Hindawi
International Journal of Alzheimer's Disease
Volume 2020, Article ID 7603015, 15 pages
https://doi.org/10.1155/2020/7603015

Review Article

Taxonomic Distribution of Medicinal Plants for Alzheimer's Disease: A Cue to Novel Drugs

Muhammad Kamran,[1] Rehana Kousar,[2] Shakir Ullah,[3] Siraj Khan,[1] Muhammad Farooq Umer,[1] Haroon Ur Rashid,[1] Zakir Khan,[1,4] Muhammad Ijaz Khan Khattak ,[1,5] and Mujeeb Ur Rehman [1]

[1]*Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan*
[2]*Department of Botany, Faculty of Sciences, Pir Mehr Ali Shah, Arid Agriculture University Rawalpindi, Pakistan*
[3]*Department of Pharmacy, University of Malakand, Lower Dir, Dir KPK, Pakistan*
[4]*Çukurova Üniversitesi, Tıp Fakültesi, Tıbbi Farmakoloji Anabilim Dalı, Sarıçam, Adana 01330, Turkey*
[5]*Department of Pharmacy, University of Swabi, Anbar, 23561 Swabi, KPK, Pakistan*

Correspondence should be addressed to Muhammad Ijaz Khan Khattak; ijazkhattak74@yahoo.com and Mujeeb Ur Rehman; mujeebkhwaja@gmail.com

Received 27 December 2019; Accepted 14 May 2020; Published 19 June 2020

Academic Editor: Francesco Panza

Alzheimer's disease (AD) is a neurodegenerative disorder manifested by decline in memory and mild cognitive impairment leading to dementia. Despite global occurrence of AD, the severity and hence onset of dementia vary among different regions, which was correlated with the customary use of medicinal herbs and exposure level to the causatives. In spite of execution of versatile therapeutic strategies to combat AD and other neurodegenerative diseases, success is only limited to symptomatic treatment. The role of natural remedies remained primitive and irreplaceable in all ages. In some examples, the extracted drugs failed to show comparable results due to lack of micro ingredients. Micro ingredients impart a peerless value to natural remedies which are difficult to isolate and/or determine their precise role during treatment. A variety of plants have been used for memory enhancement and other dementia-related complications since ages. Acetyl choline esterase inhibition, antioxidant potential, neuroprotection, mitochondrial energy restoration, and/or precipitated protein clearance put a vast taxonomic variety into a single group of anti-AD plants. Secondary metabolites derived from these medicinal plants have the potential to treat AD and other brain diseases of common pathology. This review summarizes the potential of taxonomically diverse medicinal plants in the treatment of AD serving as a guide to further exploration.

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by personality and behavioral impairments along with dementia [1]. AD is a condition of high neurofibrillary tangles and β-amyloid level due to duplication or mutation of β-amyloid precursor proteins (APP) and a presenilin-encoding gene for proteolytic enzymes [2]. Brain neurodegeneration and β-amyloid (Aβ) deposition are used as biomarkers for the identification of individuals at risk of AD [3]. Neurodegenerative disorders occur due to combined effects of environmental and genetic factors accompanied by aging [4]. AD takes years to progress without apparent clinical symptoms which ultimately lead to declined cognition [5, 6]. AD starts with changes in normal functions of the brain, initially by failure to generate new memories as it is difficult to consolidate new information and leads to rapid forgetting [7]. It is characterized by the formation of plaques followed by inflammation, lack of cholinergic activity, and stress [8]. Risk of cognitive aging and Alzheimer's disease increases due to inflammation in the central nervous system (CNS) caused by any alterations in the microglia [9].

In a normal physiological state, the oxidative stress is overcome by antioxidant enzymes, but in AD, these enzymes

fail to perform their normal function in the brain [10]. Progression of pathology in AD starts from the perirhinal region to the hippocampus complex and ultimately to temporal lobes with the basal forebrain [11]. AD is mostly linked with emotions, and it affects the quality of life of patients and the caregivers. Changes in behaviors either positive or negative are an important parameter to assess the quality of life of patients suffering from AD [12]. Aging, education, gender, genetics, and apolipoprotein E $\varepsilon 4$ allele are significant risk factors for AD [13]. Cardiovascular disease, diabetes, and smoking increases the risk of AD and dementia [14, 15].

Screening and management of cardiovascular diseases like stroke, blood pressure, and other problems significantly lowered the risk of AD [14] contrary to the earlier concept that cardiovascular risks, trauma, smoking, family history, alcohol, and use of nonsteroidal anti-inflammatory drugs (NSAIDs) have no significant impact on AD [12]. Occupational environment, physical exposure, or chemicals also have no relation to progression of AD [16]. Common cognitive activities such as reading books, watching television, and playing games reduce the risk of AD and dementia [17]. Cardiac medications, for instance, digoxin, antihistamines, and other nonpsychotropic agents, may induce cognitive impairment by interfering with neurotransmitter function [18].

The number of people suffering from AD and dementia is increasing globally due to many factors including growing population, aging, and growth. It has been estimated that this number doubled from 1990 to 2016 [19], and currently, an estimated 40–50 million people are affected by dementia [19]. Alzheimer's disease and dementia share approximately 2.5% of the total mortality toll among the 12% of global deaths caused by neurological disorders [20], and the rate of deaths due to dementia elevated by 148% between 1990 and 2016 making it the fifth largest cause of death [19]. With 7.7 million new cases each year [21], it is predicted that by the year 2050, one out of 85 people will be suffering from Alzheimer's disease or other forms of dementia. AD is widespread in older people with a 25-50% higher prevalence rate than the young people [22]. Early detection and appropriate treatment are suggested to lower the increasing incidence of AD as well as other metabolic disorders [23]. Age is considered one of the most important factors as dementia is more prevalent in the geriatric population and more than three-quarters of dementia occur as a result of AD [24]. The early onset before age 65 years is very scarce, and its prevalence before age 50 years is even less than 1 per 4000, with roughly 30% of cases being attributed to Alzheimer's disease [25]. The increasing prevalence of AD has raised concerns to understand its pathophysiology and the risk factors associated with AD to format an affordable preventive or curative strategy. Aging, sex, and genetics are the prime risk factors, but modifiable factors like lifestyle and certain treatable medical conditions play an important role in AD development [26].

An AD brain shows agglomeration of hyperphosphorylated tau protein (neurofibrillary tangle formation), a primary marker of AD, along with deposits of β-amyloid in the gray matter of the brain which ultimately leads to loss of neurons in the brain which causes cognitive impairment leading to Alzheimer's disease as shown in Figure 1 [3]. β-Amyloid accumulation activates immune cell infiltration resulting in inflammation. This not only hinders cell communication but also leads to cognitive impairment and neuronal cell death. The proteases butyrylcholinesterase (BChE), acetylcholinesterase (AChE), and β-amyloid secretase-1 (BACE-1) correlate with the aggregation and accumulation of β-amyloid plaques in the AD patients' brains [27]. The genetic component (60–80%) and the apolipoprotein E (APOE) gene are among the leading genetic risk factors [28]. Mutations in genes like presenilins (PSEN I, PSEN II) and APP are involved in the early onset of AD while the APOE gene is considered one of the most important causative genes. Overexpression of the APOE gene causes accumulation of high amount of β-amyloid, and this observation leads to the formation of β-amyloid hypothesis of AD [29]. In mitochondria, redox-active metals interact with oxidative response elements, which generates high levels of hydrogen peroxide that cause oxidative damage. In the early stage of the disease, β-amyloid and tau protein deposition compensates and downregulates this damage. But when the disease progresses, antioxidant activity becomes decreased which leads to the generation of reactive species that cause high oxidative stress in AD [30]. Decrease in acetylcholinesterase activity occurs when there is excessive deposition of tau protein and β-amyloid adding the complications in AD [31]. Leukotriene signaling inhibition in the brain cells is associated with neuroinflammation and neurodegeneration inhibition, and targeting the leukotriene signaling system will mediate several aspects of AD pathology [32]. Proper and effective diagnosis for AD is done through a postmortem brain study. Currently, new ways are developed to check levels of β-amyloid and tau proteins in blood and cerebrospinal fluid (CSF), but these ways are not reliable so better options need to be developed [33].

Appropriate therapeutic and preventive strategies may delay the progression of AD [34]. Lifestyle modifications and appropriate physical activity can reduce the overall prevalence of AD [35]. Interventions for the management of dementia are not signed up to the mark, and cost-effective programs should be started for better treatment and prevention of dementia [1]. β-Amyloid levels, tau proteins, and genetic susceptibility, along with vascular changes and hearing loss, are used for the early diagnosis of AD. Magnetic resonance imaging (MRI) and positron emission tomography (PET) scanning improved the diagnosis of AD [36]. Due to the complex nature of AD, no reliable treatment is currently available to cure this disorder. The available drugs are used to slow down the progression of the disease and have many side effects [37]. Traditionally, memory and cognitive abilities are enhanced by various plants and their preparations. Plants contain secondary metabolites which possess therapeutic potential in Alzheimer's disease. This review article will provide us the basis for the development of drugs derived from natural sources both in terms of activity and in terms of cost-effectiveness in the treatment of AD.

Secondary metabolites derived from medicinal plants showed potential against dementia and AD [8]. Moreover, natural products have diversity in terms of their structure and functions, so it is easy to develop anti-AD medicines from natural sources. Herbs have therapeutic potency, AChE

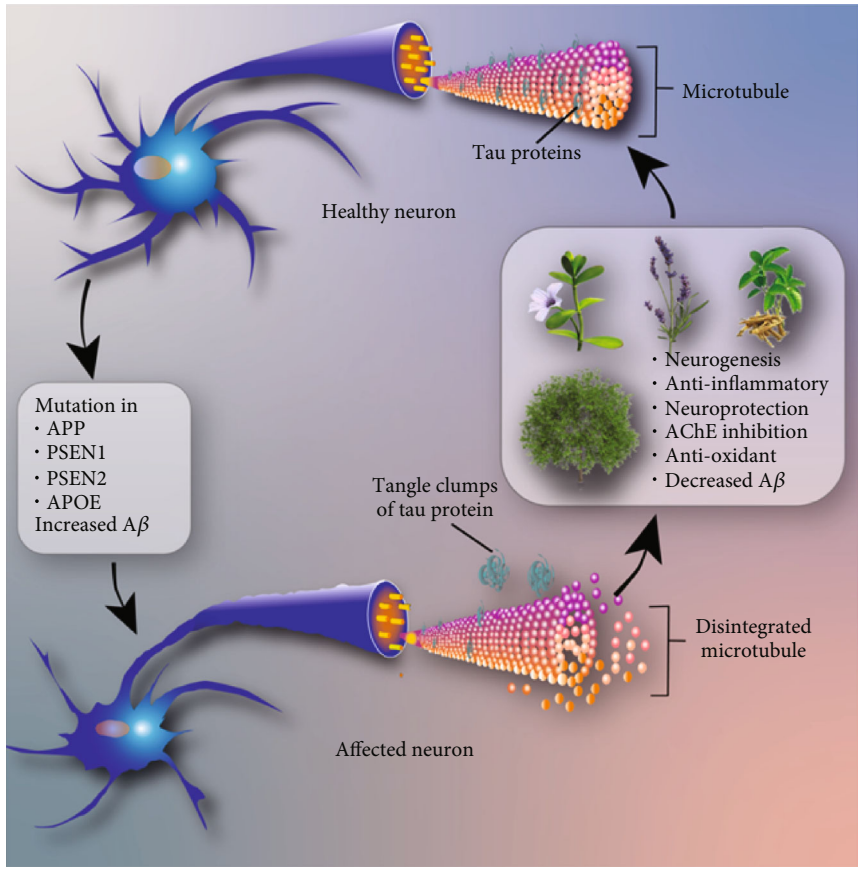

Figure 1: Alzheimer's disease. Condition of high neurofibrillary tangles and increased β-amyloid (Aβ) level due to duplication or mutation of β-amyloid precursor proteins (APP) and apolipoprotein E- (APOE-) and presenilin- (PSEN1, PSEN2) encoding genes for proteolytic enzymes. Medicinal plants reduce the effects of Alzheimer's disease by different proposed mechanisms, decrease β-amyloid level, inhibit acetylcholinesterase (AChE), and enhance neurogenesis as well as neuroprotection and anti-inflammatory and antioxidant effects.

inhibitory activity, antioxidant and anti-inflammatory capacity, and redox metal-chelating activities, inhibit Aβ aggregation, and hyperphosphorylate tau proteins [38].

However, only a few medications have been developed yet that are approved by the FDA for treatment against AD [39]. We focused on the recent studies regarding the potential of various plants and their phytochemicals in treating Alzheimer's disease. Therapeutic potential of different plant families according to their antioxidant, anti-inflammatory, neuroprotective, and anti-AChE properties is discussed and shown in Table 1 [40, 41] and Figure 1.

2. Material and Methods

2.1. Search Strategy and Selection. The current review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [42]. The published studies were searched by using the MeSH terms "medicinal plants for Alzheimer's disease", "Alzheimer's disease", "Plants and medicinal used in Alzheimer's disease", "role of medicinal plant in Alzheimer's disease", "Alzheimer's disease and treatment approaches", "new molecules in Alzheimer's disease", "medicinal plants and Alzheimer's disease", "exploration of Alzheimer's disease", "plants family and its use in Alzheimer's disease", and "taxonomic distribution of plants in Alzheimer's disease", in Google Scholar, PubMed, Ovid, Alzheimer's disease journals, MEDLINE, Embase, and the Cochrane Database of Systematic Reviews without language limitation, with the last search being updated in 2018. The reference lists were hand searched for other relevant publications.

2.2. Data Extraction/Inclusion and Exclusion Criteria. The first author name, year of publication, source of plants, and plants used in Alzheimer's disease were selected from each publication according to the following inclusion criteria: (1) plants studied in Alzheimer's disease; (2) the molecular mechanisms explored in Alzheimer's disease; and (3) the studies evaluated by limitations, consistency, directness, precision, and publication bias and having control or placebo groups. The quality of the included studies was determined according to the GRADE process, and those articles were included which were published in indexed journals.

3. Results and Discussion

Over the years, the management of AD has remained a big challenge for medical science due to the unavailability of a large number of therapeutic choices; as of today, only a few medications have been developed and approved from the US FDA. Keeping in view the diversity in structures and

Table 1: Medicinal plant species used for the treatment of Alzheimer's disease.

Serial no.	Family	Plants name	Part used	Properties	Chemical constituents	References
01	Acanthaceae	*Thunbergia grandiflora* Roxb	Leaf extract	Antioxidant, antilipoxygenase, AChE inhibitor	Iridoids, glycosides	[44]
		Andrographis paniculata (Burm.f.)	Active compound	AChE, BChE, and BACE-1 inhibitor	Grandifloric acid, phenolic acids	[27]
02	Acoraceae	*Acorus calamus* L.	Plant extract	Antioxidant, AChE inhibitor	Phenolics, flavonoids	[46]
03	Anacardiaceae	*Mangifera indica* Wall	Leaf extract	Antipyretic, antioxidant	Flavonoids, phenols	[48]
		Myracrodruon urundeuva M. Allemão	Leaf extract	Anti-inflammatory, AChE inhibitor	Phenols	[48]
		Semecarpus anacardium Buch.-Hamis.	Leaf extract	Antioxidant, anti-AChE	Flavonoids, phenols	[49]
04	Apiaceae	*Ferula asafoetida* H. Karst	Whole plant extract, resins	AChE inhibitor, antioxidant activity	Ferulic acid, umbelliferone, coumarins, and other terpenoids	[51, 128]
		Coriandrum sativum L.	Leaf extract, volatile oil	Antioxidant, antidepressant, and anxiolytic proprieties	Petroselinic acid, linalool, fatty acids	[53, 129]
05	Apocynaceae	*Hancornia speciosa* Gomes	Fruit extracts	Antioxidant, AChE inhibitor	Flavonoids, phenols, tannins	[55]
06	Araliaceae	*Eleutherococcus leucorrhizus* var. setchuenensis (Harms) C. B. Shang & J. Y. Huang and *Eleutherococcus sessiliflorus* (Rupr. & Maxim.) S. Y. Hu	Leaf extracts	Antioxidant, adaptogen, anti-inflammatory	Eleutherosides	[58, 59]
		Acanthopanax trifoliatus (L.) Voss and *Eleutherococcus senticosus* Maxim	Whole plant extract	Leukotriene signaling pathway inhibitor	Polyphenols, flavonoids	[59]
		Panax ginseng C.A. Mey	Root extract	Neuroprotective	Ginsenosides, gintonin	[61–63]
07	Arecaceae	*Syagrus romanzoffiana* (Cham.) Glassman	Leaf and fruit extract	AChE inhibitor	Stilbenoids, flavonoids, lignans, phenols, and fatty acids	[64]
08	Boraginaceae	*Nonea micrantha* Boiss. & Reut.	Whole plant extract	Antioxidant, AChE inhibitor	Saponins	[66]
09	Buxaceae	*Sarcococca saligna* Müll.Arg	Whole plant extracts	AChE inhibitor	Steroidal alkaloids	[67]
		Sarcococca hookeriana Baill	Whole plant extracts	Butylestrase inhibitor	Steroidal alkaloids, salignenamide	[69]
		Buxus papillosa C.K. Schneid	Leaf extract	Skin protectant	Vegainine, hookrianamide, buxakarachiamine	[70]
10	Convolvulaceae	*Convolvulus pluricaulis* Choisy	Leaf extracts	Antioxidant, muscarinic receptor stabilizer	Ascorbic acid, flavonoids, rivastigmine, terpenoids, steroids	[72]
11	Crassulaceae	*Rhodiola rosea* L.	Root and rhizome extract	Anti-inflammatory and adaptogenic, antioxidant	Glycoside salidroside	[58, 76]
12	Cucurbitaceae	*Caryocar coriaceum* Wittm.			Flavonoids	[77]

Table 1: Continued.

Serial no.	Family	Plants name	Part used	Properties	Chemical constituents	References
13	Fabaceae	*Bauhinia forficata* Link and *Copaifera langsdorffii* Desf	Fruit extract	Antioxidant, antifungal and antileishmaniasis	Polyphenols	[79–82]
			Fruit extract	Hypoglycemic, antioxidant, AChE inhibitor, hypoglycemic		
		Clitoria ternatea L.	Leaf and root extracts	Brain tonic antioxidant, muscarinic receptor stabilizer	Quercetin and myricetin glycosides	[72]
14	Ginkgoaceae	*Ginkgo biloba* L.	Leaf extracts	Antioxidant, AChE inhibitor	Terpenes, bilobalide, ginkgolide	[84]
15	Iridaceae	*Crocus sativus* Ten	Dry stigma powder	Antioxidant, neuroprotective	Crocin, crocetin, picrocrocin, and safranin	[84]
16	Lamiaceae	*Mentha piperita* L., *Salvia longifolia* Nutt., *Betonica officinalis* L., *Satureja montana* L., *Teucrium* L., *Chamaedrys* Moench, *Clerodendrum cephalanthum* subsp. montanum (Thomas) Verdc., *Teucrium polium* L., and *Thymus vulgaris* L.	Arial part and leaf extracts	Antioxidant, AChE inhibitor, anticholinesterase activity	Carotenoids, phenolic acids, rosmarinic acid, chlorogenic acid, caffeic acid, ferulic acid, Trolox	[92]
		Lavandula angustifolia Mill	Arial part extract	Antioxidant, neurotransmitter, antianxiety, hypnotic, anticonvulsant	Linalool, tannins, linalyl acetate, camphor, coumarins, triterpenes, flavonoids	[94, 95, 130]
17	Lessoniaceae	*Ecklonia cava*	Seaweed extract	AChE inhibitor, antioxidant, anti-inflammatory, and anticancer	Dieckol, phlorofurofukoeckol-A	[97]
18	Lythraceae	*Lawsonia inermis* L.	Leaf extract	Antioxidant, nootropic potential	Phytol, pseudoephedrine, aspidofractinine-3-methanol, phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl, methylcarbamate	[98]
19	Lycopodiaceae	*Lycopodiella cernua* (L.) Pic.Serm, *Lycopodiella riofrioi* (Sodiro) B.Øllg, *Lycopodium clavatum* f. brevipedunculatum Louis-Marie, and *Huperzia selago* var. serrata (Thunb.) Á. Löve & D. Löve	Whole plant extract	AChE inhibitor, antioxidant, AChE inhibitor	Huperzine A	[99, 100]
20	Moraceae	*Ficus carica* L.	Mesocarp extract	Antioxidant	C-Sitosterol	[21]
21	Myrtaceae	*Psidium guajava* L.	Leaf and fruit extract	Antioxidant, antidiabetic	Linoleic acid	[103]
22	Oleaceae	*Olea europaea* L.	Fruit oil	Autophagous, antioxidant, anti-inflammatory, neuroprotective	Polyphenols, oleuropein aglycone	[105–107]
23	Pedaliaceae	*Sesamum indicum* L.	Seed extract	Antioxidant, AChE inhibitor, neuroprotective	Sesamin, sesaminol, terpenes, flavonoids	[109]

Table 1: Continued.

Serial no.	Family	Plants name	Part used	Properties	Chemical constituents	References
24	Plantaginaceae	*Rehmannia glutinosa* f. lutea	Root extract	Antioxidant, neuroprotective, anti-inflammatory	Catapols, 5-hydroxymethylfurfural, bacopasaponin	[110]
		Bacopa monneiri or thyme-leaved gratiola	Leaf extracts	Antioxidant, antilipoxygenase	Brahmine, herpestine	[111]
25	Polygalaceae	*Polygala alba* var. tenuifolia S.F.Blake	Root extract	Antioxidant	Lipopolysaccharides	[112]
26	Ranunculaceae	*Nigella sativa* L.	Seed extract	Anti-inflammatory and antioxidant, AChE inhibitor, neuroprotective	Thymoquinone, phenols	[113–115]
27	Rhamnaceae	*Ziziphus jujuba* Lam	Whole plant extract	Antioxidant, immunostimulant, and anti-inflammatory	Flavonoids, polysaccharides, phenolics, terpenes	[117]
28	Sargassaceae	*Sargassum sagamianum*	Seaweed extracts	AChE inhibitor	Plastoquinones, sargachromenol, sargaquinoic acid	[119]
29	Saururaceae	*Saururus chinensis* hort. ex Loudon	Whole plant extract	Antioxidant, anti-inflammatory	Flavonoids, alkaloids, α-pinene, cinnamic acid, camphene, safrole, β-caryophyllene, linalool, and humulene	[121, 122]
30	Solanaceae	*Withania somnifera* (L.) Dunal	Root extracts	Antioxidant, adaptogenic, leukotriene signaling inhibitor	Sitoindosides, withaferin	[125]
31	Zingiberaceae	*Curcuma longa* L.	Rhizome extracts	Neuroprotective, anti-inflammatory, protein hyperphosphorylation inhibitor	Curcumins, flavonoids, phenols	[127]

functions, natural products could be the best possible source for developing an anti-AD medication. Research has shown that secondary metabolites obtained from medicinal plants have the potential to be converted into a lead molecule effective against AD. In this review, we have enlisted different plant families based on their therapeutic potential (Figure 1) to treat AD as shown in Table 1 and discussed below.

3.1. Family: Acanthaceae. Dicotyledonous plants with 2500 plant species are included in the Acanthaceae family [43]. *Thunbergia grandiflora* Roxb. commonly found in Bangladesh is an important plant of the Acanthaceae family which contains iridoids, glycosides, isounedoside, and grandifloric acid. These compounds possess anti-AChE, antioxidant, and anti-arthritic properties. The methanolic extract was analyzed for anti-AChE activities and lipid peroxidation inhibition for antioxidant activities. Results revealed the effectiveness of the *T. grandiflora* leaf extract in the treatment of AD [44]. *Andrographis paniculata* (Burm.f.), another plant from this family, also possesses neuroprotective activity. Three compounds 3,4-di-o-caffeoylquinic acid, apigenin, and 7-o-methylwogonin were reported from *A. paniculata* with maximum binding affinities for cholinesterases and BACE-1. It was predicted that these compounds are strong inhibitors of AChE, BChE, and BACE-1, thus inhibiting the formation of β-amyloid plaques, which is the main cause of dementia and neurotoxicity [27].

3.2. Family: Acoraceae. The family Acoraceae contains two species around the globe. *Acorus calamus* L. is a plant of the Acoraceae family which is used in Ayurveda and herbal treatment for centuries. It contains flavonoids, triterpenes, alkaloids, phenols, and saponins [45]. Total phenolic contents from the methanolic extract of *Acorus calamus* L. were determined through the Folin-Ciocalteu micromethod at 760 nm. A 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay was also performed at 517 nm, and anti-AChE activity was examined in male rats of the Wistar strain. Positive results were obtained, and it was suggested that total phenolics and antioxidant potential of *A. calamus* make it a probable candidate in the treatment of AD [46].

3.3. Family: Anacardiaceae. Cashew or Anacardiaceae is a family of flowering plants comprising 860 plant species [47]. *Mangifera indica* L. Wall is a noteworthy member of the Anacardiaceae family that possesses antipyretic and anti-ulcer activities. It has recently been proposed that being a rich

source of flavonoids, *M. indica* Wall have potential against oxidative stress and can be a suitable candidate for the treatment of AD. *Myracrodruon urundeuva* M. Allemão possess anti-inflammatory and acetylcholinesterase inhibitory activity. The presence of high phenolic contents makes it a good principal component for AD management [48]. *Semecarpus anacardium* Buch.-Hamis. is another member of the Anacardiaceae family that contains flavonoids and phenolics. Extracts of plant leaves were analyzed for antioxidant activity, revealing that the extract possesses antioxidant and anti-AChE activities [49].

3.4. Family: Apiaceae. Apiaceae or Umbelliferae is the 16th largest family of flowering plants. It consists of more than 3700 aromatic plant species in 434 genera [50]. Several plants from this family are reported to possess activity against neurogenerative diseases. The *Ferula asafoetida* H. Karst. aqueous extract showed acetylcholinesterase (AChE) activity-inhibiting property in an in vitro as well as in vivo assay in the nervous system of snail and in the brain of a rat. The resins of *F. asafoetida* possess the potential to inhibit monoamine oxidase B (MAO-B) [51]. The acetylcholinesterase-inhibiting and antioxidant properties of *F. asafoetida* lead to memory enhancement and thus can be employed in the treatment of Alzheimer's disease and dementia [52].

Neuroprotective effects of the *Coriandrum sativum* L. leaf ethanolic extract (volatile oil) were assessed in the β-amyloid rat model of Alzheimer's disease. The anxiolytic and antidepressant effects were evaluated in vivo, and the antioxidant property was estimated by the total content of the reduced glutathione in the hippocampus. The experiment revealed that the anxiolytic and antidepressant-like effects decreased catalase activity and increased glutathione levels in the hippocampus of the rat brain. Improvement in these parameters suggests the probable advantage of *C. sativum* in Alzheimer's disease [53].

3.5. Family: Apocynaceae. The Apocynaceae or dogbane family is a diverse family containing 348 genera of plants [54]. *Hancornia speciosa* Gomes is an important plant of the Apocynaceae family which contains flavonoids, phenols, tannins, and anthocyanidins. Volatile components of the plant exhibit antioxidant properties due to the presence of the phenolic compounds while flavonoids and tannins exhibit cytotoxic activity [55].

3.6. Family: Araliaceae. Ivy or Araliaceae is a family of flowering plants that contains 254 plant species [56]. *Eleutherococcus leucorrhizus* var. setchuenensis (Harms) C. B. Shang & J. Y. Huang and *Eleutherococcus sessiliflorus* (Rupr. & Maxim.) S. Y. Hu are two plants of this family that contain alkaloids and eleutherosides B, B1, E, and E1. Analysis of the plant extracts through spectroscopy and High-Performance Liquid Chromatography (HPLC) revealed that these alkaloids effectively improved cognitive function [57]. The *Eleutherococcus senticosus* Maxim extract was evaluated for its ability to alter gene expression in T98G neuroglia cells to question the relevance of these deregulated genes and the eicosanoid signaling pathway. It was revealed that *E. senticosus* effectively inhibited the leukotriene signaling pathway by downregulating Arachidonate 5-Lipoxygenase-Activating Protein (ALOX5AP), Dipeptidase 2 (DPEP2), and Leukotriene C4 Synthase (LTC4S) gene expression [58]. *Acanthopanax trifoliatus* (L.) Voss is another plant of this family that contains polyphenols and flavonoids as active ingredients. Activity of total flavonoid and phenols was assessed from the decoction of leaves. Significant activity was found against oxidative stress which shows promise in the treatment of AD [59]. *Panax ginseng* C.A. Mey contains various pharmacological activities and has been employed in the treatment of different diseases since ages in China [60]. *P. ginseng* C.A. Mey contains ginsenosides and gintonin that have neuroprotective effects [61]; these properties make *P. ginseng* C.A. Mey an effective candidate in the management of neurodegenerative disorders such as AD and dementia [62].

3.7. Family: Arecaceae. Arecaceae commonly known as the "palm family" consists of 181 genera and 2600 species [63]. Hydroalcoholic extracts of *Syagrus romanzoffiana* (Cham.) Glassman leaves and fruits were evaluated for their pharmacological properties and anticholinesterase activity in the rat model of aluminum chloride-induced Alzheimer disease. The plant was found to possess 39 metabolites belonging to different chemical classes, i.e., stilbenoids, flavonoids, lignans, phenols, and fatty acids. Acetylcholinesterase activity was significantly decreased by both extracts, and histopathological changes in the cerebral cortex and cerebellum were improved. These results recommend *S. romanzoffiana* Glassman as a promising candidate for AD treatment [64].

3.8. Family: Boraginaceae. The Boraginaceae family is comprised of 2000 flowering plant species [65]. *Nonea micrantha* Boiss. & Reut. is a plant of the Boraginaceae family that is reported to possess important saponins. The methanolic extract of *N. micrantha* was prepared and analyzed by DPPH and ABTS for free radical scavenging properties. The assays expressed significant antioxidant and anti-AChE activities. Thin-Layer Chromatography (TLC) and spectrophotometric analysis further revealed that this plant is rich in many important bioactive compounds that have potential in the treatment of AD [66].

3.9. Family: Buxaceae. The box or Buxaceae family comprises 123 plant species [63]. *Sarcococca saligna* Müll.Arg, an important member of this family, was evaluated for its anti-AChE activity. Five new steroidal alkaloids, namely, salignenamides C, D, E, and F; 2B-hydroxypachysamine-D; axillarines C and F; sarcorine; N-dimethyl Sara codeine; vegainine; 5,6-dehydrosarconidine; 2-hydroxy salignarine; and 2-hydroxysalignamine, were isolated from the ethanolic extract of the plant. In vitro assessment of these alkaloids exhibited anti-AChE activities. All these results signified the effectiveness of *S. saligna* in the management of AD [67]. *S. hookeriana* Baill commonly known as a hook plant is another species of the Sarcococca genus that contains four new alkaloids hookrianamides D, E, F, and G; (-) hookrianamide A; (+) hookrianamide B; and hookrianamine A and is

also reported to possess anti-AChE activities. The ethanolic extract of the plant was purified by column chromatography and TLC. Results showed that the hook plant is effective in the treatment of AD [68]. *Buxus papillosa* C.K. Schneid contains steroidal alkaloids like buxakarachiamine, buxakashmiramine, and buxahejramine, along with four known bases cycloprotobuxine C, cyclovirobuxeine A, cyclomicrophyline A, and semperviraminol which possess acetylcholinesterase as well as butylestrase inhibitory activities [69]. The ethanolic leaf extract showed that it is effective in the treatment of various skin ailments as well as neurodegenerative disorders [70].

3.10. Family: Convolvulaceae. The morning glory or Convolvulaceae family comprises 1650 plant species [71]. *Convolvulus pluricaulis* Choisy, another plant of the Convolvulaceae family, is reported to have ascorbic acid, flavonoids, terpenoids, rivastigmine, and steroids as active compounds. It not only scavenges the free radical but also stabilizes muscarinic receptors. The ethanolic extract of this plant was applied in rats. It was observed that memory and learning ability of the rats were improved; this suggested that this plant can be beneficial in AD therapy [72].

3.11. Family: Crassulaceae. The family Crassulaceae also known as stonecrop or orpine [73] consists of 34-35 genera with approximately 1400 species [74]. *Rhodiola rosea* L., a member of this family, has shown some promising effects on cognition and physical performance. Transcriptome-wide RNA sequencing was carried out to profile gene expression in T98G neuroglia cells in response to root and rhizome extracts of *R. rosea* L. It was found that the *R. rosea* L. extract downregulated the expression of *ALOX5AP*, *DPEP2*, and *LTC4S* genes and thus apprehended leukotriene signaling pathways [58]. *R. rosea* L. possess high adaptogen properties owning to its bioactive compound glycoside salidroside. It has been reported to produce anxiolytic and antidepressant effects in wild-type adult mice. *R. rosea* L. effectively reduced oxidative stress and increased antioxidant acetylcholine (ACh) and choline acetyltransferase (ChAT) levels in the cortex of Aβ1-42-injected rats [75]. These results make *R. rosea* L. a potential pharmacological tool to enhance cognition, balance mood disorders, and treat Alzheimer's disease [76].

3.12. Family: Cucurbitaceae. The Cucurbitaceae family commonly known as the gourd family comprises 965 plant species [63]. *Caryocar coriaceum* Wittm., a prominent member of this family, contains phenolics and flavonoids. The most prominent flavonoids were quercetin (QCT), isoquercetin, and rutin. Overall, it was concluded that *C. coriaceum* has potential antifungal and antileishmaniasis activity and can be a possible addition in AD management [77].

3.13. Family: Fabaceae. The Fabaceae or Leguminosae family is the economically important 3rd largest family of flowering plants with diverse 19000 plant species [50, 63, 78]. *Clitoria ternatea* L. is an eminent member of this family that contains quercetin and myricetin glycosides. Leaf and root extracts of *C. ternatea* behaved as brain tonic owing to their potential in increasing levels of acetylcholine in the brain. *Bauhinia forficata* Link, a species of the Fabaceae family, is reported to possess hypoglycemic activity and is also involved in the signaling pathway in AD. Changes in insulin metabolism lead to molecular pathogenesis and increase glucose levels in AD patients. Thus, improvement in insulin metabolism enhances cognitive functions in patients with AD. Along with hypoglycemic activity, *B. forficata* also possess anti-AChE and antioxidant activities [79, 80]. *Copaifera langsdorffii* Desf, another member of Fabaceae, is known as a protective agent for gastric mucosa, and it also contains polyphenols that possess antioxidant activity. Ethanolic and methanolic extracts of *C. langsdorffii* have antioxidant activity [81, 82].

3.14. Family: Ginkgoaceae. Ginkgoaceae is a family of the Mesozoic Era. *Ginkgo biloba* L. is a member of this family which is termed as a living fossil [83]. Chemical constituents of *G. biloba* include ginkgolides, bilobalide, and ginkgetin and other terpenes. These compounds possess remarkable anti-AChE and antioxidant properties that are useful against AD. Further clinical assessment was suggested for the methanolic extract of *G. biloba* upon revealing in vitro anti-AChE and antioxidant properties when tested [84].

3.15. Family: Iridaceae. The Iridaceae family belongs to the order Asparagales; this family got its name after iris that means rainbow because of its multiple colors. It includes 66 genera with 2244 species worldwide [63]. *Crocus sativus* Ten commonly known as saffron was assessed for its efficacy in treating AD. *C. sativus* contain a diverse set of compounds such as lipids, minerals, polypeptides, vitamins, and carbohydrates. Saffron's main bioactive ingredients are crocin, crocetin, picrocrocin, and safranin [85]. *C. sativus* dry powder was administered in AD patients aged 55 years for 3 months, and an improvement in cognitive functions was observed. *C. sativus* was as effective as donepezil in AD patients [86]. Crocin, the main component of *C. sativus*, exhibited antioxidant potential by reducing malondialdehyde (MDA) levels [87]. Dry stigma of the *C. sativus* and the water-soluble corcin have been found effective in neurodegenerative conditions such as dementia and traumatic brain injury. Crocin not only enhances cognition but also protects brain cells. It can be a promising agent for the prevention or treatment of AD [88, 89].

3.16. Family: Lamiaceae. The Lamiaceae or mint family is a large family of flowering plants comprising 236 species which are rich in carotenoids, phenolic acids, and ascorbic acid. Many plants of this family possess antioxidant and anticholinesterase activity that is particularly useful in the treatment of dementia and AD [90, 91]. Antioxidant and anticholinesterase activities of different plants from the family Lamiaceae were assessed. A total of twenty-six plant methanolic extracts were tested, and nine plants, namely, *Mentha piperita* L., *Salvia longifolia* Nutt., *Betonica officinalis* L., *Satureja montana* L., *Chamaedrys* Moench, *Clerodendrum cephalanthum* subsp. montanum (Thomas) Verdc., *Teucrium polium* L., and *Thymus vulgaris* L., showed strong (75%) AChE inhibitory activity. These results revealed that plants belonging to

the Lamiaceae family possess strong AChE inhibitory activities as well as antioxidant activities that are useful in the management of AD [92].

The *Lavandula angustifolia* Mill aqueous extract was evaluated for its effect on the spatial performance of AD rats. Promising results were obtained where spatial learning deficits in AD rats were reversed effectively by the lavender extract [93]. Lavender extract treatment reversed levels of 10 metabolite markers nearly to control including carnitine, pantothenate, isobutyrate, glutamine, alanine, isoleucine, serine, valine, glucose, and asparagine involved in AD pathogenesis. These results established a promising therapeutic potential in *L. angustifolia* in disease improvement and treatment of AD [94]. The aqueous extract of lavender was evaluated for induction of LTP in the CA1 area of the hippocampus in rats. The lavender extract exhibited positive effects on the plasticity of synaptic transmission and thus improves impaired spatial memory in the Alzheimeric animals [95]. These results suggest a potential therapeutic role of lavender in the treatment of AD.

3.17. Family: Lessoniaceae. Ecklonia cava Kjellman, an edible brown seaweed, is a member of kelps or the Lessoniaceae family found in oceans of Korea [96]. It contains polyphenols like eckol, bieckol, dieckol, and phlorofurofukoeckol-A which possess antioxidant, anti-inflammatory, and anticancer properties. A phenolic extract was made with ethanol at 50°C and then evaporated until a gummy paste is formed and further separated by ethyl acetate and water. Amyloid biosynthesis, anti-AChE, glycogen synthase kinase 3 β-amyloid inhibition, and BACE inhibition-1 assays were performed. Results showed that dieckol and phlorofurofukoeckol-A were effective against AChE and amyloid precursor protein biosynthesis that could be helpful in the treatment of AD [97].

3.18. Family: Lythraceae. The Lythraceae family includes 32 genera and 620 species of herbs, shrubs, and trees [86]. Phytochemical characterization of *Lawsonia inermis* L., a species that contains twelve various compounds, was performed in the chloroform extract of leaves. Swiss albino mice were tested for memory-enhancing and cognitive function peroral administration of *L. inermis* powder. Memory loss due to oxidative neurodegeneration was effectively reversed by *L. inermis*. The exact mechanism of this reversal is not known; however, the antioxidant potential is accounted for the nootropic potential of the plant [98].

3.19. Family: Lycopodiaceae. The Lycopodiaceae family is an important family of vascular plants which is reported to contain various alkaloids, flavonoids, and phenolic compounds that possess antioxidant and anti-AChE activities. Huperzine A is mainly involved in anti-AChE activities. Extracts of different species from the Lycopodiaceae family like *Huperzia flexibilis* (Fée) B.Øllg, *Lycopodiella cernua* (L.) Pic.Serm, *Lycopodium clavatum* f. brevipedunculatum Louis-Marie, and *Lycopodiella riofrioi* (Sodiro) B.Øllg were analyzed through Liquid Chromatography-Mass Spectroscopy (LC-MS) and TLC. *L. clavatum* showed strong anti-AChE activity [99]. *Huperzia selago* var. serrata (Thunb.) Á. Löve & D. Löve contains huperzine A as an active constituent which has potent anti-AChE activity. Safety, tolerability, and efficacy of *H. selago* var. serrata were tested on 210 AD patients, and no significant side effects were obtained [100].

3.20. Family: Moraceae. The Moraceae family, commonly known as the fig or mulberry family, is cosmopolitan in nature and is comprised of 38 genera and over 1100 species [63]. *Ficus carica* L. generally called fig possesses a remarkable antioxidant nutritional value conferring it a great protective mechanism against various ailments and AD. The bioactive metabolites in *F. carica* mesocarp were assessed for their effect on the human neuroblastoma SHSY5Y cell line via a cell viability test. Nuclear magnetic resonance (NMR) spectroscopy profiling active metabolites was carried out, and it was revealed that c-sitosterol, an aliphatic compound, is responsible for neuronal bioactivity [21].

3.21. Family: Myrtaceae. It is a dicotyledonous family widely distributed in tropical and warm temperate regions comprising 5950 plant species [63, 101, 102]. *Psidium guajava* L. commonly known as guava is the most prominent member of this family that possesses high antioxidant as well as antidiarrheal and antidiabetic potential. The leaf extract of guava was analyzed for antioxidant properties in a linoleic acid system by a thiocyanate method. A radical scavenging assay was performed with 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) ($ABTS^+$) radicals at 414 nm. Results revealed that guava leaves possess significant antioxidant activity that can be effective in the management of AD [103].

3.22. Family: Oleaceae. The family Oleaceae is comprised of 26 genera and 700 plant species. The family consists of shrubs, trees, and woody climbers which are subcosmopolitan in distribution [104]. *Olea europaea* L., an eminent member of this family, possesses certain promising effects on AD. AD progression is attributed to the accumulation of hyperphosphorylated β-amyloid and tau proteins. Elimination of the damaged organelles and aggregated proteins is carried out by autophagy through lysosomal digestion. Autophagy deficiency leads to noneffective elimination and in turn accumulation of damaged and aggregated mitochondria in the cell. This increases cell toxicity and oxidative stress. Extra virgin olive oil possessed several polyphenols, e.g., oleuropein aglycone, that cause autophagy, thus decreasing aggregated proteins and in turn cognitive impairment. Extra virgin olive oil consumption as supplement can benefit Alzheimer's patients through the induction of autophagy [105]. *O. europaea* is a rich source of natural antioxidant. The fruit ethanolic extract of *O. europaea* was analyzed for its putative neuroprotective effects in alloxan-induced cognitive impairment in mice. A behavioral study was carried out to assess neuroprotective effects. The administration of olive oil not only altered the mice's behavior but also decreased lipid peroxidation in the cells [106]. The main bioactive compounds are phenolic oleuropein and hydroxytyrosol (HT) found in the leaf extract, which are responsible for antioxidant, anti-inflammatory, and neuroprotective properties [107].

3.23. Family: Pedaliaceae. Pedaliaceae commonly known as the pedalium or sesame family is a small family of flowering plants comprising about 79 species [108]. *Sesamum indicum* L. is an important plant of the Pedaliaceae family which contains sesamol that possesses antioxidant and neuroprotective activities mainly in dementia and Huntington disease. It also contains flavonoids, terpenes, alkaloids, and chemicals like sesamin and sesaminol. Different extracts were tested, and it was found that *S. indicum* possess anti-AChE as well as antioxidant activities [109].

3.24. Family: Plantaginaceae. Plantaginaceae is a very diverse family of flowering plants with 1900 plant species [63]. *Rehmannia glutinosa* f. lutea from this family contains catapols and 5-hydroxymethylfurfual, which has been reported to possess antioxidant, neuroprotective, and anti-inflammatory activities. The *R. glutinosa* lutea root extract was analyzed for its neuroprotective effects in vitro in hippocampal neurons, and it showed remarkable activity against AD, but its efficacy is still not well established in humans [110]. *Bacopa monnieri* (L.) Wettst. or thyme-leaved gratiola is another important plant of this family that possesses antioxidant and antilipoxygenase properties. Various alkaloids like brahmine, herpestine, B-sterols, betulic acid, bacopasaponins (bacopasides A, B, C, I, II, X, and N2), and bacopasaponin E (III, IV, V, and N1) were scrutinized from the leaf extract of *B. monnieri*, and promising results were obtained. These alkaloids improved cognitive function and memory capacity in patients of AD [111].

3.25. Family: Polygalaceae. Polygalaceae is commonly known as the milkwort family with 900 known plant species. Use of *Polygala alba* var. tenuifolia S.F.Blake, an important plant of the Polygalaceae family, in certain disorders like insomnia and cognitive impairment has been reported. The aqueous extract of *P. alba* var. tenuifolia improved memory and other behavioral disorders in rats. These promising results suggest further research on *P. alba* var. tenuifolia for the effective treatment of AD [112].

3.26. Family: Ranunculaceae. Ranunculaceae is a family of over 2000 flowering plant species in 43 genera and is distributed worldwide commonly known as the buttercup family [63]. *Nigella sativa* L. belongs to the family Ranunculaceae and is reported to possess several phenolic compounds such as stearic acid, linoleic acid, palmitic acid, oleic acid, arachidic acid, and eicosadienoic acid. *N. sativa* has potent antioxidative effects and can effectively improve scopolamine-induced cognitive impairment and reduced the AChE activity and oxidative stress of the rat's brain [113]. Thymoquinone, a major component of *N. sativa*, exhibited neuroprotective effects on various neuronal disorders such as epilepsy, Alzheimer's disease, and neurotoxicity [114]. The increased cognitive functions and neuroprotective effects of thymoquinone (TQ) are attributed to its substantial anti-inflammatory and antioxidant potential [115]. *N. sativa* prevented the damage of the spatial memory in scopolamine administration-induced oxidative stress of the brain tissue in rats [113]. Seeds of *N. sativa* are reported to exhibit positive effects on memory impairment and neurotoxicity [114].

3.27. Family: Rhamnaceae. Buckthorn or Rhamnaceae is a family of 950 flowering plant species [43]. *Ziziphus jujuba* Lam is a plant belonging to the Rhamnaceae family that activates choline acetyltransferase which prevents loss of cholinergic neurons [116]. *Z. jujuba* contains flavonoids, polysaccharides, terpenoids, and phenolics that have antioxidant, immunostimulant, and anti-inflammatory properties. The polysaccharide fraction of the hydroalcoholic extract of *Z. jujuba* displays a promising antioxidant profile that is useful in the treatment of AD [117].

3.28. Family: Sargassaceae. Sargassum, a member of Sargassaceae, is a brown seaweed that possesses compounds like proteins, fibers, and carotenoids and particularly plastoquinones which possess anti-AChE activity [118]. Four compounds that possess anti-AChE activity were isolated, namely: sargaquinoic acid, sargachromenol, dihydro-mono-oxofarnesyl acetone, and mono-oxofarnesyl acetone. Enzymatic activity of the methanolic extract of *Sargassum sagamianum* (Yamada) Yoshida & T. Konno and its compound sargaquinoic acid was found effective in the inhibition of acetylcholinesterase as well as butyl cholinesterase which is remarkable in the treatment of AD [119].

3.29. Family: Saururaceae. Saururaceae is a small family of flowering plants comprising only four genera and seven species mainly herbaceous plants inhabiting eastern and southern Asia and North America [120]. *Saururus chinensis* hort. ex Loudon, a plant of this family, was assessed for neuroinflammatory responses in BV-2 microglial cells and for antioxidant potential was estimated by DPPH and alkyl radical scavenging assays [121]. Chemistry of *S. chinensis* revealed the presence of flavonoid, fatty acid, alkaloid, quinone, amino acid, and essence oils. Hyperin, isoquercetin, quercetin, and quercitrin were reported from the stem and leaf [122, 123]. *S. chinensis* showed significant antioxidant and anti-inflammatory activity against tumor necrosis factor-alpha. Quercetin (QCT) was revealed as one of the major constituents of *S. chinensis*. QCT inhibited the excessive release of Nitric Oxide (NO) in Lipopolysaccharide- (LPS-) stimulated BV-2 cells [121].

3.30. Family: Solanaceae. Solanaceae or nightshade is an important family of 27000 flowering plants. Plants of the Solanaceae family contain many important alkaloids that have therapeutic importance [124]. *Withania somnifera* (L.) Dunal, a valuable plant of the Solanaceae family, contains sitoindosides VII-X and withaferin A that has mainly antioxidant activities. The root extract of *W. somnifera* was beneficial in reversing the effects of memory impairment in transgenic mice when it was administered to them for 30 days. These results recommend *W. somnifera* as a good candidate target for the treatment of AD [125]. Anti-inflammatory lipoxin signaling pathways were upregulated by *W. somnifera* (L.) extracts, while proinflammatory signaling pathways (ALOX5AP, DPEP2, and LTC4S genes) were downregulated to inhibit the biosynthesis of prostaglandins, leukotrienes, and thromboxanes [58]. This leads to reduced

neuroinflammation and neurodegeneration, declined tau phosphorylation and β-amyloid plague load, activation of neurogenesis, elevated neuronal survival, and synaptic integrity, all the pathological hallmarks of Alzheimer disease [32].

3.31. Family: Zingiberaceae. The Zingiberaceae or ginger family is an important family of monocotyledonous flowering plants with 1600 species. Plants in the Zingiberaceae family are also known as pseudostems [126]. Turmeric or *Curcuma longa* L. is an important plant of this family which is commonly used as a spice and traditionally used in the management of cough, hepatic disorders, diabetes, and inflammations. Turmeric rhizome possesses pharmacological activities and contains curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin as chemical constituents. Various glycosides flavonoids and terpenoids are reported from *C. longa* [127]. In another study, it was found that oral administration of curcumin inhibits Aβ fibril deposition and hyperphosphorylation of tau proteins that is an important pathway leading to AD [127]. Extracts of *C. longa* rhizome upregulated the expression of the prostaglandin E receptor 3 gene and downregulated *ALOX12* expression, suggesting a positive role of *C. longa* which inhibit the neurotoxicity [127].

4. Conclusion

AD is the most prevalent neurodegenerative disease over the entire globe with no effective drugs or therapy to treat the conditions. It appeals for the exploration of new chemical entities where medicinal plants can play a pivotal role being the rich source of pharmacological principles and vast diversity. The secondary metabolites of plants including alkaloids, flavonoids, and phenolic acids play a key role in improving regeneration and/or inhibiting neurodegeneration. Various natural remedies and individual plant parts have shown significant potential in the treatment and management of AD. Diversified medicinal plants of the same taxonomic origin share some common pharmacological properties. This review will provide basis for further exploration of anti-AD drugs by screening unexplored species from the already reported effective families.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] A. Wimo, L. Jönsson, J. Bond, M. Prince, B. Winblad, and Alzheimer Disease International, "The worldwide economic impact of dementia 2010," *Alzheimer's & Dementia*, vol. 9, no. 1, pp. 1–11.e3, 2013.

[2] R. E. Tanzi and L. Bertram, "Twenty years of the Alzheimer's disease amyloid hypothesis: a genetic perspective," *Cell*, vol. 120, no. 4, pp. 545–555, 2005.

[3] G. N. Bischof, "Alzheimer's disease risk: amyloid versus neurodegeneration," *The Lancet Neurology*, vol. 15, no. 10, pp. 1000-1001, 2016.

[4] R. G. Urdinguio, J. V. Sanchez-Mut, and M. Esteller, "Epigenetic mechanisms in neurological diseases: genes, syndromes, and therapies," *The Lancet Neurology*, vol. 8, no. 11, pp. 1056–1072, 2009.

[5] D. P. Salmon and M. W. Bondi, "Neuropsychological assessment of dementia," *Annual Review of Psychology*, vol. 60, no. 1, pp. 257–282, 2009.

[6] B. J. Kelley and R. C. Petersen, "Alzheimer's disease and mild cognitive impairment," *Neurologic Clinics*, vol. 25, no. 3, pp. 577–609, 2007.

[7] S. Weintraub, A. H. Wicklund, and D. P. Salmon, "The neuropsychological profile of Alzheimer disease," *Cold Spring Harbor Perspectives in Medicine*, vol. 2, no. 4, 2012.

[8] K. Dastmalchi, H. D. Dorman, H. Vuorela, and R. Hiltunen, "Plants as potential sources for drug development against Alzheimer's disease," *International Journal of Biomedical and Pharmaceutical Sciences*, vol. 1, no. 2, pp. 83–104, 2007.

[9] M. R. Irwin and M. V. Vitiello, "Implications of sleep disturbance and inflammation for Alzheimer's disease dementia," *The Lancet Neurology*, vol. 18, no. 3, pp. 296–306, 2019.

[10] J. Sharma, R. Chawla, R. Kumar, A. Sharma, R. K. Sharma, and R. Arora, "Camellia sinensis as a safe neuroprotective radiation counter measure agent," *International Journal of Pharmaceutical Science Invention*, vol. 2, pp. 26–33, 2013.

[11] D. E. Bredesen, "Neurodegeneration in Alzheimer's disease: caspases and synaptic element interdependence," *Molecular Neurodegeneration*, vol. 4, no. 1, p. 27, 2009.

[12] C. Zucchella, M. Bartolo, S. Bernini, M. Picascia, and E. Sinforiani, "Quality of life in Alzheimer disease: a comparison of patients' and caregivers' points of view," *Alzheimer Disease & Associated Disorders*, vol. 29, no. 1, pp. 50–54, 2015.

[13] J. Lindsay, D. Laurin, R. Verreault et al., "Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging," *American Journal of Epidemiology*, vol. 156, no. 5, pp. 445–453, 2002.

[14] R. A. Whitmer, S. Sidney, J. Selby, S. C. Johnston, and K. Yaffe, "Midlife cardiovascular risk factors and risk of dementia in late life," *Neurology*, vol. 64, no. 2, pp. 277–281, 2005.

[15] J. A. Luchsinger, C. Reitz, L. S. Honig, M. X. Tang, S. Shea, and R. Mayeux, "Aggregation of vascular risk factors and risk of incident Alzheimer disease," *Neurology*, vol. 65, no. 4, pp. 545–551, 2005.

[16] R. T. Gun, A. E. Korten, A. F. Jorm et al., "Occupational risk factors for Alzheimer disease: a case-control study," *Alzheimer Disease & Associated Disorders*, vol. 11, no. 1, pp. 21–27, 1997.

[17] R. S. Wilson, C. F. Mendes de Leon, L. L. Barnes et al., "Participation in cognitively stimulating activities and risk of incident Alzheimer disease," *Journal of the American Medical Association*, vol. 287, no. 6, pp. 742–748, 2002.

[18] A. R. Moore and S. T. O'Keeffe, "Drug-induced cognitive impairment in the elderly," *Drugs & Aging*, vol. 15, no. 1, pp. 15–28, 1999.

[19] Collaborators GD, "Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016," *The Lancet Neurology*, vol. 18, no. 1, pp. 88–106, 2019.

[20] Organization WH, *Neurological Disorders: Public Health Challenges*, World Health Organization, 2006.

[21] H. Khojah and R. Edrada-Ebel, "P43 the isolation and purification of bioactive metabolites from Ficus carica and their neuroprotective effects in Alzheimer's disease," *Biochemical Pharmacology*, vol. 139, p. 140, 2017.

[22] D. M. Barten and C. F. Albright, "Therapeutic strategies for Alzheimer's disease," *Molecular Neurobiology*, vol. 37, no. 2-3, pp. 171–186, 2008.

[23] N. K. Seetlani, N. Kumar, K. Imran, A. Ali, N. Shams, and T. Sheikh, "Alzheimer and vascular dementia in the elderly patients," *Pakistan Journal of Medical Sciences*, vol. 32, no. 5, pp. 1286–1290, 2016.

[24] A. Ott, M. M. B. Breteler, F. van Harskamp et al., "Prevalence of Alzheimer's disease and vascular dementia: association with education. The Rotterdam Study," *BMJ*, vol. 310, no. 6985, pp. 970–973, 1995.

[25] M. A. Lambert, H. Bickel, M. Prince et al., "Estimating the burden of early onset dementia; systematic review of disease prevalence," *European Journal of Neurology*, vol. 21, no. 4, pp. 563–569, 2014.

[26] G. A. Edwards III, N. Gamez, G. Escobedo Jr., O. Calderon, and I. Moreno-Gonzalez, "Modifiable risk factors for Alzheimer's disease," *Frontiers in aging neuroscience*, vol. 11, 2019.

[27] A. N. Panche, S. Chandra, and A. Diwan, "Multi-target β-protease inhibitors from Andrographis paniculata: in silico and in vitro studies," *Plants*, vol. 8, no. 7, p. 231, 2019.

[28] L. Schneider, "Alzheimer's disease and other dementias: update on research," *The Lancet Neurology*, vol. 16, no. 1, pp. 4-5, 2017.

[29] B. P. Imbimbo, J. Lombard, and N. Pomara, "Pathophysiology of Alzheimer's disease," *Neuroimaging Clinics of North America*, vol. 15, no. 4, pp. 727–753, 2005.

[30] P. I. Moreira, K. Honda, Q. Liu et al., "Oxidative stress: the old enemy in Alzheimer's disease pathophysiology," *Current Alzheimer Research*, vol. 2, no. 4, pp. 403–408, 2005.

[31] E. K. Perry, B. E. Tomlinson, G. Blessed, K. Bergmann, P. H. Gibson, and R. H. Perry, "Correlation of cholinergic abnormalities with senile plaques and mental test scores in senile dementia," *British Medical Journal*, vol. 2, no. 6150, pp. 1457–1459, 1978.

[32] J. Michael, J. Marschallinger, and L. Aigner, "The leukotriene signaling pathway: a druggable target in Alzheimer's disease," *Drug Discovery Today*, vol. 24, no. 2, pp. 505–516, 2019.

[33] A. Delacourte, "Diagnosis of Alzheimer's disease," *Annales de Biologie Clinique*, vol. 56, no. 2, pp. 133–142, 1998.

[34] R. Brookmeyer, E. Johnson, K. Ziegler-Graham, and H. M. Arrighi, "Forecasting the global burden of Alzheimer's disease," *Alzheimer's & Dementia*, vol. 3, no. 3, pp. 186–191, 2007.

[35] S. Norton, F. E. Matthews, D. E. Barnes, K. Yaffe, and C. Brayne, "Potential for primary prevention of Alzheimer's disease: an analysis of population-based data," *The Lancet Neurology*, vol. 13, no. 8, pp. 788–794, 2014.

[36] R. Barnett, *Case histories Alzheimer's disease*, 2019, https://dl.uswr.ac.ir/bitstream/Hannan/80095/1/2019%20Lancet%20Volume%20393%20Issue%2010181%20April%20%2828%29.pdf.

[37] A. K. Singhal, O. P. Bangar, and V. Naithani, "Medicinal plants with a potential to treat Alzheimer and associated symptoms," *International Journal of Nutrition, Pharmacology, Neurological Diseases*, vol. 2, no. 2, p. 84, 2012.

[38] M. Simunkova, S. H. Alwasel, I. M. Alhazza et al., "Management of oxidative stress and other pathologies in Alzheimer's disease," *Archives of Toxicology*, vol. 93, no. 9, pp. 2491–2513, 2019.

[39] K.-Y. Yoo and S.-Y. Park, "Terpenoids as potential anti-Alzheimer's disease therapeutics," *Molecules*, vol. 17, no. 3, pp. 3524–3538, 2012.

[40] D. E. Moerman, "An analysis of the food plants and drug plants of native North America," *Journal of Ethnopharmacology*, vol. 52, no. 1, pp. 1–22, 1996.

[41] O. Phillips and A. H. Gentry, "The useful plants of Tambopata, Peru: I. Statistical hypotheses tests with a new quantitative technique," *Economic Botany*, vol. 47, no. 1, pp. 15–32, 1993.

[42] D. Moher, A. Liberati, J. Tetzlaff, D. G. Altman, and PRISMA Group, "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement," *International Journal of Surgery*, vol. 8, no. 5, pp. 336–341, 2010.

[43] The Angiosperm Phylogeny Group, "An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG II," *Botanical Journal of the Linnean Society*, vol. 141, no. 4, pp. 399–436, 2003.

[44] M. J. Uddin, M. N. Alam, K. Biswas, and M. A. Rahman, "In vitro antioxidative and cholinesterase inhibitory properties of Thunbergia grandiflora leaf extract," *Cogent Food & Agriculture*, vol. 2, no. 1, 2016.

[45] V. Tanigasalam, B. Vishnu Bhat, B. Adhisivam, N. Plakkal, and K. T. Harichandra Kumar, "Vasambu (*Acorus calamus*) administration: a harmful infant rearing practice in South India," *Indian Journal of Pediatrics*, vol. 84, no. 10, pp. 802-803, 2017.

[46] F. Ahmeda, J. N. Chandra, A. Urooj, and K. S. Rangappa, "In vitro antioxidant and anticholinesterase activity of Acorus calamus and Nardostachys jatamansi rhizomes," *Journal of Pharmacy Research*, vol. 2, no. 5, 2009.

[47] C. Aguilar-Ortigoza, V. Sosa, and G. Angeles, "Phylogenetic relationships of three genera in Anacardiaceae: Bonetiella, Pseudosmodingium, and Smodingium," *Brittonia*, vol. 56, no. 2, pp. 169–184, 2004.

[48] A. B. Penido, S. M. de Morais, A. B. Ribeiro et al., "Medicinal plants from Northeastern Brazil against Alzheimer's disease," *Evidence-Based Complementary and Alternative Medicine*, vol. 2017, Article ID 1753673, 7 pages, 2017.

[49] R. Sobhani, A. K. Pal, A. Bhattacharjee, S. Mitra, and K. Aguan, "Screening indigenous medicinal plants of Northeast India for their anti-Alzheimer's properties," *Pharmacognosy Journal*, vol. 9, no. 1, pp. 46–54, 2016.

[50] P. F. Stevens, *Angiosperm Phylogeny Website, Version 6*, 2005.

[51] N. O. Zarmouh, S. S. Messeha, F. M. Elshami, and K. F. Soliman, "Natural products screening for the identification of selective monoamine oxidase-B inhibitors," *European Journal of Medicinal Plants*, vol. 15, no. 1, pp. 1–16, 2016.

[52] Vijayalakshmi, S. Adiga, P. Bhat, A. Chaturvedi, K. L. Bairy, and S. Kamath, "Evaluation of the effect of *Ferula asafoetida* Linn. gum extract on learning and memory in Wistar rats," *Indian journal of pharmacology*, vol. 44, no. 1, pp. 82–87, 2012.

[53] O. Cioanca, L. Hritcu, M. Mihasan, A. Trifan, and M. Hancianu, "Inhalation of coriander volatile oil increased anxiolytic–antidepressant-like behaviors and decreased oxidative status in beta-amyloid (1–42) rat model of Alzheimer's disease," *Physiology & Behavior*, vol. 131, pp. 68–74, 2014.

[54] M. E. Endress and P. V. Bruyns, "A revised classification of the Apocynaceae s.l," *The Botanical Review*, vol. 66, no. 1, pp. 1–56, 2000.

[55] C. F. Assumpção, P. Bachiega, M. C. Morzelle et al., "Characterization, antioxidant potential and cytotoxic study of mangaba fruits," *Ciência Rural*, vol. 44, no. 7, pp. 1297–1303, 2014.

[56] E. Haston, J. E. Richardson, P. F. Stevens, M. W. Chase, and D. J. Harris, "The Linear Angiosperm Phylogeny Group (LAPG) III: a linear sequence of the families in APG III," *Botanical Journal of the Linnean Society*, vol. 161, no. 2, pp. 128–131, 2009.

[57] D. Załuski and R. Kuźniewski, "*In vitro* anti-AChE, anti-BuChE, and antioxidant activity of 12 extracts of *Eleutherococcus* species," *Oxidative Medicine and Cellular Longevity*, vol. 2016, Article ID 4135135, 7 pages, 2016.

[58] A. Panossian, E.-J. Seo, and T. Efferth, "Effects of anti-inflammatory and adaptogenic herbal extracts on gene expression of eicosanoids signaling pathways in isolated brain cells," *Phytomedicine*, vol. 60, p. 152881, 2019.

[59] P. Sithisarn and S. Jarikasem, "Antioxidant activity of Acanthopanax trifoliatus," *Medical Principles and Practice*, vol. 18, no. 5, pp. 393–398, 2009.

[60] A. Rajabian, M. Rameshrad, and H. Hosseinzadeh, "Therapeutic potential of Panax ginseng and its constituents, ginsenosides and gintonin, in neurological and neurodegenerative disorders: a patent review," *Expert Opinion on Therapeutic Patents*, vol. 29, no. 1, pp. 55–72, 2018.

[61] X. Huang, N. Li, Y. Pu, T. Zhang, and B. Wang, "Neuroprotective effects of ginseng phytochemicals: recent perspectives," *Molecules*, vol. 24, no. 16, p. 2939, 2019.

[62] J. H. Heo, S. T. Lee, K. Chu et al., "An open-label trial of Korean red ginseng as an adjuvant treatment for cognitive impairment in patients with Alzheimer's disease," *European Journal of Neurology*, vol. 15, no. 8, pp. 865–868, 2008.

[63] M. J. M. Christenhusz and J. W. Byng, "The number of known plants species in the world and its annual increase," *Phytotaxa*, vol. 261, no. 3, pp. 201–217, 2016.

[64] S. S. El-Hawary, F. I. Fathy, A. A. Sleem, F. A. Morsy, M. S. Khadar, and M. K. Mansour, "Anticholinesterase activity and metabolite profiling of *Syagrus romanzoffiana* (Cham.) Glassman leaves and fruits via UPLC–QTOF–PDA–MS," *Natural Product Research*, pp. 1–5, 2019.

[65] L. Chang, "Boraginaceae," in *Identification and Control of Common Weeds*, pp. 149–161, Springer, 2017.

[66] M. Imran, F. Ullah, M. Ayaz et al., "Anticholinesterase and antioxidant potentials of Nonea micrantha Bioss. & Reut along with GC-MS analysis," *BMC Complementary and Alternative Medicine*, vol. 17, no. 1, p. 499, 2017.

[67] A.-u. Rahman, F. Feroz, I. Naeem et al., "New pregnane-type steroidal alkaloids from *Sarcococca saligna* and their cholinesterase inhibitory activity," *Steroids*, vol. 69, no. 11-12, pp. 735–741, 2004.

[68] M. I. Choudhary, K. P. Devkota, S. A. Nawaz, R. Ranjit, and A. U. Rahman, "Cholinesterase inhibitory pregnane-type steroidal alkaloids from *Sarcococca hookeriana*," *Steroids*, vol. 70, no. 4, pp. 295–303, 2005.

[69] A.-u. Rahman, S. Parveen, A. Khalid, A. Farooq, and M. I. Choudhary, "Acetyl and butyrylcholinesterase-inhibiting triterpenoid alkaloids from *Buxus papillosa*," *Phytochemistry*, vol. 58, no. 6, pp. 963–968, 2001.

[70] K. Hostettmann, A. Borloz, A. Urbain, and A. Marston, "Natural product inhibitors of acetylcholinesterase," *Current Organic Chemistry*, vol. 10, no. 8, pp. 825–847, 2006.

[71] U. Steiner, M. A. Ahimsa-Müller, A. Markert et al., "Molecular characterization of a seed transmitted clavicipitaceous fungus occurring on dicotyledoneous plants (Convolvulaceae)," *Planta*, vol. 224, no. 3, pp. 533–544, 2006.

[72] N. Kaur, B. Sarkar, I. Gill et al., "Indian herbs and their therapeutic potential against Alzheimer's disease and other neurological disorders," *Neuroprotective Effects of Phytochemicals in Neurological Disorders*, vol. 79, 2017.

[73] M. Mort, T. O'Leary, P. Carrillo-Reyes, T. Nowell, J. Archibald, and C. Randle, "Phylogeny and evolution of Crassulaceae: past, present, and future," *Schumannia*, vol. 6, pp. 69–86, 2010.

[74] Z. Xu and M. Deng, "Crassulaceae," in *Identification and Control of Common Weeds*, pp. 475–486, Springer, 2017.

[75] X. Zhang, X. Wang, X. Hu, X. Chu, X. Li, and F. Han, "Neuroprotective effects of a Rhodiola crenulata extract on amyloid-β peptides (Aβ1-42)-induced cognitive deficits in rat models of Alzheimer's disease," *Phytomedicine*, vol. 57, pp. 331–338, 2019.

[76] A. Palmeri, L. Mammana, M. R. Tropea, W. Gulisano, and D. Puzzo, "Salidroside, a bioactive compound of Rhodiola rosea, ameliorates memory and emotional behavior in adult mice," *Journal of Alzheimer's Disease*, vol. 52, no. 1, pp. 65–75, 2016.

[77] D. R. Alves, S. Maia de Morais, F. Tomiotto-Pellissier et al., "Flavonoid composition and biological activities of ethanol extracts of *Caryocar coriaceum* Wittm., a native plant from Caatinga biome," *Evidence-Based Complementary and Alternative Medicine*, vol. 2017, Article ID 6834218, 7 pages, 2017.

[78] W. S. Judd, C. S. Campbell, E. Kellogg, P. Stevens, and M. Donoghue, "Plant systematics: a phylogenetic approach," *Ecologia Mediterranea*, vol. 25, no. 2, p. 215, 1999.

[79] Y. Chen, J. Zhang, B. Zhang, and C.-X. Gong, "Targeting insulin signaling for the treatment of Alzheimer's disease," *Current Topics in Medicinal Chemistry*, vol. 16, no. 5, pp. 485–492, 2016.

[80] A. De Falco, D. S. Cukierman, R. A. Hauser-Davis, and N. A. Rey, "Alzheimer's disease: etiological hypotheses and treatment perspectives," *Quimica Nova*, vol. 39, no. 1, pp. 63–80, 2015.

[81] M. Lemos, J. R. Santin, C. S. Mizuno et al., "Copaifera langsdorffii: evaluation of potential gastroprotective of extract and isolated compounds obtained from leaves," *Revista Brasileira de Farmacognosia*, vol. 25, no. 3, pp. 238–245, 2015.

[82] Â. G. Batista, A. S. Ferrari, D. C. da Cunha et al., "Polyphenols, antioxidants, and antimutagenic effects of Copaifera langsdorffii fruit," *Food Chemistry*, vol. 197, pp. 1153–1159, 2016.

[83] S. Gnaedinger, "Ginkgoalean woods from the Jurassic of Argentina: taxonomic considerations and palaeogeographical distribution," *Geobios*, vol. 45, no. 2, pp. 187–198, 2012.

[84] P. K. Mukherjee, V. Kumar, M. Mal, and P. J. Houghton, "Acetylcholinesterase inhibitors from plants," *Phytomedicine*, vol. 14, no. 4, pp. 289–300, 2007.

[85] S. Z. Bathaie and S. Z. Mousavi, "New applications and mechanisms of action of saffron and its important ingredients," *Critical Reviews in Food Science and Nutrition*, vol. 50, no. 8, pp. 761–786, 2010.

[86] S. Akhondzadeh, M. Shafiee Sabet, M. H. Harirchian et al., "A 22-week, multicenter, randomized, double-blind controlled trial of *Crocus sativus* in the treatment of mild-to-moderate Alzheimer's disease," *Psychopharmacology*, vol. 207, no. 4, pp. 637–643, 2010.

[87] M. R. Khazdair, A. Anaeigoudari, M. Hashemzehi, and R. Mohebbati, "Neuroprotective potency of some spice herbs, a literature review," *Journal of Traditional and Complementary Medicine*, vol. 9, no. 2, pp. 98–105, 2019.

[88] J. W. Finley and S. Gao, "A perspective on *Crocus sativus* L. (Saffron) constituent crocin: a potent water-soluble antioxidant and potential therapy for Alzheimer's disease," *Journal of Agricultural and Food Chemistry*, vol. 65, no. 5, pp. 1005–1020, 2017.

[89] S. Akhondzadeh, M. S. Sabet, M. H. Harirchian et al., "Saffron in the treatment of patients with mild to moderate Alzheimer's disease: a 16-week, randomized and placebo-controlled trial," *Journal of Clinical Pharmacy and Therapeutics*, vol. 35, no. 5, pp. 581–588, 2010.

[90] S. Venkateshappa and K. Sreenath, "Potential medicinal plants of Lamiaceae," *American International Journal of Research in Formal, Applied & Natural Sciences*, vol. 3, no. 1, pp. 82–87, 2013.

[91] G. Zgórka and K. Głowniak, "Variation of free phenolic acids in medicinal plants belonging to the Lamiaceae family," *Journal of Pharmaceutical and Biomedical Analysis*, vol. 26, no. 1, pp. 79–87, 2001.

[92] S. Vladimir-Knežević, B. Blažeković, M. Kindl, J. Vladić, A. D. Lower-Nedza, and A. H. Brantner, "Acetylcholinesterase inhibitory, antioxidant and phytochemical properties of selected medicinal plants of the Lamiaceae family," *Molecules*, vol. 19, no. 1, pp. 767–782, 2014.

[93] M. S. Kashani, M. R. Tavirani, S. A. Talaei, and M. Salami, "Aqueous extract of lavender (*Lavandula angustifolia*) improves the spatial performance of a rat model of Alzheimer's disease," *Neuroscience Bulletin*, vol. 27, no. 2, pp. 99–106, 2011.

[94] A. A. Oskouie, R. F. Yekta, M. R. Tavirani, M. S. Kashani, and F. Goshadrou, "*Lavandula angustifolia* effects on rat models of Alzheimer's disease through the investigation of serum metabolic features using NMR metabolomics," *Avicenna Journal of Medical Biotechnology*, vol. 10, no. 2, pp. 83–92, 2018.

[95] M. Soheili, M. R. Tavirani, and M. Salami, "Lavandula angustifolia extract improves deteriorated synaptic plasticity in an animal model of Alzheimer's disease," *Iranian Journal of Basic Medical Sciences*, vol. 18, no. 11, pp. 1147–1152, 2015.

[96] R. E. Lee, *Phycology*, Cambridge University Press, 2008.

[97] B. W. Choi, H. S. Lee, H. C. Shin, and B. H. Lee, "Multifunctional activity of polyphenolic compounds associated with a potential for Alzheimer's disease therapy from *Ecklonia cava*," *Phytotherapy Research*, vol. 29, no. 4, pp. 549–553, 2015.

[98] N. T. Mir, U. Saleem, F. Anwar et al., "Lawsonia inermis markedly improves cognitive functions in animal models and modulate oxidative stress markers in the brain," *Medicina*, vol. 55, no. 5, p. 192, 2019.

[99] A. I. Calderón, J. Simithy-Williams, R. Sanchez, A. Espinosa, I. Valdespino, and M. P. Gupta, "Lycopodiaceae from Panama: a new source of acetylcholinesterase inhibitors," *Natural Product Research*, vol. 27, no. 4-5, pp. 500–505, 2013.

[100] M. S. Rafii, S. Walsh, J. T. Little et al., "A phase II trial of huperzine A in mild to moderate Alzheimer disease," *Neurology*, vol. 76, no. 16, pp. 1389–1394, 2011.

[101] R. Govaerts, M. Sobral, P. Ashton et al., *World Checklist of Myrtaceae*, Royal Botanic Gardens, 2008.

[102] K. J. Sytsma and A. Litt, "Tropical disjunctions in and among the Myrtaceae clade (Myrtaceae, Heteropyxidaceae, Psiloxylaceae, Vochysiaceae): Gondwanan vicariance or dispersal," in *Botany 2002 Conference, University of Wisconsin*, pp. 4–7, Madison, WS, USA, 2002.

[103] H.-Y. Chen and G.-C. Yen, "Antioxidant activity and free radical-scavenging capacity of extracts from guava (Psidium guajava L.) leaves," *Food Chemistry*, vol. 101, no. 2, pp. 686–694, 2007.

[104] Y. L. Huang, M. B. Oppong, Y. Guo et al., *The Oleaceae family: a source of secoiridoids with multiple biological activities*, Fitoterapia, 2019.

[105] J. G. Cordero, R. García-Escudero, J. Avila, R. Gargini, and V. García-Escudero, "Benefit of oleuropein aglycone for Alzheimer's disease by promoting autophagy," *Oxidative Medicine and Cellular Longevity*, vol. 2018, Article ID 5010741, 12 pages, 2018.

[106] A. Mamum, M. Uddin, and F. Wahid, "Neurodefensive effect of Olea europaea L. alloxan-induced cognitive dysfunction and brain tissue oxidative stress in mice: incredible natural nootropic," *Journal of Neurology and Neuroscience*, vol. 7, pp. 1–9, 2016.

[107] M. Sarbishegi, "Antioxidant effects of olive leaf extract in prevention of Alzheimer's disease and Parkinson's disease," *Gene, Cell and Tissue*, vol. 5, no. 1, 2018.

[108] I. C. Gormley, D. Bedigian, and R. G. Olmstead, "Phylogeny of Pedaliaceae and Martyniaceae and the placement of *Trapella* in Plantaginaceae s. l," *Systematic Botany*, vol. 40, no. 1, pp. 259–268, 2015.

[109] S. Choudhary, P. Kumar, and J. Malik, "Plants and phytochemicals for Huntington's disease," *Pharmacognosy Reviews*, vol. 7, no. 14, pp. 81–91, 2013.

[110] M.-J. R. Howes, R. Fang, and P. J. Houghton, "Effect of Chinese Herbal Medicine on Alzheimer's Disease," *International Review of Neurobiology*, vol. 135, pp. 29–56, 2017.

[111] C. Dwivedi, K. Chandrakar, V. Singh et al., "Indian herbal medicines used for treatment of dementia: an overview," *International Journal of Pharmacognosy*, vol. 1, pp. 553–571, 2014.

[112] P. K. Mukherjee, V. Kumar, M. Mal, and P. J. Houghton, "*In vitro* acetylcholinesterase inhibitory activity of the essential oil from *Acorus calamus* and its main constituents," *Planta Medica*, vol. 73, no. 3, pp. 283–285, 2007.

[113] M. Hosseini, T. Mohammadpour, R. Karami, Z. Rajaei, H. Reza Sadeghnia, and M. Soukhtanloo, "Effects of the hydro-alcoholic extract of Nigella sativa on scopolamine-induced spatial memory impairment in rats and its possible mechanism," *Chinese Journal of Integrative Medicine*, vol. 21, no. 6, pp. 438–444, 2015.

[114] M. R. Khazdair, "The protective effects of *Nigella sativa* and its constituents on induced neurotoxicity," *Journal of Toxicology*, vol. 2015, Article ID 841823, 7 pages, 2015.

[115] M. Cascella, S. Bimonte, A. Barbieri et al., "Dissecting the potential roles of *Nigella sativa* and its constituent thymoquinone on the prevention and on the progression of Alzheimer's disease," *Frontiers in Aging Neuroscience*, vol. 10, p. 16, 2018.

[116] Z. Rabiei, M. Rafieian-kopaei, E. Heidarian, E. Saghaei, and S. Mokhtari, "Effects of *Zizyphus jujube* extract on memory and learning impairment induced by bilateral electric lesions of the nucleus basalis of Meynert in rat," *Neurochemical Research*, vol. 39, no. 2, pp. 353–360, 2014.

[117] B. Wang, "Chemical characterization and ameliorating effect of polysaccharide from Chinese jujube on intestine oxidative

injury by ischemia and reperfusion," *International Journal of Biological Macromolecules*, vol. 48, no. 3, pp. 386–391, 2011.

[118] S. R. Yende, B. B. Chaugule, and U. N. Harle, "Therapeutic potential and health benefits of *Sargassum species*," *Pharmacognosy Reviews*, vol. 8, no. 15, pp. 1–7, 2014.

[119] B. W. Choi, G. Ryu, S. H. Park et al., "Anticholinesterase activity of plastoquinones from *Sargassum sagamianum*: lead compounds for Alzheimer's disease therapy," *Phytotherapy Research*, vol. 21, no. 5, pp. 423–426, 2007.

[120] The Angiosperm Phylogeny Group, "An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG IV," *Botanical Journal of the Linnean Society*, vol. 181, no. 1, pp. 1–20, 2016.

[121] B.-W. Kim, S. Koppula, S. Y. Park et al., "Attenuation of inflammatory-mediated neurotoxicity by *Saururus chinensis* extract in LPS-induced BV-2 microglia cells via regulation of NF-κB signaling and anti-oxidant properties," *BMC Complementary and Alternative Medicine*, vol. 14, no. 1, 2014.

[122] S. H. Sung, S. H. Kwon, N. J. Cho, and Y. C. Kim, "Hepatoprotective flavonol glycosides of *Saururus chinensis* herbs," *Phytotherapy Research*, vol. 11, no. 7, pp. 500–503, 1997.

[123] K.-H. Choe, C.-H. Yoon, and S.-J. Kwon, "A study on chemical composition of Saururaceae growing in Korea (5) on flavonoid constituents of Saururus chinensis," *Analytical Science and Technology*, vol. 7, no. 1, pp. 11–15, 1994.

[124] S. L. González, G. G. Bazán, and L. C. Chávez, "*Solanum lycopersicum* l."tomate" y *solanum muricatum* aiton "Pepino"(solanaceae), dos frutas utilizadas en el perú prehispánico," *Arnaldoa*, vol. 22, no. 1, pp. 201–224, 2015.

[125] N. Sehgal, A. Gupta, R. K. Valli et al., "Withania somnifera reverses Alzheimer's disease pathology by enhancing low-density lipoprotein receptor-related protein in liver," *Proceedings of the National Academy of Sciences*, vol. 109, no. 9, pp. 3510–3515, 2012.

[126] Z. Xu and L. Chang, "Zingiberaceae," in *Identification and Control of Common Weeds*, pp. 909–911, Springer, 2017.

[127] S. Bhattacharjee, N. Banerjee, S. Chatterjee et al., "Role of turmeric in management of different non-communicable diseases," *World Journal of Pharmacy and Pharmaceutical Sciences*, vol. 6, pp. 1767–1778, 2017.

[128] A. Amalraj and S. Gopi, "Biological activities and medicinal properties of Asafoetida: a review," *Journal of Traditional and Complementary Medicine*, vol. 7, no. 3, pp. 347–359, 2017.

[129] S. Mandal and M. Mandal, "Coriander (*Coriandrum sativum* L.) essential oil: chemistry and biological activity," *Asian Pacific Journal of Tropical Biomedicine*, vol. 5, no. 6, pp. 421–428, 2015.

[130] M. Rychlik, "Quantification of free coumarin and its liberation from glucosylated precursors by stable isotope dilution assays based on liquid chromatography–tandem mass spectrometric detection," *Journal of Agricultural and Food Chemistry*|, vol. 56, no. 3, pp. 796–801, 2008.