer's disease. In initial stages, terrible loss of brain function can cause malnutrition, dehydration or infection. The brain shrunk significantly in the final stage. The pathological symptom is the frontal and temporal cortices has enlarged sulcal spaces with atrophy. Complications of Alzheimer's disease cause the bladder and bowel problems. This condition results from restricted movement and limited communication to other people. The symptoms of depression may include sleeping problem and changes in mood. These symptoms are minimized with the nutraceutical products. The nutraceutical are formulation with the herbal plants which helps in prevention and treatment of some diseases. The drugs includes the almonds, walnuts, pomegranate seeds and dates, etc… These are helps for reducing certain diseases.

Keywords: Nutraceutical, Alzheimer's Disease

INTRODUCTION

Alzheimer's disease is the neurodegenerative disease that is identified before 100 years and today the cardinal features of amyloid plaques and neurofibrillary tangles that is identified with pathological diagnosis. This disease is explained as *paralysis agitans* or *shacking palsy.* It is one of the progressive neurodegenerative disease produce the symptoms of damaging of memory power, affect the behavior, speech and motor system[1]. The Alzheimer's disease is developed after 65 years old , it is reaching around 15% -20% of the entire population.Industrialized countries estimated this disease at 0.5% of the general population[2].

In human brain contains over 100 billion nerve cells and other cells. The nerve cells work together to fulfill all the communication needed to perform functions such as thinking, learning, remembering and

planing.Scientist are believed that amyloid protein build up in brain cells, forming larger masses called plaques. Corrupt fibers of another protein called tau form in tangles. That plaques and tangles block the communication between the nerve cells, prevents them from carrying out their communication processes. The slow and ongoing death of the nerve cells results in the symptoms of Alzheimer's disease[3].

The risk of developing Alzheimer's disease is feeding habits and generic problems. It is one of the worldwide severe problem. In recent times, the number of people with dementia(impaired ability to remember) is rapidly increasing[4].

Medical costs for dementia patients is also increased. So, understanding dementia is the primary step to minimize the negative perspectives of dementia patients.The absolute cause of disease is still a mystery, but many pathogenic factors such as oxidative stress, free radical formation, mitochondria dysfunction, apoptosis(process of cell death), neuro inflammation and genetic susceptibility are critically involved in Alzheimer's disease[5].

History

Alzheimer's disease has occurred in human history long before it was named. In about 2000 B.C, the ancient Egyptians were already aware that memory declines as people age. Pythagoras(570-495 B.C.), a doctor and mathematician in Greece, classified lifetime of human into six stages such as infancy(Age 0-6), adolescence(age 7-21), adulthood(age 22-49), middle age (age 50-62), senescence(age 63-79) and old age(age 80 or older).Of these stages, senescence and old age people were regarded as a declining phase of mind and body, and some people who survive this time were expected to degenerate in mind to a level of suckling baby and finally become stupid. Hippocrates(460-370 B.C.), a philosopher in Greece, believed that brain injury leads to cognitive disorder and Plato, mentioned that the principle causes of dementia is old age itself because of mental performance is destined to inevitably degrade. Emil kraepelin (1856-1926), classified dementia into senile dementia and presenile dementia in 1910. He was the first named the disease as"Alzheimer's disease". After Alois Alzheimer (1864-1915), discovered pathological features of presenile dementia[6].

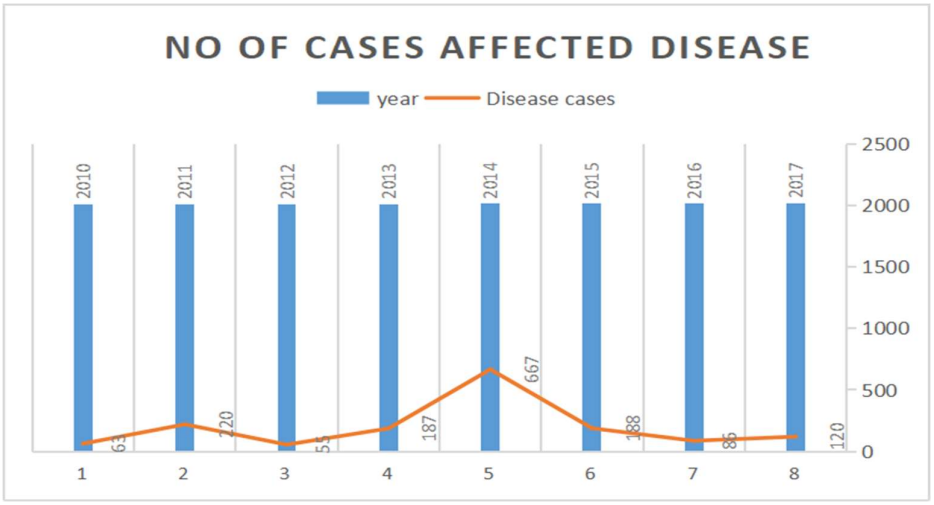

Table1: In Food and Drug Administration (FDA), drugs approved for Alzheimer's disease according to the year

APPROVAL YEAR	DRUGS
Ketamine	1970
Piracetam	1971
Rivastigmine	1985
Donenepezil	1996
Galantamine	2000
Memantine	2003

Symptoms

There are many symptoms in Alzheimer's disease, one of the key symptom is memory loss. In these early sign includes difficulty in remembering recent event or conversations. But memory loss increases in higher degree and other symptoms develop as the disease progresses. At early stage, some one with this Alzheimer's disease maybe aware of having trouble remembering things and thinking clearly. As symptoms get worse, a family member or friend maybe more likely to notice the changes in their behavior. Brain changes associated with

Alzheimer's disease lead to growing difficulty with memory, thinking and reasoning, making judgements and decisions, planning and performing familiar tasks, changes in personality, behavior and preserved skills. Every human being has memory lapses at times but the memory loss associated with Alzheimer's disease persist and gets worse. One of the main symptom of Alzheimer's disease in early stage is forgetting recently learned information. Others are forgetting important dates or events, asking the same question over and over, and increasingly needing to rely on memory aids or family members for things they used to handle on their own.
In later stages of Alzheimer's disease, the symptoms become increasingly severe and distressing for the person with the condition, as well as their career, friends and family. Hallucinations and delusions may come and go over the course of illness, but it can get worse as the condition progresses.

A number of other symptoms may also develop as Alzheimer's disease progresses such as difficulty in eating and swallowing[dysphagia], difficulty in changing position or moving around without the assistances, weight loss in sometimes severe, unintentional passing of urine or stools, loss of speech, and primary problem with short and long term memory. In critical stages of Alzheimer's disease, patients may need full time care and assistance with eating, moving and personal care[7].

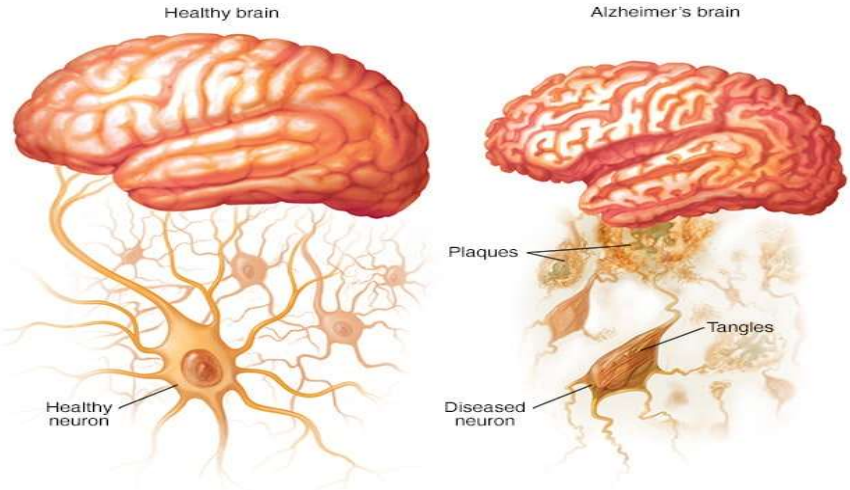

Figure : 01 Brain parts damaged due to Alzheimer's disease

Diagnosis

Alzheimer's disease is always clinically diagnosed, includes normal aging and essential tremors. Laboratory tests can includes blood test, such as complete blood count, a chemistry panel, urine analysis and blood glucose testing. Dementia describes the state of a persons mental functions. Its not a specific disease and declines in mental function from a previously higher level, that's severe enough to interfere with daily living. A person with dementia has two or more of these certain difficulties, including a change in memory, reasoning and dealing of complex tasks, language, understanding visual form and space relationship, behavior and personality. Very few quantity of medication has approved by Food and Drug Administration for Alzheimer's disease treatment.

Test of memory and thinking skills also help diagnose Alzheimer's disease. Alzheimer's disease was diagnosed, when looking at the brain with a microscope revealed plaques and tangles. Health care professional and researchers are able to diagnosing diseases. And also, the Biomarkers can detect the presence of plaques and tangles. Biomarkers tests include particular types of PET(Positron Emission Tomography) scans and tests that determine amyloid and tau proteins in the fluid part of blood and cerebral spinal fluid. A neurological exam may include testing is reflexes, muscle tone, strength, ability to get up from a chair and walk across the room, sense of sight and hearing, coordination and balance.

Lab tests – Blood tests can measure levels of beta – amyloid protein and tau protein , but these tests aren't widely available. It may help rule out other potential causes of memory loss and confusion, such as a thyroid disorder or vitamin levels that are too low. Mental status and neuropsychological testing may provide more details about mental function that can be compared with people of a similar age and education level. Future diagnostic tests and Researchers are working to develop tests that can measure biological symptoms of disease processes in the brain. Family history of early onset Alzheimer's disease may consider it. Alzheimer's disease organization and healthcare providers various terms to explain the stages of Alzheimer's disease based on the symptoms[8].

Causes and risk factors

Alzheimer's disease is a disorder that causes destruction of brain cells and it is the main cause of dementia characterized by affecting memory, thinking and social abilities[9]. These includes increase in the aging,

anatomical pathway degenerated, environmental factors includes heavy metals, head injury, genetic factors includes sudden mutations of amyloid precursor protein and presenillin genes and variations in(ApoLipoprotein E)APOE, mitochondrial dysfunction, immune system dysfunction and infection causing agents[10].More than 20 risk factors in Alzheimer's disease have proposed in literature. It includes age, familial inheritance, Aluminium, exposed to environment, brain cells destroyed and associated factors such as cardiovascular diseases and infectious agents. In recent times, these risk factors are identified and discussed about how they cause Alzheimer's disease. In rarely , early onset -family hereditary Alzheimer's disease[EO-FAD] are strongly linked to gene. Sudden changes in amyloid precursor protein and presenilin genes. Late onset sporadic Alzheimer's disease[LO-SAD] is a multifactor disorder includes age related changes and other risk factors associated with immune system[11].Severe loss of brain function can cause dehydration, malnutrition or infection. In briefly discuss about aging Alzheimer's risk older age does not cause Alzheimer's , but it is the most important risk factor for the disease.

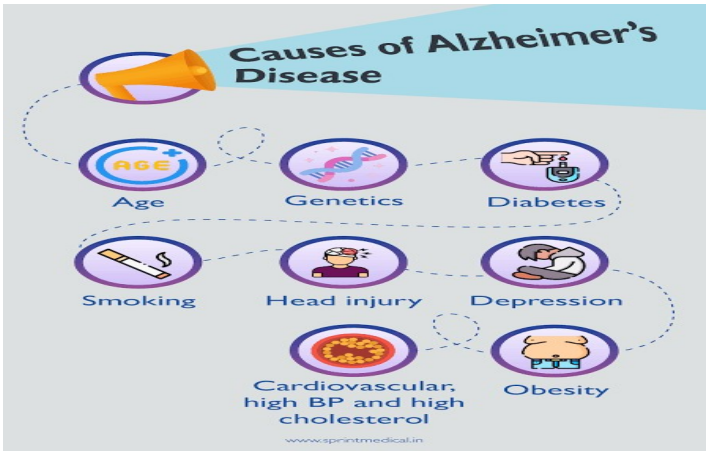

Fig 2: Causes of Alzheimer's disease

The number of people with Alzheimer's disease doubles about every five beyond age 65. Genetic risk factors are chances are differences in genes that can influence the chance of getting a disease. The understanding of Alzheimer's disease process is difficult. But in a basic level, brain protein fails to function as usual. Neurons connections are loss with each other and eventually die.The damage most often starts in the region of the brain that controls memory. The brain has shrunk significantly in the later stage of the disease. The researchers trying to understand the causes of Alzheimer's disease are focused on the role of two proteins. The two proteins are plaques and tangles.

Plaques: Beta amyloid is a fragment of larger protein. When these fragments clump together, they appear to have a toxic effect on neurons and disrupt communication between brain cells. The clumps form bigger deposits called amyloid plaques, which also include other cellular debris.

Tangles: Tau proteins play a major role in brain cells internal support and transport system to carry a nutrients and other essential materials. In Alzheimer's disease, tau proteins change shape and organize into structures called neuro fibrillary tangles. The tangles disturbed the transport system and causes damage to the brain cells.

Downsyndrome develops in many people of Alzheimer's disease.This is related to having three copies of chromosome 21. It is the gene involve in the production of protein that leads to creation of beta amyloid. This amyloid fragments become plaques in brain with symptoms tend to appeared 10 to 20 years. Estimates suggest that 50% or more of the people with down syndrome with develop Alzheimer's with symptoms appearing in their 50s and 60s. Another genetic variations in the APOE gene, which has several forms is known to influence the risk of Alzheimer's disease.

Conditions associated with cardiovascular disease can increases the risk of Alzheimer's disease. This includes smoking, obesity, high blood pressure and cholesterol. The latest research suggest in other factors are also important, this is not mean these factors are directly responsible for causing dementia. These includes hearing loss, untreated depression(though depression can also be one of the main symptoms of Alzheimer's disease), loneliness or social isolation. The risk of developing vascular dementia appear to increased by many condition that damages the heart and blood vessels[12].

Complications

- People those who are diagnosed with Alzheimer's disease commonly have periods of agitation and anxiousness. Alzheimer's disease having patients ability to reason and understand certain situation can also

decline as the disease progresses. Patient cannot make sense of confusing world, because of that they become fearful and agitated.

- There is also other complications of Alzheimer's disease, they are bladder and bowel problems. As the Alzheimer's disease progresses, the patient may no longer recognize the sensation of needing to use the bathroom and also unable to respond quickly to urges. This condition results from restricted movement or limited communication to other people.
- This bladder and bowel related problems in Alzheimer's disease patient make them more confused and use the restroom in inappropriate places. Some patients with Alzheimer's disease also have depressed mind and don't know how to maintain with a loss of cognitive functions. The symptoms of depression may include sleeping problems,changes in mood, withdrawing from friends and relatives, difficulty concentrating in particular activity.
- The patient suffering from Alzheimer's disease can also affect the balance and coordination in their physical activities. The rate of falling increases as the disease worsens. This can lead to head injury and damaged the skeletal system. Alzheimer's disease affected patients can also lose control of normal internal functions and they may forget how to chew the food and swallow the food.
- If this condition continues, they have increased risk of eating food and consuming drinks. Alzheimer's disease can cause pulmonary aspiration and also pneumonia which can leads to the life-threatening condition. This disease can also cause infections such as fever, cough, shortness of breath and excess phlegm.
- Wandering is also another complication of Alzheimer's disease. Patient can experience restlessness and sleeplessness due to sleep pattern is disturbed, which results in wander of the home believing that they are running or going to work. In this kind of disease, we can see many patient leave home and forget their way back.
- In rare cases of this disease patients wander from home at night when everyone is asleep. Another major complications of Alzheimer's disease is malnutrition and dehydration. It is important for every patient to eat and drink enough solids and fluids. But for Alzheimer diseased patient may refuse to eat or drink. Also, they maybe unable to consume food and drink properly because of difficulty in swallowing. The symptoms of dehydration includes dry mouth, headache, dry skin, sleepiness and irritability[13].
- In the Alzheimer's disease gets complicated the patients forget to take care of their teeth or dentures. Alzheimer's disease affected patients can face the problem such as sores, decayed teeth, food "pocketed" in the cheek or on roof of the mouth, lumps[14].
- One of the rare complication of Alzheimer's disease is nasal packing aspiration. Nasal bleeding is the general problem of patient suffering from Alzheimer's disease who are receiving anticoagulant agents. Most of the cases of Alzheimer's disease are successfully managed with anterior or posterior nasal packing. However the complication of nasal packing in Alzheimer's disease patient should be considered.
- The complications of Alzheimer's disease patient also include imbalance in thyroid hormone have been linked with dementia. Several studies related to Alzheimer's disease have reported an association between thyroid disorder such as hyperthyroidism and hypothyroidism[15].

Pathophysiology

Alzheimer's disease in brain often moderate cortical atrophy. It is one the most important multimodal association cortices and limbic lobe structures. The frontal and temporal cortices has enlarged sulcal spaces with atrophy of the gyri. After Alzheimer's disease it produces the major symptom such as enlargement of the frontal and temporal horns of lateral ventricles and produces decreased brain weight[16].

Oxidative stress is one of the major problem of Alzheimer's disease. Oxygen level is inadequate for the aerobic metabolic processes. Thus forms reduced oxygen species such as superoxide radicals, hydroxyl radicals and singlet oxygen.

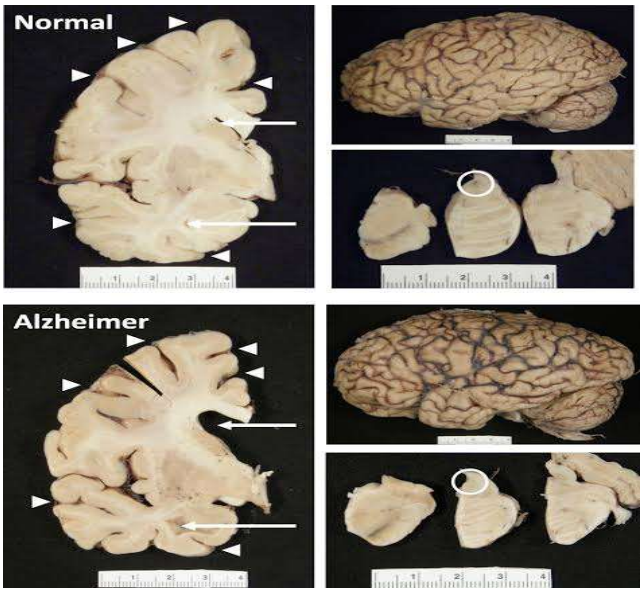

Fig 3: Pathophysiology

Results in life threatening condition because reactive oxygen species interfere with nucleic acid, proteins, enzymes and lipids which leads to the pathological conditions of Heart attack, Aging ,Cancer, Neurodegenerative diseases. Nowadays, many Microbial Ribo Nucleic Acids are known to be a biomarkers for Alzheimer's disease. Some Microbial Ribo Nucleic Acids is attributed to irregulation in Alzheimer's disease through alteration in gene expression[17].

In Alzheimer's disease pathology maybe seen particularly in the hippocampus, amygdala, endorhinal cortex and the cortical association areas of the frontal, temporal and parietal cortices, but also with subcortical nuclei such as the serotonergic dorsal raphe, nor adrenergic locus coreleus and the cholinergic basal nucleus[18].

Usually, the pathophysiology of Alzheimer's disease is very complicated.We do know that amyloid is central to the pathophysiology of Alzheimer's disease . Amyloid is present in more number of species. It starts as a monomer. It means one molecule then it changes nature and aggregate to become more complicated. First it is dimer and then changes into trimer. These process will continued until it becomes an oligomer, which contains many molecules.

Eventually, it forms the plaques.In the human brain, there are a whole variety of species of amyloid ranging from the very simple into the complex plaque itself.It is a plaque that we can see with amyloid imaging and it is the monomer or the very most simple species,that can be assessed with spinal fluid analysis.

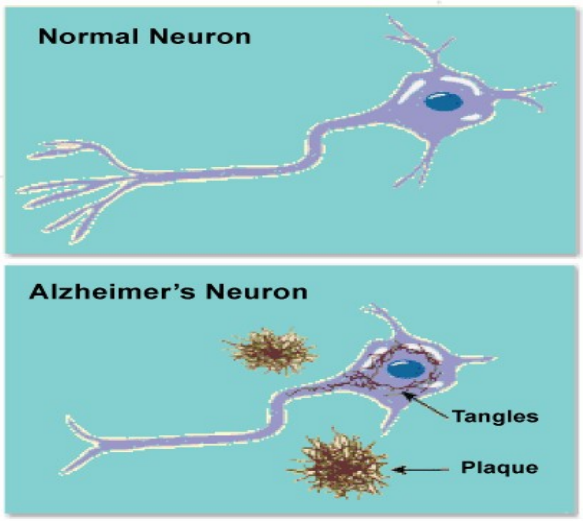

Fig 4: Neurons communication damage

There are a lot of species of amyloid molecules in between that we can see in the cerebrospinal fluid and also in positron emission tomography.Our brain also show the neurofibillary tangles. The neurofibillary tangles tends to be associated with cell death and consequently the appearance of symptoms of Alzheimer's disease. The condition called cognitive decline can be result of many different types of damages to the brain.

We can see that the patient with cognitive impairment, we can think about broad array of neurodegenerative disease and you're also going to think about other posible influences, such as hypothyroidism or vitamin B12 deficiency, that can either contribute to the cognitive impairment of a demanded individual or in some cases cause the cognitive impairment. There is an another type known as the phenotype of Alzhiemr's disease is mainly memory impairment and then the patient suffering Alzheimer's disease, due to the worsening of disease suffer from language deficits and visual spatial abnormalities[19].

Allopathic remedies

Allopathic drugs are prescribed to prevent or slow the development of Alzheimer's disease symptoms. These drugs effects vary from one person to another person. Food and Drug Administration has approved different types of drugs specific to treat symptoms of Alzheimer's disease.

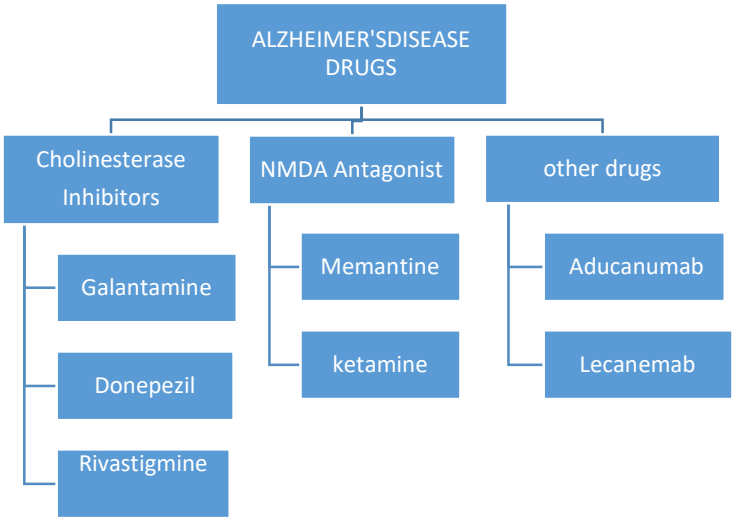

Fig 5: Classification of Alzheimer's disease drugs

1. Cholinesterase inhibitors.
2. NMDA Antagonist.
3. Other drugs.

These are two types of drugs approved for specific stages of Alzheimer's disease includes mild, moderate and severe are based on the scores on test that memory, awareness of time and place , thinking and reasoning.

Cholinesterase inhibitors

Alzheimer's disease harms the brain by decreasing the level of a chemical messenger of Acetylcholine that is important for alertness, memory, thought and judgement. Cholinesterase inhibitors increase the amount of Acetylcholine available to nerve cells by preventing its breakdown in the brain.

SIDE EFFECTS: Nausea, vomiting and Diarrhoea.

a) *Galantamine(Razadyne):* Galantamine is treat mild to moderate Alzheimer's disease.It is taken a pill once a day or as an extended - release capsule twice a day.
   SIDE EFFECTS: Nausea, Vomiting, Diarrhoea,Dizziness, Headache, Decreased appetite, Skin rashes, Weight loss, Slow heart rate, Tiredness and fainting.
b) *Donepezil(Aricept)*: These drugs are used to delay or slow the symptoms of mild, moderate and severe Alzheimer's disease. It comes in a tablet or disintegrating tablet. It is taken once a day as a pill.
   SIDE EFFECTS: Muscle cramp, Stomach bleeding, Difficulty urinating, Seizures, Trouble sleepiness, Nausea , Diarrhoea and Worsening asthma or COPD.
c) *Rivastigmine(Exelon):* It is approved for mild to moderate Alzheimer's disease.Rivastigmine is taken as pill.
   SIDE EFFECTS: Bladder pain, Bloody or cloudy urine, Lower back or side pain, Blurred vision,Nervousness, Slow or fast heartbeat and pounding in the ears.

NMDA Antagonist

These are the drugs used for block the NMDA Receptor.

a) *Memantine*: It is approved by Food and Drug Administration for treatment of moderate to severe Alzheimer's disease. This drug are taken as a pill or syrup.
SIDE EFFECTS: Confusion, Constipation, Dizzinesss, Bloodclot , Agitation, Insomnia and Headache.

b) *Ketamine:* It is generally maintains normal pharyngeal and laryngeal reflexes and permits spontaneous respiration.It is also interaction with opioid receptors.
SIDE EFFECTS: Chest pain, Confusion, Dizziness, Drowsiness,Double vision, Loss of motor coordination and Hallucinations[20].

Other drugs

It includes Aducanumab and Lecanemab.

a) *Aducanumab*: The intraveneous infusion therapy is the first drug of kind to be approved for Alzheimer's disease.It is approved for patients with mild cognitive impairment and mild dementia caused by the Alzheimer's disease.
SIDE EFFECTS: Amyloid Related Imaging Abnormalities - Edema(ARIA-E) which means brain swells, Amyloid Related Imaging Abnormalities - Hemosiderin deposition(ARIA-H) which means low bleeding in the brain.

b) *Lecanemab:* In 2023, the united states of food and drug administration has approved lecanemab for people with mild Alzheimer's disease and mild cognitive impairment due to Alzheimer's disease. It is given as I.v infusion every two weeks.
SIDE EFFECTS: Infusion related to reaction such as fever, Flu like symptoms. changes in heart rate and Shortness of breath, Dizziness, Vomiting , Nausea and seizures[21].

Nutraceutical management of alzheimer's disease

Nutraceuticals are the formulation of nutrients which helps in prevention and treatment of some diseases, in addition to a supplement diet. It is a term given by Dr. Stephen De Felice in 1989 and came from two words "Nutrition" and "Pharmaceutical".These products can be considered non specific biological therapies used to promote general well being , control symptoms, and prevent malignant processes.

The nutraceutical drugs are used for Alzheimer's disease includes,

- ✓ Centella asiatica
- ✓ Cluster beans
- ✓ Walnuts
- ✓ Almonds
- ✓ Brown rice
- ✓ Oats
- ✓ Pumpkin seeds
- ✓ Pomegranate
- ✓ Pistha
- ✓ Dates

- ● **Centella asiatica :**

Family : Apiaceae

Biological source : Obtained from plants of *Centella asiatica*

Chemical constituents : Asiatic acid and cassic acid

- The commonly named *gotu kola* is an ayurvedic herb used to enhance memory and nerve function. It is an Indian medicinal plant, has been described as possessing central nervous system activity, such as improving intelligence.
- In addition property is that having the cognitive enhancing and antioxidant property. Centella asiatica possess various health promoting activities with bioactive compounds such as triterpenes, flavonoids and vitamins[22].
- . The major constituents of centella asiatica are saponins, which includes asiaticosides, in which a trisaccharide moiety is linked to the aglycone asiatic acid, madecassoside and madasiatic acid. Phytoconstituents identified as the isoprenoids(plant sterols, pentacyclic triterpenoids and saponins) and phenylpropanoid derivatives(eugenol derivatives, caffeoylquinic acids and flavonoids). These constituents are having the antioxidant property with curing the Alzheimer's disease[23].

Cluster beans

Family : Leguminosae

Biological source : Obtained from plant of *Cyamopsis tetragonolob*us

Chemical constituents : crude protein, crude fiber and carbohydrate contents

- Cluster bean having the wide range of adaptability having antioxidant, antidiabetic, antimicrobial and cytotoxic potential.
- Cluster bean plant has received tremendous attention as functional food s based on their high nutritional profile like 28.3 to 35% crude protein, 8% crude fiber, 59% carbohydrate contents, 7.35% oil and moisture contents along with polyphenols, tannins, flavonoids and phytic acid upto 25mg. The cluster bean seeds with important fatty acids such as linoleic acid, palmitic acid and oleic acids is that used for the neurodegenerative diseases[24].

Walnuts

Family : Juglandaceae

Biological source : Obtained from the tree of the *Genus julgan*s

Chemical constituents : palmitic acid, stearic acid, oleic acid and linoleic acid

- Walnuts contain several components that have antioxidant and anti inflammatory effects. So the supplements of walnut is suggested to add in the diet to improve cognition and reduce the risk of Alzheimer's disease.
- Enhanced oxidative damage as evidenced by increased lipid peroxidation, protein oxidation and DNA oxidation has been demonstrated in human brain, CSF and blood samples of individuals with Alzheimer's disease was studies and walnut decreases the symptoms.
- Walnut used in Alzheimer patient decreased the oxidative stress such as reduces the free radical level, increases the antioxidants, decreases the lipid peroxidation, decreases protein oxidation and decreases amyloid beta protein - induced cell death, membrane damage and DNA damage.
- Walnut also decreases amyloid beta protein fibrillation, amyloid beta protein oligomers and inflammation in brain. Walnuts have polyunsaturated fat, eicosapentaenoic acid which have the anti inflammatory effects.

Recent studies also shows in walnut the ALA (Alpha Linoleic Acid) inhibits inflammation by decreasing COX - 2 and inflammatory cytokines thus reduces the Alzheimer's disease[25].

Almonds

Family : Rosaceae
Biological source : Obtained from edible nuts of *Prunus dulcis*
Chemical constituents :Lipids, proteins, Tannins and soluble sugars

- Almonds having the primary metabolites contains Fumaric acid, Lactic acid and Ethanol.Almonds is having the essential source of nutrients. The characterization of almond macro and micro nutrients have many nutritious ingredients such as fatty acids, lipids, amino acids, proteins, carbohydrates, vitamins and minerals and also having secondary metabolite.
- Among the compounds with beneficial properties for health profile, predominantly monounsaturated fatty acids(MUFA, 60%) followed by poly unsaturated fatty acids(PUFA,30%), fibers, vitamins,minerals, phytosterols and polyphenols.
- Good source of protein is having almond is monosaturated fatty acids, dietary fiber(Insoluble /soluble fiber), vitamin E, Riboflavin and essential minerals(manganese, magnesium, copper and phosphorus). The selection of the variety depends on the yield, performance of the yield, performance of the field in specific region, resistant to disease and marketability[26].

Brown rice

Family : Grancineae
Biological source :Obtained from the *Oryza sativa*
Chemical constituents : Phenolics, flavanoids, caffeic acid, ferulic aacid and luteolin

- Pre-germinated brown rice having high level of nutrients GABA. Alzheimer's disease is described by numerous senile plaques resulting in damaging neuronal communication.
- study found that the brown rice which has been soaked in water to induce slight germination and contains around 13 times the amount of oryzanol and 15 times the Gama Amino Butyric Acid (GABA) then polished rice.
- Suggest that large amount of GABA on the brown rice may enhance Glutamate release and the sensitivity of NMDA receptors. Activation of these receptors is thought to underlie learning and memory[27].

Oats

Family : Poaceae
Biological source : Obtained from the edible seeds of *oat grass*
Chemical constituents : lipids, protein, beta glucan and starch

- Oats seedlings contain more protein, beta glucan, free amino acids and phenolic compounds. The progressive neuro degenerative disorder of Alzheimer is accompained by worsening memory and cognitive function.
- In recent studies oats extract has been identified as a new therapeutic value for Alzheimer's disease, this is due to its antioxidant activity and Alzheimer's disease specific mechanism of action.
- Alzheimer's disease is prevented done with the combination of Antioxidant as well as the nutrition rich diet . Hence oats focuses on nutraceutical and Antioxidant treatment of Alzheimer's disease[28].

Pumpkin seeds

Family : Curcurbitaceae
Biological source : Obtained from *Pumpkin fruits*
Chemical constituents : Carbohydrates, fat, protein and water

- The pumpkin is a very well known as the edible plant that is a member of the *curcubitaceae* family. Pumpkins includes many chemical components which is also rich in phytoestrogens, unsaturated fatty acids,and vitamin E in their seeds that will have medicinal, nutritional and cosmetic benefits.
- Pumpkin seeds are rich in primary and secondary metabolites such as carbohydrates, proteins, monounsaturated fatty acids, poly saturated fatty acids, carotenoids, tocopherols,tryptophan, delta-7-sterols and numerous other phytochemicals are abundant in the pumpkin seeds.
- The pumpkin seeds has the activities such as anti-diabetic,hypoglycemic, cardiovascular preventive and anti-cancer,anti-depressants,anti-helmintics,and anti-oxidants.
- Pumpkin is consumed because of its nutritional and phytochemical constituents.The phytocompounds can be listed as alpha and gamma -tocopherol,beta-carotene,beta-cryptoxanthin,lutein and zeaxanthin,beta-sitosterol. These are help to improve Alzheimer's disease patients mental condition and improves the memory[29].

Pomegranate

Family : Puniaceae
Biological source : Obtained from fruits of *punica granatum*
Chemical constituents : Flavonoids, anthocyanins, alkaloids, fructose and glucose

- Oxidative stress plays an important role in Alzheimer's disease. To prevent oxidative stress, this contribution first identified and quantified phenolic bioactives present in the pulp and peel of pomegranate.
- Extract obtained from the peel showed much higher phenolic contents and antioxidant properties than that of the pulp, hence being selected as potential inhibitor of acetyl cholinesterase, a key enzyme involved in the progress of Alzheimer's disease. Phenolics from pomegranate peel helps for inhibition of acetylcholinesterase, which was dependent on the phenolic concentration.
- Based on preclinical trails, it appears that pomegranate may prove valuable in treating neurodegenerative disorders, including Alzheimer's disease and Parkinson's disease. Based on the previous preclinical studies, pomegranate juice, extracts and its bioactive constituents have shown many mitigating properties, including suppression of inflammatory cell signaling, reduction in expression of genes associated with oxidative stress.
- It also decreases the expression of soluble amyloid protein precursor Beta -Secretase and Carboxyl Terminal Fragment Beta. So pomegranate supplementation has been shown to impart cognitive aid by production of neurons against Alzheimer's disease[30].

Pista

Family : Anacardiaceae
Biological source : Obtained from edible seeds of pistacia vera
Chemical constituents : Anacardic acids, fatty acids and phytosterols

- Pistachios are one of the only nuts that contain the carotenoids lutein and zeaxanthin. These components may also helps to develop blood flow to the brain, helping to keep your mind sharp and focused.
- Pistha may be good for health as they contain source of protein, antioxidants and fiber. Possible benefits include developing heart health, managing blood sugar and reducing colon cancer.
- Pistachios contain many essential nutrients,

Calories - 159, protein - 5.7 g, fat - 12.8g, carbohydrates - 7.7g, fiber - 3g, sugars 2.2g and magnesium - 34.3mg. That is having the high antioxidant content, they prevent the cell damage and play a key role in reducing risk of Alzheimer's disease.pistha are especially rich in lutein and zeaxanthin, both of which are very important in antioxidants[31].

Dates

Family : Arecaceae
Biological source : Obtained from sweet fruits of *phoenix dactylifera*
Chemical constituents : carbohydrates, dietary fibre, protein, vitamins and carotenoids

- At present time, treatment options available to delay the onset or slow down the progression of Alzheimer's disease are not effective
- . Recent studies have suggested that diet and lifestyle factors may represent protective strategies to minimize the risk of developing Alzheimer's disease.
- Date palm fruits are a good source of dietary fiber and are rich in total phenolics and natural antioxidants, such as anthocyanins, ferulic acid, protocatechuic acid and caffeic acid. These polyphenolic compounds have been neuroprotective in different model systems[32].

CONCLUSION

Alzheimer's disease is the neurodegenerative disorder caused by brain cells death. After the studies of nutraceutical management of Alzheimer's disease, we understand that the allopathic remedies causes more side effects that can leads to life-threatening condition. so, we can use nutraceutical products to minimize the side effects and to increase the therapeutic activity by taking it as a food in our day to day life. In the past years, studies have demonstrated that nutraceutical products is reducing cognitive deficits, preventing and protecting against neuronal damage, pathological changes and symptomatology of Alzheimer's disease. The nutraceutical products such as Centella asiatica, Cluster beans, Walnuts, Almonds, Oats, Brown rice, Pumpkin seeds, Pomegranate, Dates and Pista contains chemical components such as carotenoids, Flavanoids, zexanthine, beta glucan, phenols, tannins, triterpenoids, linoleic acid, palmitic acid and oleic acid .In these,the major chemical constituent is *flavanoids, it* has the anti-oxidative and anti-inflammation activity. By the way these nutraceuticals reduces the efficacy of Alzheimer's disease in patient, which can helps to increase the patient's memory towards their daily routine such as eating and physical activity leads to improvement of their health and also improve their self confidence according to their status in society. The flavanoid constituent above nutraceutical drugs maybe cure the Alzheimer's disease is that hypothesis can be studied with the future clinical research.

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