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Review on Treatment of Alzheimer's Disease by managing oxidative stress using Herbal Drugs

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ABSTRACT: Alzheimer's disease(AD) is a progressive neurodegenerative disease which gradually impairs the person's memory and ability to learn, reasoning, judgement,communication and daily activities.Mostly cause in the old age people. AD can be clinically identified bycognitive Impairment and pathologically by the deposition of beta amyloidplaques neurofibrillary tangles and the degeneration of the cholinergic basal forebrain. During the progression of AD patient may produce the changes in personality and behaviour like anxiety ,paranoia, confusion, hallucination, etc. Currently there is no cure for AD but in new treatments they reveal a horizon on the biology of the disease. The objective of this article is to throw a light on the prevelence, causes, symptoms and preventionof and h Alzheimer's disease.People will more aware about the consequencesof Alzheimer's disease

KEYWORDS:anoia,amyloidplaques,paranoia.

I. INTRODUCTION

The health promotive, disease preventive and innovation approach available in the Indian systems of prescription like 'Ayurveda' is gaining greater attention and popularity in various regions of the world. Ayurveda is one of the renowned systems of medicine invented from 'Vedas'. Ancient ayurveda physicians has classified 'Ayurveda' in eight divisions by specifying the meaning of each one like 'Kaya chikitsa' (General medicine), 'Tantra' (Surgery), 'Shalaya Tantra' (disease of eye, ear, nose and throat), 'Kumarbhritya' (children diseases, obstetrics and gynecology), 'Agada Tantra' (Toxicology), 'BhutaVidya' (Psychiatry), 'Vaji Karana' (Aphrodisiac/sexology) and 'Rasayana' (rejuvenation) [charakayurveda] [1]. Learning is the progression of acquiring information about the world and memory is the retaining of the acquired knowledge which can be regained as and when required [2]. Memory is a vital part of Cognition for which the brain plays interesting games of neurotransmitter with billions of neurons. Different forms of memory are associated with different parts of the brain. For example; Short term memory is associated with prefrontal cortex, Long term memory occurs in hippocampus and temporary lobe and skill memory processed in cerebellum [3]. The disturbance in such area indications to amnesia and hence memory loss [4]. Alzheimer's disease (AD) is a progressive, irreversible neurological disorder that occurs gradually and results in memory loss, unusual behavior, personality changes, and loss of the ability to thinking[5]. AD has affected 15 million people worldwide which is estimated. AD has dementia like symptom in the geriatrics. AD is a developing neurological impairment with time period of nearly 8.5 years from beginning of onset of clinical symptoms and death. The early stage symptoms of ADare loss of short term memory, forgetting names and addresses, as further this condition progressively become more marked and even individuals cannot remember the home way and his own identity. Unfortunately, AD has no cure but it's progressing condition can be prevented by proper treatment. Seventy percent of causes for AD is due to genetic factor and 21% is due toenvoirmental factors[6]. At present, the most efficient AD treatment therapy include the use of cholinesterase inhibitors these drugs diminish the function of the acetylcholinesterase (AChE) enzyme in order to increase acetylcholine neurotransmitter levels in the brain. Acetylcholinesterase inhibitors include tacrine, Rivastigmine, galantamine, and donepezil whereas memantine(methyl-D-aspartate receptor antagonist) has been prescribed recently for AD. However, there is no such therapy for cure AD, except to getrelief from symptoms of the disease[7].

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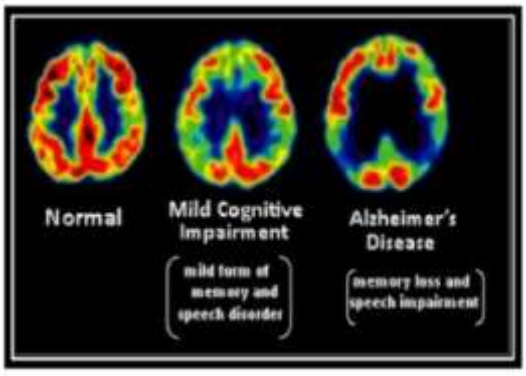
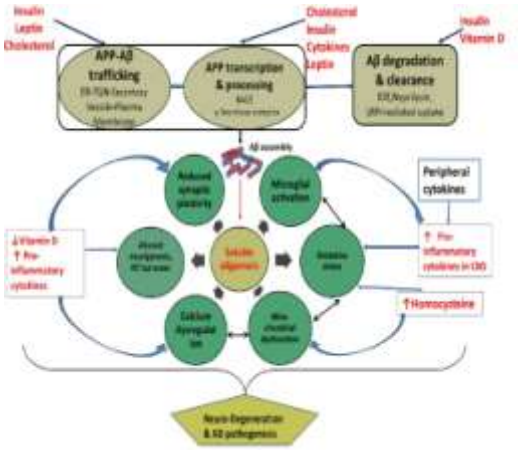


PATHOGENEISOFAD

Impairment of memory and learning, the most characteristic manifestation of dementia can be chemically induced by scopolamine in experimental animals . Scopolamine is a anticholinergic drug that involve the transmission of acetylcholine to the central nervous system[8]. This Cholinergic transmission can be terminated by hydrolysis of acetylcholine by the enzyme called acetylcholinesterase,the function of AChEis to degrade acetylcholine in to the acetate and choline within synaptic cleft[9]. Scopolamine-induced amnesia in experimental animals is widely used to screen the drughavinga potential therapeutic efficacy for the treatment of dementia[10]. Cognitive impairment was observed in AD patient due to lack of acetylcholinetransferase enzyme activity and low amount of cholinergic neuron in basal part of brain in frontal area[11].

The understanding and awareness of cholinergic cortical system is studied by lession pattern of nucleus basallis of myenert and also cognitive deficit of AD are indicated[12].Decrease in level of cholinergic marker is shown by destruction of NBM in animal model. These cholinergic marker represent level of acetylcholine,acetylcholine release and turnover, ACh uptake, number of cholinergic muscarinic receptor in frontal cortex and AChE activity[13]. Because cholinergic unexpected consequences are sent from meynertneuclei to cortex and septal area ,the death of cholinergic cell is due to destruction of NBM and also decrease amount of acetylcholine in cortex[14].Role of learning and memory is played by hippocampus.This activity include acquisition,consolidation and retrieval of information[15].The generation of new nerve cell involved in memory formation in hippocampus is called neurogenesis.Spatial memory come with improved neurogenesis whereas poor cognitive function indicate impaired neurogenesis[16]. Some of feature of AD also include the accumulation of amyloid plaque in brain tissue, meningeal blood vessel.Some time neurofibrillary tangles are present in hippocampus and cerebral cortex of brain [17]. Some studies revealed that AD has inflamatory process , second messenger like reactive oxidative species can damage cellular components by inflamation .Therefore antioxidants can also be used to treat AD[18]. Oxidative stress play important role in pathogenesis of AD as it imbalance and disturb the free radicals and antioxidant system.The cellular function and integrity is disrupted by attack oxygen free radical on the protein, neuclic acid and lipid membranes.The polyunsaturated fatty acids contained in brain tissue are more exposed of being attack by free radical .Most destructive form of oxidative degradation is lipid peropxidation which damage cell membrane and produce secondary product,both of loop and splitting form of oxygenated fatty acid have neurotoxic effect [19]. Lipid peroxidation indicator include important oxidative species out of which one of important is malondialdehyde(MDA) [20].



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MEDICINAL PLANTS USED FOR THE TREATMENT OF AD

Hypericumperforatum

Hypericum is herbaceous perennial plant with a height of 30-80 cm. It has creepy and glabrous stem. Leaves of plant are spoon-shaped and sessile, with various cavities of essential oil and feature from specific name (Perforatum).The chemical constituents of leaf branches and flowers are containing compounds like essential oils, tannins, hayperciyn, hayperpyron, choline and flavonoids. Clinical effects of Hypericum include enhancement of neurological diseases,

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antidepressant, anti-anxiety, anti-inflammatory, wound healing and analgesic effects[21]

Lepidiummeyenii

Maca (Lepidiummeyenii) grows height of 3 500 to 4500 meters in the Andes of Peru. Macais one of species of plant that can survive at the difficult and unfavorable condition of high Andes altitude, hot days, burning sun, dry winds and cold nights[22].The investigation of memory deficit in animal model induced by 1mg /kg of scopolamine by administrating diffrent doses of aqeuos and hydroalcoholic extract of Macca is studiedfor 35d.

Prunella vulgaris (P. vulgaris)

P. vulgaris is most widely founded in Korea, china, Japan and Europe. Prunella vulgaris is a traditional medicine used byKorean and Chinese community for treatment of inflamatory diseases ,headache ,eyepain and dizziness[23]. Oleic acid ,ursolicacid,butyricacid,flavonoids and rosmarinic acid are some of the active ingredient of P.vulgaris as demonstrated by previous studies[24].

Cyperusrotundus (C. rotundus)

C. rotunduswhich is also called as sedge which belongs to the family named asCyperaceae. The rhizome of Cyperus is enrich in essential oils , these essential oil contents are pinene, a little cineole, terpenes, and a new alcohol moiety called asisociprol. Many of chemical compounds have been isolated by ethanolic extraction of C.roduntus species by their rhizome these chemicals posses AChE activity[25].

Zizyphus jujube

At the immature period jujube fruit is green in color, but as ripe, it becomes red and changes colouralso begins to wrinkle. The jujube fruit has elongated and long nucleus and is fully ripe in autumn weather condition. It is edible, sweet in taste and has therapeutic medicinal properties. Jujube has soothing and anti-grouch properties, and has been used as traditional therapy in Korean and chinesecountries as they can also reduce anxiety and strengthen stomach ,spleen and gastrointestinal system[26].

Lavandulaofficinalis

Lavandulaofficinalisalso called as lavender, has been traditionallywell known. This plant has wide variety of distrbution and it's essential oil and flowers are used in cosmetic product and for making perfumes . Lavender is a plant that belong to the genus Lavandula, their leaves looks like thyme leave but thinner and longer and has white petals of flower[27].

Salvia officinalis (S. officinalis)

S. officinalis has a very old and well known drug that hold reputation for improving memory. It is particularly has function that is good for the brain and head [28]. Antioxidants and anti-inflammatory properties are potential pharmacological effects of these kind of herbs and also has AChE inhibitory effect for alzheimers disease. The leaves of the plant S. officinalis L. (sage) are very well known for their antioxidative properties and effect overAD[29].

Melissa officinalis (M. officinalis)

M. officinalisalso called as lemon balm is a cultivated that posses perennial lemon scented herb. As per the records concerning its use date back over 2000 years with entries in the HistoriaPlantarum. In traditional medicine M. officinalis L. (Lamiaceae) has been used in the form of remedy for over 2000 years, and also claimed to promote long healthy life and enhancement of memory been acclaimed for promoting long life and for restoring memory[30].

Ginseng

From last thousands of years, ginseng root, particularly the main root, has been used as an East Asian medicinal herb for treatment of several diseases[31]. Ginseng are foundmainly inNortheastern Asia. As per thetraditional Korean and Chinese medicines, ginseng root is purposefully used for increase and boost energy.

HERBAL EXTRACTION OF CASSIA OCCIDENTALIS

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Preparation of herbal extract

Collection and authentication of plant materials

Generally in the month of November the leaves of cassia occidentalis which belong to the family of fabaceae were collected from the local areas].

Processing of sample

Course powder was prepared by drying the leaves in shade . Further extraction is performed by using this powder stored in air tight container.

Preparation of methanolic extract of cassia occidentalis leaves

The coarse was introduced in to the methanol extraction by the process of maceration in the ratio of 7:3. In this procedure of maceration,stirring was performed at regular interval of time when the powdered leaves were macerated. Then the macerated solution was filtered and concentrated and later on it was dried by process of evaporation.

Phytochemical screening

Standard procedures were performed for diffrent types of chemical test to carry out methanolic extraction for identifying chemical constituents by Sofawara (1993), Trease and Evans(1989), and Edeoga(2005).Qualitative analysis on phytochemical constituents.

Drug administration

COE was added in specific amount of distilled water for use. And scopolamine were administeredi.p. at dose of 2mg/kg. In the scopolamine induced memory impairment study COE (200,400 mg/kg, p.o.) were given half hour before a test trial in the elevated plus -maze task, and half hour before the first trial session every consecutive day in the water maze task. In the control group, normal saline solution was injected using the similar time schedule. Each task require 30 minute and according to that memory impairment was induced by scopolamine treatment at dose of 2mg/ kg ,i.p.

ANIMAL STUDY

Elevated plus maze task

Modified elevated plus maze test(mEPM) it was used to measure Spatial learning, EPM learning task . Transfer latency is the term defined as the time required in which the animal show movement from open arm to enclosed arm which is used as an index of learning process.The apparatus is made up of woods that consist of two open arms which are sorrounded by a small Plexi glass edge that prevents fall and for enclosing arms they are arranged such that they can open and close arms are opposite to each other. A central platform is used to connect both the arms to each other and the maze was poured with alcohol water solution for cleaning purpose after every rat to remove any co-founding olfactorycuez. The concept of the experiment is depend upon the eversive behaviour shown by rodentsin to open and high spaces. For the protection of animal from open to high area the animals are preferred to move to open and enclosed arms. The procedure described by Hilnak and Krejci was performed . Diffrent experimental and control group allotted animals randomly where each group has 6 animals (N=6). On the day 1 acquisition was performed in which every rat was gently placed at the distal end an open arm of apparatus on the face opposite to the central platform and time required from animal to show movement from open arm to either of enclosed arm is called as transfer latency which is recorded on repeated exposure of the animal open arms called trainee shorten this parameter, possibly as of consequence of learning acquisition and retention .The enclosed arm from central space having all four legs are separated by crossing and imagenary line by entering animal by the proper criterion. As rat enters enclosed arm it was allowded to move freely for the 10 second. Then rat was allowed to return to its homecage.The experiments were conducted between 10:00and 14:00 are in a semi sound proof room under natural elimination. (hlinak and krejci,2002).

Morris water maze task

The Morris water maze has featureless inner structure with a circular pool . This pool was filled to a depth with water containing tank was placed in a dimly lit, sound-proof test room with several visual cues was then stored in one of the pool quadrants parts . The first experimental day was assignedfor the swimming training for 60 secondswithout using any kind of the platform. While in another four subsequent days, the mice were given two trial sessions each day with the platform in place. Each trial session has time interval of 30 minutes in between.In one of the pool quadrants part mice was placed facing towards the pool wall for the two trial sessions.Each day entry point we're changed in the diffrent order. The administration of drug or the vehicle was performed before the 1hour of first training trial. Mouse permitted to remain for 10 second as it located the platform . If the rat is not able to locate on the platform within 120 second then it was placed on the platform for 10 seconds. After each trial animal was exposed to infrared lamp after

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each trial before returning to its homecage. During each trial session, the time occupied by animal to find out the hidden platform is called as latency which was recorded using a video camera-based Ethovision System (Nodulus, Wageningen, The Netherlands). One day after the last training trial sessions, mice were subjected to a probe.

II. CONCLUSION

It is concluded that their is no such treatment available to slow or stop the Alzheimer's disease. Their are five drugs approved by the U.S. Food and Drug Administration for improvement of symptoms temporarily . As the effectibeness of drug varies across the population. None of the treatments are available now to alter the underlying course of this terminal disease.Herbs has shownconfirming therapeutic activity in AD treatment because of their cognitive benefits and more importantly, their mechanisms of action of the herbs in order of the fundamental pathophysiology of the disease. In summary, preliminary clinical evidence demonstrated that some herbal medicines can improve the learning an memory power of individual having mild to moderate type of AD . Potential beneficial actions were imparted by the active chemical constituents of these herbs which are not limited to the inhibition of AChE and include the modification of Aβ processing, protection against cell destruction called apoptosis and anti-inflammatory effects, and oxidative stressin AD

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