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Ayurveda and Yoga practices: a synergistic approach for the treatment of Alzheimer's disease

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ABSTRACT: Alzheimer's disease (AD) is an irreversible and progressive neurodegenerative disease which affects about over 30 million people worldwide. There is no suitable treatment for AD nowadays. The current scenario of the research in the field of the search for suitable therapeutic approaches for the treatment of Alzheimer's disease should be a shift towards the combinatorial approach of Ayurveda and Yoga. This review is mainly focused on to adapt Ayurveda and Yoga approaches for the treatment of Alzheimer's disease.

Keywords: Neurodegenerative disease; Alzheimer's disease; Ayurveda; Yoga; Therapeutic approaches.

1. INTRODUCTION

Alzheimer's disease (AD) is an irreversible and progressive neurodegenerative disease. Dementia is the leading cause of AD that affects about over 30 million people worldwide [1]. According to the world Alzheimer report 2018, new case of dementia develops in every three seconds around the world. AD is a major disease that has no effective ways to cure, reverse and slowdown of disease progression once symptoms start. AD is the multifactorial disease in which genetic and environment both involve [2] and progression of inflammation is significant cause of the pathogenesis of the AD [3]. In AD patients, there are three more common changes are appeared in the brain tissues as neurofibrillary tangle, neuritic plaques and senile plaques. AD affects the three main processes that keep neurons healthy as communication, metabolism and repair. The degeneration of the nerve cells is responsible to cause the memory loss, personality changes and problems in routine workout etc. Many researchers are used multi-target strategies for the treatment of AD such as β -amyloid peptide aggregation inhibitors, γ and β -secretase inhibitors & modulators, anti-amyloid immunotherapy, tau hyperphosphorylation inhibitors (e.g. JNK3, CDK5, GSK3 β & Fyn kinase), tau aggregation inhibitors, microtubules stabilization, anti-tau immunotherapy, AChE inhibitors, 5-HT6 antagonism, anti-diabetic/metabolic regulation therapies and Cdk5 inhibitors but these approaches have a limited success to cure the AD [4]. In this article, we have tried to collect an ample data that demonstrates Ayurveda and Yoga are significantly contributed in several distinctive treatment modalities for the Alzheimer's treatment, in spite the use of above medicinal treatments. We have initially discussed about various ayurvedic medicinal therapeutics approaches that effective to prevent the AD progression and then discussed the several yoga practices which significant for AD's treatment.

2. AYURVEDIC THERAPEUTIC APPROACHES IN AD

In Ayurveda, various herbal formulations in which Rasayana is essential for management of mental and cognitive disorders including AD [5]. The Rasayana is mainly focused to enhance oxygenation that helps to promote neurogenesis by the homeostatic regulation re-establishment [6]. It can be noticed that the Ayurvedic medicinal therapeutics approaches are showed the same mechanisms to the modern medicine in a mechanistic study and effective to prevent the AD progression at some extent through various ways showing in Figure 1. They are bio-available and comparatively less toxic. Ayurveda drugs are not only modulated the neuro-endocrine-immune system but also provide rich source of antioxidant, strengthen cognitive power and memory and improve intellects [7]. Affluent sources of anti-oxidant, anti-amyloidogenic, anti-inflammatory, neuroprotective and immunomodulatory compounds are found in Ayurvedic nootropic herbs and formulations. The researchers have been found that these features are essential to modulate the neuro-immune activities, enhance memory, intellect, rejuvenate brain functions, allay neurodegenerative cascades of AD and improve quality life [8]. In recent times, some phytodrugs have been methodically tested in *in-vivo* and *in-vitro* models of AD and also in clinical trials. *Ginkgo biloba*, *Curcuma longa*, *Withania somnifera*, *Angelica sinensis* extracts have been found to regulate APP metabolism towards α -secretase pathway and even restrict the formation, extension and stabilization of A β fibrils. These studies might be provided significant lead for the discovering an appropriate medicine for AD [9]. For the treatment of AD, *Ginkgo biloba* has been under prevention trials [10, 11]. Some study has reported that three plants *Buchanania axillaris* Desr. (Anacardiaceae), *Hemidesmus indicus* Linn. (Apocynaceae) and *Rhus mysorensis* Heyne (Anacardiaceae) were identified as multifunctional therapeutics remedy for the treatment of AD [12]. It has found that *Bramhi Ghrita* has features like as improving cognition, anti-inflammatory properties, clearance of small channels, rejuvenator and blood purification that is perfect for clearing up the toxic metabolic byproducts in the brain and also work to stop neurodegeneration and to support neuroprotection [13].

Several studies have been shown that ayurvedic medicines play a vital role to treat the AD such as *Ginkgo biloba* for slow progression of AD, *Galanthus caucasicus* for treating memory impairments, *Huperzia serrata* for improving memory and mental functioning in AD patients, *Catharanthus roseus* for treating memory loss and mental impairments, *Melissa officinalis* for improving cognitive function and reducing the agitation, *Curcuma longa* (curcumin) increases phagocytosis of amyloid-beta that effectively clearing them from the brains of patients with AD and *Withania somnifera* (Ashwagandha) for stopping reverse and removing the neuritic atrophy and synaptic loss that is the main cause of neurodegeneration [14]. In recent years, some studies have been reported that AD disease could be treated by biomolecules extracted by plants such as kaempferol, is flavonoid, have been found to reduce the neurotoxic motor and cognitive impairments in AD flies [15] and oleanolic acid extracted from a Chinese herb, is pentacyclic triterpene, found to enhance A β induced memory loss and to restore synaptic plasticity in AD rats [16]. Various isolated compounds (alkaloids) have extracted from *Esenbeckia leiocarpa* (Rutaceae) [17], *Coptidis rhizoma* [18] and *Corydalis cava* (Fumariaceae) [19, 20] plants that were reported for acetylcholinesterase and butyrylcholinesterase inhibitory activity.

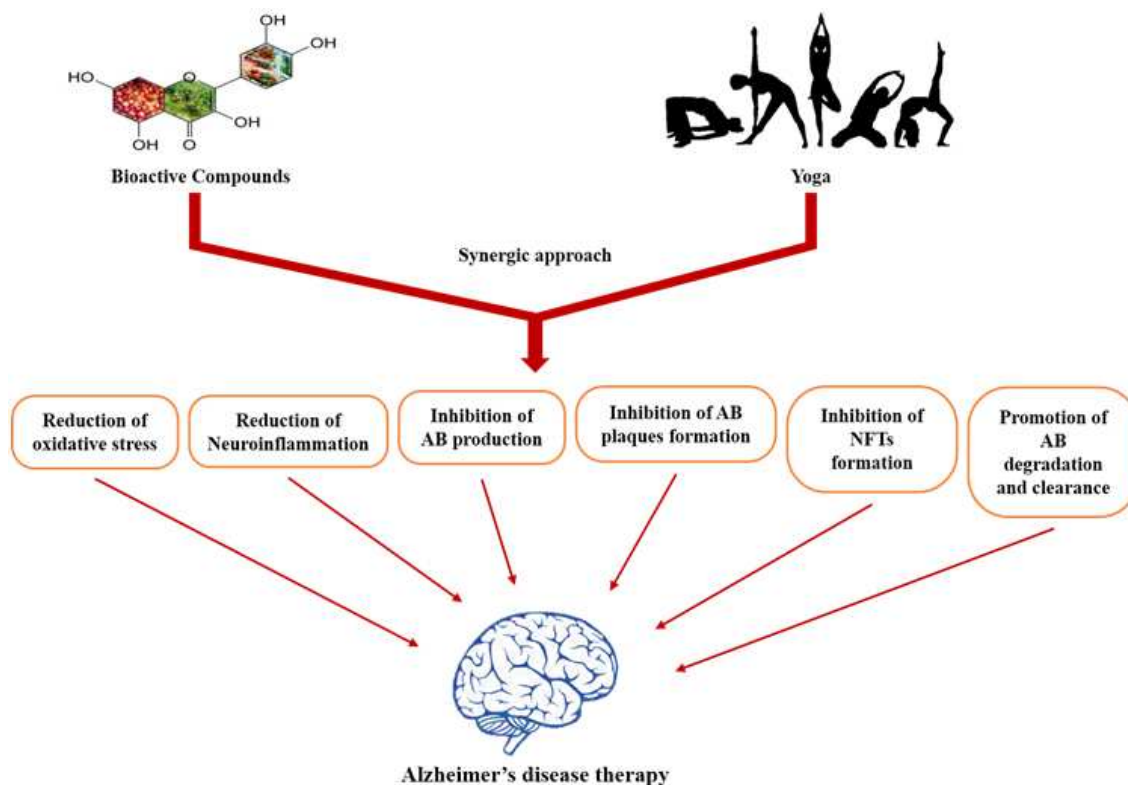


Figure 1. Synergistic neuroprotective effect of Ayurvedic herbs and Yoga practices on AD progression through various aspects.

3. ANTI-OXIDANT PROPERTY

Anti-oxidant present in ayurvedic plants are scavenged the free radicals, which are played vital role in the progression of Alzheimer's disease. Many ayurvedic herbs are contained wide range of bioactive compounds that have a strong anti-oxidant and neuroprotective properties (Table 1) such as *Terminalia chebula* [21], *Passiflora incarnata* [22], *Typhonium trilobatum* [23], *Satureja cuneifolia* [24], *Anisomeles indica* [25], *Curcuma longa* [26], *Bacopa monnieri* [27], *Crocus sativus L.* [28, 29] *Macrosphyra longistyla* [30], *Cinnamomum zeylanicum* [31], *Melissa officinalis* [32, 33], *Caesalpinia crista* [34], *Camellia sinensis* [35], *Scoparia dulcis* [35]. These medicinal plants can be a potent alternative drug for Alzheimer's disease treatment.

4. ANTI-AMYLOIDOGENIC PROPERTY

Natural extracts (e.g. polyphenols, alkaloids, cannabinoid) of medicinal plants that have shown anti-amyloidogenic activities which is crucial to potent drug discovery to treat the AD without any side effects. These medicinal plants are *Grewia tiliaefolia* [36], *Cassia tora* [37], *Elettaria cardamomum* [38], *Caesalpinia crista* [39], *Perilla frutescens* [40], *Guettarda speciose* [41], *Dryopteris crassirhizoma* [42], *Dracocephalum moldavica L.* [43], *Bacopa monnieri (L.) Wettst* [44], *Perilla frutescens* [45], *Lawsonia inermis* [46], *Sargassum horridum* [47] that involve in anti-amyloid activity (Table 1).

5. ANTI-INFLAMMATORY PROPERTY

Various medicinal plants extract (polyphenols, alkaloids, cannabinoid) has shown anti-inflammatory activities in in-vitro/vivo experiments which is vital to develop a potential drug to treat the AD with no any

side effects. These medicinal plants are *Terminalia chebula* [21], *Crocus sativus L.* [28, 29], *Lagerstroemia indica* [48], *Limonium spathulatum* [49], *Okinawa propolis* [50], *Corydalis dubia* [51], *Pancreaticum parvum* [52] that reducing the inflammatory effects in brain tissues (Table 1).

6. NEUROPROTECTIVE PROPERTY

Alkaloids, flavonoids and phenolic acids, secondary metabolites of plants, are played a major role in improving regeneration or inhibiting neurodegeneration [53]. The plants compounds with neuroprotective property are widespread in clinical use but many is undergoing in clinical trials for the treatment of AD include nerve growth factor, valproate and other GSK inhibitors, various nicotinic agonists, the CEP-1347 stress kinase inhibitor, minocycline as caspase inhibitor and metal chelators [54]. *Bacopa monnieri* (L.) Wettst [44], *Grewia tiliaefolia* [55], *Vernonia amygdalina* [56], *Levisticum officinale* [57], *Schisandra chinensis* [58], *Withania somnifera* [59], *Ginkgo biloba* [60], *Kigelia africana* [61] have the potentials of the neuroprotection through the improving regeneration of the neuron cells and inhibiting the neurodegeneration (Table 1).

Table 1. Showing the name and type of herbal compounds used in in-vivo/in-vitro and their properties.

Botanical name of medicinal plants	Plant compound	Type of study	Activity	References
<i>Terminalia chebula</i>	Phenolic	<i>In-vivo</i>	Antioxidant, Anti-inflammatory, Neuroprotective	[21]
<i>Passiflora incarnata</i>	Butanolic	<i>In-vitro</i>	Antioxidant	[22]
<i>Typhonium trilobatum</i>	Flavonoids	<i>In-vitro</i>	Antioxidant	[23]
<i>Satureja cuneifolia</i>	Phenolic	<i>In-vitro</i>	Antioxidant	[24]
<i>Anisomeles indica</i>	Polyphenol	<i>In-vivo</i>	Antioxidant, Anti-cholinesterase	[25]
<i>Curcuma longa</i>	Hydroxynonenal	<i>In-vivo</i>	Antioxidant	[26, 35]
<i>Bacopa monnieri</i>	Bacoside A, Bacoside B, Bacosaponins, Betulinic acid	<i>In-vivo</i>	Neuroprotective	[27]
<i>Crocus sativus L.</i>	Carotenoid	<i>In-vivo</i>	Antioxidants, Anti-inflammatory, Neuroprotective	[28, 29]
<i>Macrosphyra longistyla</i>	Tannins, Flavonoids, Phenolics, Terpenoids, Saponins	<i>In-vitro</i>	Antioxidant, Anti-cholinesterase	[30]
<i>Cinnamomum zeylanicum</i>	Cinnamaldehyde Cinnamyl acetate	<i>In-vitro</i>	Antioxidant, Anti-cholinesterase	[31]
<i>Melissa officinalis</i>	Rosmarinic acid	<i>In-vivo</i>	Antioxidant, Anti-cholinesterase, Anti-inflammatory	[32, 33]
<i>Caesalpinia crista</i>	Methanolic	<i>In-vivo</i>	Antioxidant, Anti-cholinesterase, Neuroprotective, Anti-amyloidogenic	[34, 39]
<i>Camellia sinensis</i>	Catechin	<i>In-vitro</i>	Antioxidant	[35]
<i>Scoparia dulcis</i>	Flavones	<i>In-vitro</i>	Anti-amyloidogenic	[35]
<i>Grewia tiliaefolia</i>	Vitexin	<i>In-vitro</i>	Anti-amyloidogenic Anti-cholinesterase	[36]
<i>Cassia tora</i>	Polyphenols	<i>In-vitro</i>	Antioxidant, Anti-cholinesterase	[37]
<i>Elettaria cardamomum</i>	Alpha-terpinyl acetate	<i>In-vitro</i>	Antioxidant, Anti-cholinesterase, Neuroprotective, Anti-amyloidogenic	[38]
<i>Perilla frutescens</i>	Asarone	<i>In-vitro</i>	Anti-amyloidogenic	[40]

Botanical name of medicinal plants	Plant compound	Type of study	Activity	References
<i>Guettarda speciose</i>	Iridoids, Phenolics	<i>In-vivo</i>	Anti-inflammatory, Anti-amyloidogenic	[41]
<i>Dryopteris crassirhizoma</i>	Butanolic	<i>In-vitro</i>	Anti-amyloidogenic	[42]
<i>Dracocephalum moldavica</i> L.	Flavonoids	<i>In-vitro</i> , <i>In-vivo</i>	Neuroprotective, Anti-amyloidogenic	[43]
<i>Bacopa monnieri</i> (L.) Wettst	Phenolics, Flavonoids	<i>In-vivo</i>	Antioxidant, Anti-amyloidogenic	[44]
<i>Perilla frutescens</i>	Luteolin, Rosmarinic acid, Flavonoids	<i>In-vitro</i>	Anti-amyloidogenic	[45]
<i>Lawsonia inermis</i>	1,2,4-trihydroxynaphthal-ene-2-O-β-D-glucopyranoside	<i>In-vitro</i>	Antioxidant, Anti-amyloidogenic	[46]
<i>Sargassum horridum</i>	Fucosterol	<i>In-vitro</i>	Anti-amyloidogenic	[47]
<i>Lagerstroemia indica</i>	Alkaloids, Phenolics, Flavonoids	<i>In-vitro</i>	Antioxidant, Anti-inflammatory	[48]
<i>Limonium spathulatum</i>	Phenolics	<i>In-vitro</i>	Antioxidant, Anti-cholinesterase, Anti-inflammatory	[49]
<i>Okinawa propolis</i>	Flavonoids	<i>In-vivo</i>	Anti-inflammatory	[50]
<i>Corydalis dubia</i>	Scoulerine	<i>In-vitro</i>	Anti-cholinesterase, Anti-inflammatory	[51]
<i>Panacratium parvum</i>	Flavonoids	<i>In-vitro</i>	Antioxidant, Anti-inflammatory	[52]
<i>Grewia tiliaefolia</i>	Vitexin	<i>In-vitro</i>	Anti-cholinesterase, Neuroprotective	[55]
<i>Vernonia amygdalina</i>	Alkaloid	<i>In-vitro</i> , <i>In-vivo</i>	Antioxidant, Neuroprotective	[56]
<i>Levisticum officinale</i>	Polyphenol	<i>In-vivo</i>	Antioxidant, Anti-cholinesterase, Anti-inflammatory, Neuroprotective	[57]
<i>Schisandra chinensis</i>	Lignan	<i>In-vitro</i> , <i>In-vivo</i>	Neuroprotective	[58]
<i>Withania somnifera</i>	Acrolein	<i>In-vitro</i>	Antioxidant, Anti-cholinesterase, Neuroprotective	[59]
<i>Ginkgo biloba</i>	EGb761	<i>In-vitro</i> , <i>In-vivo</i>	Antioxidant, Anti-inflammatory, Neuroprotective	[60]
<i>Kigelia africana</i>	Flavonoids	<i>In-vivo</i>	Antioxidant, Neuroprotective	[61]

7. YOGA PRACTICES ARE VITAL IN AD

Yoga is a non-religious mind-body approach of ancient India that integrates the spiritual, mental and physical components to improve the health and well-being [62, 63]. Yoga has several essential benefits and positive impactful for various body systems such as musculoskeletal system, cardiopulmonary, nervous and endocrine systems. Meditation has great potentials in stress reducing effects that is the beneficial for preventing cognitive and memory loss. Stress is depended upon the level of cortisol in body that responsible to progression of the Alzheimer's disease, which can be regulated by a regular practice of meditation, however, very limited studies have been conducted with Alzheimer's patients [64]. Some neurotransmitters secreted during the Yoga that provides the potential biological mechanism, which is responsible to improvement in AD neuropathology [65]. There has been found that long-term aerobic exercise has the potential to increase cognitive functioning and decreases in the hippocampal loss that help in prevention of the

AD [66] and the aerobic exercise may also a necessary part of the treatment for AD [67]. It can be noted that the aerobic training induces important beneficial effects on health that improving the executive function, attentional capacity, processing speed, episodic memory and procedural memory [68-70]. Several studies have been reported that physical exercise may be able to prevent and reverse these behavioral impairments in specific model of AD [70] and reducing the symptoms of dementia [71]. A recent study is presented that meditation may present themselves significant role for improving cognition and related outcomes in AD patients [72].

8. CONCLUSION

The current scenario of the research in the field of the search of suitable therapeutic approaches for the treatment of Alzheimer's disease should be shift towards the combinatorial approach of Ayurveda and Yoga, the reason behind this is that, there is no side effect of anyone out of these two, while these must be beneficial for any type of human disease. Non-drug interventions like memory training, mental and social stimulation and physical exercise programs could be possibly improved people's cognitive performance [73]. By going through different available literature on concern topic, we found that Ayurvedic therapeutic approaches and Yoga practices have been widely used for the health promotion, disease prevention and possible treatment of the Alzheimer's disease. Many Ayurvedic formulations, they are bio-available, have been used for modifying the treatment of AD. They have many special features like less toxic, anti-oxidant, anti-amyloidogenic, anti-inflammatory, neuroprotective and immunomodulatory that are essential to discover appropriate potent drugs for the AD and also significant for reduction in the cost and time. Many studies have shown that yoga is vital for treating the neurodegenerative disorders by several combine yogic exercises. The combination of the Ayurveda and Yoga would provide significant outcome for noble strategy of the treatment of Alzheimer's disease. These combinations might be proved to provide the better panacea for AD in future.

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