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Research Article

A review of the most important medicinal plants effective On Alzheimer's disease

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ABSTRACT

Objective: Alzheimer's disease is usually characterized by chronic and progressive memory disorder alongside speech difficulties and deficits of visual-spatial skills and executive functions. In patients with Alzheimer's disease, choline acetyletransferase decreases especially in temporal cortex and hippocampus. Currently, medicinal plants are considered a good pharmaceutical source to treat nervous system diseases especially Alzheimer's disease. In this review article, the most important medicinal plants that are used to treat Alzheimer's disease are reported.

Methods: Relevant articles were retrieved from Information Sciences Institute, Web of Science, PubMed, Scopus, GoogleScholar, and Scientific Information Databases using the search terms Alzheimer's disease, oxidative stress, medicinal plants, extract, essentialoil, and antioxidant and then studied.

Results: According to the findings, Prunella vulgaris, Hypericum perfortu, Cyperus rotondu, Lepidium meyenii, Lavandoula officinalis, Morinda citrifolia, Curcuma longa Linn, Zizyphus jujube, etc. were found to be effective on Alzheimer's disease. Hypericin, choline, flavonoids, oleic acid, betulinic acid, ursolic acid, and rosmarinic acid as well as triterpenoid compounds, jujuphenoside, geraniol, linalool, linalyl acetate, cineole, borneol, alpha-pinene, camphor, butyric acid, valerenic acid, ursolic acid, and luteolin flavonoids are important compounds of Prunella vulgaris, Hypericum perfortu, Cyperus rotondu, Lepidium meyenii, Lavandoula officinalis, Morinda citrifolia, Curcuma longa Linn, Zizyphus jujube that are effective on Alzheimer's disease.

Conclusions: These compounds can be considered pharmaceutically effective compounds on Alzheimer's disease that can be used to produce nature-based and potent drugs used to effectively treat Alzheimer's disease.

Keywords: Neurological disorders, Alzheimer's disease, medicinal plants

1. INTRODUCTION

Alzheimer's disease is usually characterized by progressive and chronic memory disorders alongside speech disorders and deficits of visual-spatial skills and executive functions. This disease is an age-dependent neurodegenerative disease in old age that is characterized by neurons loss in the brain and dementia [1]. The risk of acquiring Alzheimer's disease is 15% and 40% in people aged over 65 years and 80 years, respectively. In the USA, Alzheimer's disease is the seventh leading cause of death [2,3]. The biological mechanism of Alzheimer's disease is unknown. Ageing, the genotype of lipoprotein E4, vascular factors, obesity, insulin resistance, dyslipidemia, hypertension, and inflammatory markers are involved in Alzheimer's disease pathophysiology

and dementia-induced disorders [4]. In patients with Alzheimer's disease, acetylcholine transferase decreases especially in temporal cortex and hippocampus [5]. Acetylcholine concentration in cerebrospinal fluid decreases in Alzheimer's disease patients has been demonstrated to be positively correlated with dementia [5]. Throughout the course of Alzheimer's disease, which can be due to oxidative stress, some disequilibrium is seen between free radicals and antioxidant system [6,7]. Free radicals attack unsaturated fatty acids of the cells of brain tissue and cause oxidative damage [8]. Use of fruits and vegetables that have high antioxidant activities can reduce the incidence of oxidative stress-induced various diseases including Alzheimer's disease through decline in oxidative stress and subsequently free radicals [9-17]. Pharmacologic treatments for Alzheimer's disease include selegiline, vitamin E, and cholinesterase inhibitors. Pychotherapy is another approach to treat Alzheimer's disease [18].

Plants are considered as a pharmaceutical source to treat various disorders and diseases [19-24]. In this review article, the medicinal plants effective on Alzheimer's disease are reported.

2. METHODS

Initially, key words of Alzheimer's disease, medicinal plants, essential oils, extracts were searched and downloaded these articles. Then, searched articles one by one were studied and related articles were selected. Relevant articles were retrieved from *Information Sciences Institute*, *Web of Science*, *PubMed*, *Scopus*, *GoogleScholar*, and *Scientific Information Databases* using the search terms *Alzheimer's disease*, *oxidative stress*, *medicinal plants*, *extract*, *essentialoil*, and *antioxidant* and then studied. During the review process, as well as a number of other low related articles were excluded.The reasons for exclusion papers after the first stage, exclusion the research question or biases due to non-compliance with the articles. Exclusion of articles due to non-compliance with research questions or it was biases articles.

3. RESULTS

According to the findings, Prunella vulgaris, Hypericum perfortu, Cyperus rotondu, Lepidium meyenii, Lavandoula officinalis, Morinda citrifolia, Curcuma longa Linn, Zizyphus jujubewere reported to be effective on Alzheimer's disease (Table 1).

Table 1: Medicinal plants effective on Alzheimer's disease.

Row	Scientific name	Family	Common name	Main findings
1	*Prunella vulgaris*	Lamiaceae	Common self-heal	Decreased secondary delay improved in the mice administered with 25 mg and 50 mg of *Prunella vulgaris* extract in shuttle box and in Y-maze tests. [25].
2	*Hypericum perfortum*	Hypericaceae	St John's wort	Scopolamine administration causes Learning disabilities and memory disorders along with increase in malondialdehyde (MDA) and the activity of cerebral glutamine peroxidase as well as decrease in cerebral glutathione, and reactive oxygen species (ROS). Pretreatment with 4 mg, 8 mg, and 12 mg *Hypericum perforatum* 30 min before scopolamine administration enhanced antioxidant activity and improved inactive avoidance memory through shuttle box in mice [26].
3	*Lepidium meyenii*	Brassicaceae	Maka	Aqueous and hydroalcoholic *Lepidium meyenii* extracts decreased cerebral acetylcholinesterase activity and caused improvement of memory disorders, spatial learning, memory disorders, and inactive avoidance memory induced by scopolamine. [27].
4	*Lavandoula officinalis*	Lamiaceae	lavender	The inhibitory effect of *Lavandula officinalis* extract, at different concentrations, has been confirmed on acetylcholinesterase in different tests on cell lines [28].
5	*Cyperus rotondus*	Cyperaceae	Soed Kofi	Having an anti-acetylcholinesterase property, *C. rotondus* extract caused improvement of memory, spatial learning, and inactive avoidance learning [29].
6	*Morinda citrifolia*	Rubiaceae	Toot Hanoodi	Scopolamine-induced memory loss was associated with decreased CBF, increased oxidative stress and cerebral acetylcholinesterase activity in mice and *M. citrifolia* extract decreased cerebral acetylcholinesterase activity and memory disorders in a dose-dependent manner [30].
77	*Curcuma longa* Linn	Zingiberoidea e	Turmeric	Antioxidant, anti-inflammatory, and immunomodulatory effects of *C. longa* contribute to improving metabolism and preventing cell damage in patients with Alzheimer's disease *C.*

				longa intensified the activity of monocytes and macrophages in patients with Alzheimer's disease throughout beta amyloid removal. [31].
8	*Zizyphus jujube*	Rhamnaceae	Jujube	Due to increasing acetylcholine in cholinergic terminals, *Z. jujube* can play a role in alleviating Alzheimer's disease symptoms and motor deficits. *Z. jujube* extract showed a high effect in activating acetylcholinesterase (34.1%) in vitro mainly because of containing cis-9-octadecenoamide or oleamide [32].
9	*Angelica archangelica* L.	Apiaceae	Garden angelica	The plant has been used for neuro-psychological diseases. *A. archangelica* is able to inhibit Acetyl choline esterase (AChE) activity in-vitro, displace nicotine binding to its receptors in a dose dependent manner and increase cerebral blood flow [41].
10	*Artemisia absinthium* L.	Asteraceae	Absinthe	The plant is able to displace nicotine binding to its receptors in a dose dependent manner. Traditionally, *A. absinthium* has been used to restore the loss of cognitive functions. [41].
11	*Bacopa monniera*	Plantaginaceae	Waterhyssop	*B. monniera* has been reported to have antioxidant property in frontal cortex of rat and improve learning and memory [41].
12	*Biota orientalis* Endl.	Cupressaceae	Biota	Traditionally, *B. orientalis* has been used to improve amnesia and memory registration [41].
13	*Codonopsis pilulosa* Franch	Campanulaceae	Dang shen	*C. pilulosa* is used to improve amnesia, promote blood circulation and increase vitality [41].
14	*Coptis chinensis* French.	Ranunculaceae	Chinese goldthread	*C. chinensis* is a potent inhibitor of monoamine oxidase enzyme. Hence it seems potentially to have anti-depressant activity [41].
15	*Crocus sativus* L.	Iridaceae	Saffron	*C. sativus* has been traditionally used to improve nervous systems disorders, especially, learning impairments [41].
16	*Evodia rutaecarpa* Hook f. & Thoms			The bioactive components of the plant possess anti-nociceptive as well as anti-inflammatory activities. Dehydro-evodiamine, one of its components has inhibited AChE in-vitro and improved memory impairment induced by scopolamine [41].
17	*Hypericum calycimum*	Hypericaceae	Rose-of-Sharon	Hyperfurin improved memory acquisition and consolidation, and completely scopolamine-induced amnesia in mice [41].
18	*Lippia steochadifolia*	Verbenaceae	Augustus Lippi	*L. steochadifolia* and its bioactive components have inhibited the AChE enzyme activity, in-vitro [41].
19	*Magnolia officinalis* Rehder & wilson	Magnoliaceae	Houpu magnolia	*M. officinalis* has antioxidant activity and has been used to treat nervous disturbances, especially anxiety[41].
20	*Angelica sinensis*	Apiaceae	Dong quai	*A. sinensis* has neuro-protective potential for treating *Alzheimer's* disease, as well as vascular *dementia* [42].
21	*Evodia rutaecarpae*			*E. rutaecarpae* has the potential to be used for the treatment of various diseases such as endo-toxemia, diabetes, obesity, *Alzheimer's* disease and cardiovascular diseases [42].
22	*Ginkgo biloba*	Ginkgoaceae	Ginkgo	*G. biloba* is a plant with several compounds with protective effects on brain cells and improves the *Alzheimer's* Disease [42].
23	*Huperzia serrata*	Huperziaceae	Toothed clubmoss	*H. serrate* has a compound named Huperzine which is able to improve Alzheimer's disease and might be used for Alzheimer's *treatment* [42].
24	*Nicotiana tabacum*	Solanaceae	Tobacco	*N. tabacum* might be used for treatment of *Alzheimer's* [42].
25	*Panax ginseng*	Araliaceae	Ginseng	A randomized clinical trial with *Korean* red *ginseng* revealed improvement of patients with *Alzheimer's* disease [42].
26	*Paeonia suffruticosa*	Paeoniaceae	Culture varieties	*P. suffruticosa* and its active components possess potent anti-aggregation activities on *Alzheimer's* amyloid beta proteins [42].
27	*Physostigma venenosa*	Fabaceae	Calabar bean	*P. venenosa* has cognitive benefit on patients with *Alzheimer's* disease [42].

4. DISCUSSION

Prunella vulgaris, Hypericum perfortu, Cyperus rotondu, Lepidium meyenii, Lavandoula officinalis, Morinda citrifolia, Curcuma longa Linn, Zizyphus jujube are some of the plants effective on Alzheimer's disease. *H. perforatum* has antidepressant effects, can alleviate some neurological disorders and exert anti-anxiety, anti-inflammatory, antimigrain and analgesic effects, and is effective in healing wounds [33]. The flowering shoots and leaves of *H. perforatum* contains certain compounds such as tannin, hypericin, choline, and flavonoids [33]. *P. vulgaris* has anti-allergy, anti-inflammatory, anti-oxidative, antimicrobial, and antiviral properties [34].

Phytochemical investigations have demonstrated that *P. vulgaris* contains several active compounds including oleic acid, betulinic acid, ursolic acid, flavonoids, and rosmarinic acid [35]. According to traditional medicine, *Z. jujube* has sedative, anti-bad mood, anxiety-relieving, and stomach, spleen, and gastrointestinal tract-reinforcing properties. It improves motor coordination impairment induced by bilateral electric lesions of the nucleus basalis of meynert in rat [36]. *Z. jujube* fruit has triterpenoid, flavonoid, and jujuphenoside compounds [37], most important of which exist in *L. officinalis*, including geraniol, linalool, linalyl acetate, cineole, borneol, alpha-pinene, camphor, butyric acid, valerenic acid, ursolic acid, and luteolin flavonoids [38]. In traditional medicine, *M. citrifolia* is used to treat different diseases such as arthritis, diabetes, hypertension, gastric ulcer, depression, and atherosclerosis [39].

C. longa has antioxidant, anti-inflammatory, anticancer, antimicrobial, and hepatoprotective effects. Curcumin is the most important active compound of *C. longa* [40]. Hypericin, choline, flavonoids, oleic acid, betulinic acid, ursolic acid, and rosmarinic acid as well as triterpenoid compounds, jujuphenoside, geraniol, linalool, linalyl acetate, cineole, borneol, alpha-pinene, camphor, butyric acid, valerenic acid, ursolic acid, and luteolin flavonoids are important compounds of Prunella vulgaris, Hypericum perfortu, Cyperus rotondu, Lepidium meyenii, Lavandoula officinalis, Morinda Ccitrifolia, Curcuma longa Linn, Zizyphus jujube that are effective on Alzheimer's disease. Therefore, these compounds can be considered pharmaceutically effective on Alzheimer's disease that can be used to produce nature-based and potent drugs used to effectively treat Alzheimer's disease.

More importantly, Alzheimer's disease is associate with oxidative stress and antioxidants benefit this disease [6,7]. Oxidative stress is also associated with variety of other diseases such as neurological disorders, inflammation, infectious diseases, diabetes, athrosclerosis, cardiovascular diseases and wound complication. Oxidative stress causes changes and alterations in redox state. Medicinal plants with antioxidant activity have been shown to be capable of counteracting these conditions. The promising results of plants with antioxidant activity on these diseases have been demonstrated. Medicinal plants introduced here for Alzheimer's disease have antioxidant activities. Therefore, they may have acted with their antioxidant properties.

It has also been demonstrated that excessive activity of acetylcholinesterase and consequently decreased acetylcholine and synaptic transmission can contribute to development of Alzheimer's disease and loss of spatial memory. [28]. Most plants presented in this article have inhibitory effects on acetylcholinesterase resulting in increase in acetylcholine and alleviating memory loss. Hence, medicinal plants may improve Alzheimer's disease by various mechanisms especially through acetylcholine enhancement and antioxidant activity. Medicinal plants with antioxidant activity are also effective in a wide variety of other diseases as well as counteracting with toxic agents induced complications. Therefore, they may also be beneficial for other disease which might be associated with Alzheimer' disease.

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