ACCSCIENCE PUBLISHING

Advanced Neurology

REVIEW ARTICLE

Medicinal plants commonly used in Africa with neuroprotective potential in Alzheimer's disease: Mechanisms and translational relevance

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Abstract

Alzheimer's disease (AD) is a prevalent neurodegenerative disorder, and currently available pharmacological interventions provide only limited symptomatic relief and do not halt disease progression, emphasizing the need for alternative therapeutics. Herbal medicine, particularly from regions rich in plant biodiversity such as Africa, is gaining attention for its cognitive-enhancing and neuroprotective potential. This study reviews the potential benefits of common medicinal plants used in Africa for the treatment of AD, their traditional uses, phytochemical properties, and mechanisms of action reported in pre-clinical/clinical studies. A comprehensive search targeting 19 medicinal plant species with potential benefits for AD treatment was conducted across PubMed, Google Scholar, and African Journals Online up to 2025 using specific keywords related to African medicinal plants and AD. This review focused on medicinal plants utilized in African herbal medicine. However, some species included in this review are non-native but have been introduced, cultivated, and integrated into local herbal practices in Africa. Plants such as *Persea americana*, *Cuminum cyminum*, *Huperzia serrata*, and *Astragalus membranaceus* exhibit antioxidant, anti-inflammatory, and anticholinesterase activities, modulating major AD pathological processes, such as amyloid-beta aggregation, oxidative stress, and cholinergic dysfunction. Preclinical evidence suggests neuroprotective effects in animal models, while clinical data, though limited, show cognitive benefits. Regulatory challenges and the lack of standardization in the development and dosing of herbal extracts remain significant barriers to the clinical translation of African herbal medicine. Hence, further research and clinical validation, alongside the development of regulatory frameworks and standardization protocols, are needed to bridge the gap between traditional knowledge and evidence-based medicine and to develop effective, accessible, and sustainable AD treatment options.

Keywords: Alzheimer's disease; Herbal medicine; Plants; Africa; Alternative medicine; Mechanism

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Citation: Gbayisomore TJ, Alex GS, Iteire KA, Adedotun OA. Medicinal plants commonly used in Africa with neuroprotective potential in Alzheimer's disease: Mechanisms and translational relevance. *Adv Neurol*. doi: 10.36922/AN025190050

Received: May 7, 2025

1st revised: September 15, 2025

2nd revised: September 28, 2025

Accepted: October 10, 2025

Published online: December 3, 2025

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1. Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder that adversely affects memory, cognitive, and behavioral function in an individual. AD is termed the most prevalent type of dementia and affects >55 million people globally.[1] The pathological processes in AD include amyloid-beta (Aβ) plaque accumulation and neurofibrillary tangle formation, causing neuronal damage and synaptic loss.[2-4] Research on pharmacological interventions has been conducted for the prevention and treatment of this disease. Pharmacological interventions include N-methyl-D-aspartate receptor antagonists (memantine), cholinesterase inhibitors (donepezil, galantamine, and rivastigmine), and monoclonal antibodies targeting Aβ plaques (aducanumab).[5-10] These pharmacological interventions have shown promising results in mitigating AD symptoms but do not stop or reverse disease progression.[11] On the other hand, non-pharmacological interventions encompass a range of strategies, including memory training and encouraging social activities; however, there is still a gap in understanding these interventions.[12,13] This highlights the consistent need for developing new and alternative therapeutic approaches to address this disease.

African traditional medicine is an ancient medical system with a history of thousands of years, and it incorporates cultural and spiritual practices while remaining highly relevant in primary healthcare systems, especially in rural areas with limited access to modern medicine.[2] This reliance on common indigenous plants and traditional knowledge is significant in exploring other alternative options for complex neurodegenerative diseases like AD. Over the past decade, more than 200 potential drugs have failed clinical trials, further highlighting the complexity of AD.[14] The adoption of herbal medicine in developing treatments for AD has been gaining attention, especially in regions with abundant medicinal plants, such as Africa.[15] For centuries, numerous African medicinal plants have been used as traditional medicine to treat various diseases, but only some are documented.[16,17] Animal studies have demonstrated the cognitive- and memory-enhancing properties of medicinal plants, as well as their potential in mitigating AD phenotypic symptoms.[18,19] It is noteworthy that the vast potential of these plants is related to the diverse composition of bioactive compounds, including flavonoids, alkaloids, terpenoids, and phenolics, available in them at varying concentrations. These compounds contribute to the antioxidant, anti-inflammatory, anti-aggregation, anti-cholinesterase, and anti-apoptotic effects of medicinal plants.[20] These medicinal plants with distinct phytochemical properties are readily accessible and culturally accepted, making them cost-effective options for developing alternative treatments for AD.[21] Existing research evidence indicates that these plants exhibit neuroprotective, anti-inflammatory, antioxidant, and anti-cholinesterase properties that modulate AD pathology.[22,23] These studies examined pathophysiological pathways implicated in AD, including oxidative stress, inflammation, and cholinergic dysfunction.[22,23] For instance, bioactive compounds in *Ginkgo biloba*, *Garcinia kola*, and *Curcuma longa* showed significant neuroprotective effects in AD animal models with Aβ aggregation, oxidative stress, tau hyperphosphorylation, and brain inflammation.[24,25] However, the potential of these plants remains understudied and under-applied in clinical settings. In addition, regulations governing the use of herbal medicine further limit its application in AD treatment protocols. Nevertheless, the distinct phytochemical properties in these plants provide a promising avenue for drug discovery and design. This review provides an overview of the therapeutic potential of medicinal plants utilized in African herbal medicine for treating AD, focusing on their traditional uses, phytochemical profiles, and evidence from pre-clinical and clinical studies. The findings aim to highlight the role of medicinal plants in developing effective, accessible, and sustainable strategies for managing AD.

2. Literature review methodology

This review evaluated the therapeutic potential of African medicinal plants in treating AD by narratively comparing current evidence from existing preclinical and clinical studies. A literature search was conducted across databases encompassing PubMed, Google Scholar, and Africa Journals Online using specific keywords related to African medicinal plants and AD. The literature search included the following plants known for their potential neuroprotective properties: the selection of plants used in African herbal medicine included both native and non-native taxa that are currently used or cultivated within African traditional systems. These include *Persea americana* (avocado), *Cuminum cyminum* (cumin), *Huperzia serrata* (club moss), *Astragalus membranaceus* (astragalus), *G. biloba* (ginkgo), *C. longa* (turmeric), *Withania somnifera* (ashwagandha), *Moringa oleifera* (moringa), *Sutherlandia frutescens* (cancer bush), *Centella asiatica* (gotu kola), *Salvia officinalis* (sage), *Bacopa monnieri* (brahmi), *G. kola* (bitter kola), *Aspalathus linearis* (rooibos), *Vernonia amygdalina* (bitter leaf), *Zingiber officinale* (ginger), *Ocimum sanctum* (holy basil), *Camellia sinensis* (green tea), and *Phyllanthus amarus* (stonebreaker).

As a narrative review, no formal inclusion or exclusion criteria, time frame, or quality assessment protocols were employed. However, relevant and representative studies were selected after the search to provide a comprehensive understanding and contextual overview of the therapeutic

potentials of the plants used in AD. These plants were selected based on a combination of factors, including common traditional medicinal uses, preliminary scientific evidence, and the presence of bioactive compounds known to target major pathological features of AD, such as oxidative stress, neuroinflammation, Aβ aggregation, and cholinergic dysfunction.

3. Plant characteristics, bioactive compounds, and neuroprotective mechanisms

3.1. Avocado

Avocado (*P. americana* Mill.), from the Lauraceae family, is a fruit with high nutritional value, rich in essential fatty acids, proteins, vitamins (E, B1, B2, and D), minerals (calcium and iron), and bioactive compounds (carotenoids and phenolics).[26,27] Avocado has scavenging activity against free radicals and can inhibit lipid peroxidation,[24] an effect attributed to its rich active compounds and secondary metabolites, such as flavonoids, phenolics, tannins, tocopherols, fatty alcohols, carotenoids, and anthocyanins.[28-30] These antioxidants and phytochemicals may enhance synaptic function and neuroplasticity by reducing the accumulation of Aβ plaques, thereby enhancing memory and cognitive capabilities.[31] Avocados contain phytochemicals with antioxidant and anti-inflammatory properties that mitigate microglial activation in AD. In addition, oleic acid present in avocado can promote the clearance of Aβ plaques. Animal studies on the effects of avocado extract against aluminum chloride ($AlCl_3$)-induced AD have shown highly promising potential in ameliorating AD-like pathologies.[32] The neuroprotective properties are associated with its constituents, such as xanthophylls and flavonoids. Analysis of the microarchitecture of the hippocampus in a study by Ndé *et al.*[33] revealed that the extra-virgin avocado oil caused a notable reduction of neuronal loss in the hippocampal region (cornu ammonis region [CA]1 and CA3), restoring cognitive function and preventing the onset of AD. Oboh *et al.*[34] investigated the anti-cholinesterase and antioxidant properties of aqueous extracts of avocado pear leaves and seeds, revealing that both extracts reduced acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) activities linked to AD.[34] The seed extract demonstrated a greater inhibitory effect on AChE and BChE activity in comparison to the leaf extract, and both extracts demonstrated antioxidant properties, as evidenced by the iron(II)- and sodium nitroprusside-induced formation of thiobarbituric acid reactive substances in rats,[34] highlighting the benefits of avocado pear leaves and seeds in managing AD.

3.2. Cumin

Cumin, scientifically known as *C. cyminum* L., is a medicinal plant of the Apiaceae family and Apiales order. It is a medicinal plant in Southwest Asia and the Mediterranean.[35] The neuroprotective and nootropic effects of cuminaldehyde and cumin extracts hold promise as a potential treatment for AD. Cuminaldehyde and cumin possess antioxidant, anti-inflammatory, and cholinesterase-inhibitory effects by the suppression of pro-inflammatory cytokines, microglia, and other immune cells involved in neuroinflammation and oxidative stress.[36] Clinical research has shown cumin's potential for AD, including its ability to improve memory and cognition. One of the major compounds in cumin is cuminaldehyde, which has been shown to promote synaptic plasticity and neuroprotective factors through memory enhancement and spatial learning development.[37,38] Moreover, studies utilizing cumin extract on animal models of AD have elucidated the increase in antioxidant enzyme levels in the brain. Meanwhile, cuminaldehyde inhibited AChE, a contributor to AD development.[38] In addition, cumin oil, in various forms, can prevent the aggregation of α-synuclein, a hallmark of other neurodegenerative diseases.[39] Specifically, cuminaldehyde has shown potential as a monoamine oxidase-B (MAO-B) inhibitor, presenting as an alternative treatment option for AD. The increase in MAO-B in the AD brain deactivates important neurotransmitters, and inhibiting MAO-B is a possible treatment option.[40,41] Therapeutic effects of cumin extract in AD treatment have been reported in previous studies. The study by Kumar and Chowdhury[42] reported that the aqueous extract of cumin seed was the most potent inhibitor of BChE and showed mixed competitive inhibition kinetics. Compounds extracted from cumin, such as the BChE inhibitor, reduced oxidative stress and improved memory and cholinergic signaling in the brain.[43] Koppula and Choi[44] reported that cumin extract is a potent stress and anxiety reliever in a rat model, emphasizing its potential for translation to humans. The results indicated that cumin extract significantly mitigated stress-induced changes in the urinary biochemical profile in a dose-dependent manner, without affecting the control group. In addition, cumin extracts enhanced memory and cognitive functions associated with the cholinergic system of the brain, inhibiting lipid peroxidation in brain tissues, and were comparable to ascorbic acid.[44] This antioxidant activity may contribute to its neuroprotective effects, potentially reducing neuroinflammation linked to AD.

3.3. Club moss

Alkaloids, triterpenes, flavones, and phenolic acids are chemical compounds that can be extracted from the Huperziaceae plants, such as club moss. Huperzine A

(Hup A) is a natural chemical extracted from club moss.[45] Evidence suggests that Hup A possesses cytoprotective potential against numerous challenges, including epithelial apoptosis and apoptosis induced by Aβ protein, glutamate, ischemia, and staurosporine. It reduces oxidative apoptosis and decreases the levels of apoptosis-inducing factors, such as Bcl-2, Bax, p53, and caspase-3, while simultaneously protecting mitochondrial integrity. Moreover, Hup A also modulates amyloid precursor protein (APP) metabolism and antagonizes N-methyl-D-aspartate receptors and potassium currents, thereby enhancing its neuroprotective effect.[46] Phase IV clinical trials conducted in China reported that Hup A can substantially ameliorate memory deficits among older people with benign senescent forgetfulness and those with AD, with a slight peripheral cholinergic effect and no unexpected toxic effects.[47] Previous studies reported that administering Hup A to AD patients within 8 weeks resulted in improvements in task switching and a notable reduction in cognitive problems.[48] In a multicenter, randomized study involving 50 patients, improved cognitive and memory function was observed in 58% of patients with no severe side effects with the intake of 0.2 mg of Hup A.[49] A previous study reported a very promising club moss extract (NSP01) for preventing AD and impaired memory. It exerts anti-inflammatory, immunomodulatory, and antioxidant effects, including cholinesterase inhibition and free radical scavenging, and promotes neuronal survival through brain-derived neurotrophic factor (BDNF).[50] Preliminary studies have also reported the neuroprotective potential of club moss compounds, including their ability to prevent cell death, reduce reactive oxygen species (ROS) production, and inhibit AChE activity.[51] Despite research evidence supporting the use of Hup A, its translation into clinical application is limited by methodological constraints and the issue of standard dosage. To strengthen the role of Hup A as an AD treatment, extensive, randomized, and placebo-controlled trials are required.

3.4. Astragalus

Astragalus polysaccharide (APS) is a mixture of polysaccharides obtained from *A. membranaceus* in the form of white or light-yellow powder. APS is mainly composed of fructose, rhamnose, arabinose, hexuronic acid, glucose, galacturonic acid, and glucuronic acid, and it is soluble in water but insoluble in alcohol.[52,53] Shi *et al.*[54] reported that astragali (dried roots of astragalus) reversed the reduction of muscarinic cholinergic receptors in the brains of senile rats, thereby improving memory and hindering neurodegeneration. A separate study reported that APS mitigated AD symptoms by improving insulin sensitivity, thereby reducing blood sugar levels. The study showed that APS improved glucose tolerance and reduced insulin levels in AD mice induced with a high-fat diet combined with streptozotocin.[55] A study by Li *et al.*[56] using a fruit fly model showed that APS improved gut conditions, mitigated sleep disorders, delayed the onset of AD symptoms, and exhibited an anti-aging effect through modulating several signaling pathways (JAK/STAT, toll-like receptor [TLR] signaling pathway, and immune deficiency pathway). Subsequent activation of the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway explains how APS increases nuclear Nrf2 expression, decreases its cytoplasmic retention, restores antioxidant enzyme levels (Kelch-like enoyl-CoA hydratase-associated protein 1, superoxide dismutase, and glutathione peroxidase), and reduces the oxidative stress marker (malondialdehyde [MDA]) in mouse cells. In APP/PS1 mice, APS markedly enhanced cognitive function, lowered cell death, and stopped Aβ deposition.[57] Furthermore, APS has been shown to reduce cell apoptosis by inhibiting Cyt C and Caspases-3 and -9 expression, thereby providing neuroprotection.[58] Another study further demonstrated the beneficial effects of APS on the cognitive function of AD rodent models after Aβ injection. APS treatment was associated with increased organ weight index, reduced brain water content and Evans blue staining, and improved hippocampal CA3 integrity, including neuronal morphology, nuclear membrane integrity, and mitochondrial structure.[59] Similarly, APS was shown to inhibit the aggregation of disease-related proteins and reduce astrocyte injuries caused by the herpes virus, thereby mitigating inflammation, oxidative stress, and other factors associated with neurodegeneration.[60] Research on the pharmacokinetics of APS remains limited; to optimize its therapeutic potential, future research should prioritize its pharmacodynamics and pharmacokinetic properties. In addition, extensive research on the effect of individual characteristics, such as age, sex, and genetic background, on the pharmacokinetic and pharmacodynamic properties of APS is required.

3.5. Ginkgo

G. biloba is one of the oldest living species of plants, commonly found in Asia, and has been widely used by Africans as a medicinal plant for more than 1,000 years due to its therapeutic properties and its phytochemicals, including flavonoids, terpenoids, ginkgolides, and bilobalide.[64] These phytochemicals render ginkgo a powerful anti-inflammatory, antioxidant, and neuroprotective agent for the treatment of AD. Flavonoids, such as quercetin and kaempferol, act as free radical scavengers and can suppress oxidative stress associated with AD. Ginkgolides and bilobalide, bioactive compounds from ginkgo, inhibit platelet aggregation through vasodilation, protect against

oxidative stress, modulate neurotransmitter release, and enhance energy production in brain cells.[66] Bilobalide, according to Maclennan *et al.*,[61] promotes mitochondrial membrane stabilization and ATP production, thereby preventing neuronal death caused by oxidative stress and mitochondrial dysfunction. Apart from its anti-inflammatory and antioxidant properties, ginkgo enhances cerebral blood flow, thereby preserving cognitive function in the elderly and those with cerebrovascular impairment. The vasodilatory effect of ginkgo is primarily mediated by its stimulation of nitric oxide production in vascular endothelial cells, enhancing blood flow and delivering more nutrients to the brain. Faster blood flow to the brain is not only essential for cognitive health but also ensures that sufficient oxygen and vital nutrients are delivered to neuronal tissues. In a clinical study conducted by Ahlemeyer and Krieglstein,[62] ginkgo extract improved cognitive function in patients with cerebral insufficiency by enhancing cerebral blood flow. The role of ginkgo extract in enhancing cognitive function and reversing neurodegeneration is also significantly associated with its capacity to regulate cholinergic, serotonergic, and dopaminergic pathways. Ginkgo can improve learning and memory by inhibiting AChE and modulating muscarinic and nicotinic receptor activity. Weinmann *et al.*[63] reported that treatment with ginkgo was a natural method to improve brain function for patients with mild-to-moderate AD, significantly enhancing cognitive abilities, focus, and memory. Silberstein *et al.*[65] also highlighted ginkgo's role in activating notable brain regions, such as the left temporal and left prefrontal cortex, which are involved in memory processing and function.

3.6. Turmeric

C. longa, commonly known as turmeric, is an herbaceous plant from the Zingiberaceae family, with curcumin as its primary active component. Its potential therapeutic benefits in neurodegenerative diseases lie in its ability to exert direct ameliorative effects in the brain by modulating multiple molecular targets.[67] A study showed that curcumin inhibits Aβ plaque formation and aggregation in AD mice.[68] Recent findings by Iteire *et al.*[69] demonstrated that curcumin attenuates inflammation by inhibiting microglial activation and enhances memory in mice. Its involvement in the oxidative pathway, by inhibiting neuronal damage and neutralizing ROS production, is a significant mechanism for protecting the neurons against oxidative stress.[70] Pre-clinical studies suggested that curcumin exhibited neuroprotective effects in AD models through inhibiting the aggregation of Aβ plaques. Inhibition of Aβ aggregation is thought to occur through two main mechanisms. First, curcumin binds to Aβ peptides, blocking their aggregation into oligomers and fibrils, destabilizing preformed fibrils by disrupting β-sheet structures, and interacting with the 17LVFFA21 domain of Aβ, as reported in the *in vivo* and *in vitro* studies.[71,72] The second mechanistic option is reducing plaque burden, as Aβ levels were reported to be reduced by 39% and plaque burden by 43% post administration of a low dose of curcumin, whereas a higher dose prevented Aβ assembly.[68] Curcumin reduces tau protein and tangles in aged transgenic mice, lowering soluble tau dimer levels without altering insoluble tau protein, thereby improving cognitive function.[73] In molecular pathways, curcumin notably inhibits nuclear factor kappa B (NF-κB), a key regulator of inflammatory responses during neuroinflammation.[74] In addition, curcumin plays significant roles in modulating additional signaling pathways implicated in neurodegeneration, such as the serine/threonine kinase AKT and the Nrf2 pathway.[75,76] Despite the existing and promising preclinical findings, clinical trials of curcumin remain limited. Cox *et al.*[77] conducted a randomized, double-blind, placebo-controlled study and reported memory- and attention-improving effects of curcumin supplementation in non-dementia adults and highlighted its potential for cognitive enhancement.[77] Recently, curcumin-loaded nanoparticles have been studied, yielding notable findings. Fontana *et al.*[78] reported that it ameliorated the expression of inflammatory markers in lipopolysaccharide-inflamed cells of atherosclerosis. Its potential to cross the blood–brain barrier and achieve targeted drug delivery for glioma treatment was also shown in a mouse model.[79] Although there is a need for more research to elucidate curcumin's therapeutic potential against AD and specific dosing for the treatment of neurodegenerative diseases, there is also a need for more studies on nanoformulation of optimum delivery systems, in terms of the size and functionalization needed on the surface of nanoparticles to bind to receptors and transporters, for successful delivery in the brain cells.[80,81]

3.7. Ashwagandha

W. somnifera, commonly known as ashwagandha, is widely used as a medicinal plant for various ailments in Africa and is a key component of Ayurvedic medicine.[82,83] The major factor contributing to its therapeutic potential is the active compounds, withanolides.[83] In view of the various pharmacological properties of ashwagandha, including anti-inflammatory, neuroprotective, and antioxidant effects, it possesses components essential in the management and treatment of AD. There are several potential mechanisms underlying Ashwagandha's ability to improve cognition and mitigate AD-like pathology. Ashwagandha exhibits antioxidant effects against oxidative

stress to mitigate neuronal damage and neutralize free radicals owing to its high flavonoid, phenolic compound, and withanolide content (notably withaferin A and withanolide D).[84,85] Withaferin A, a withanolide compound, activates Nrf2, resulting in the production of cytoprotective molecules to overcome oxidative stress.[86,87] This mechanistic reaction by withaferin A is achieved by the inhibition of the phosphatase and tensin homolog protein and activating the PI3K/AKT/mTOR and PI3K/AKT/GSK3β pathways necessary for neuronal growth and survival, as well as protection against neuronal apoptosis. There is also a close interaction between the major phytoconstituents of ashwagandha, including withanolide A, withanolide B, withanoside IV, and withanoside V, with the hydrophobic core of Aβ 1–42 in the form of an oligomer, in reducing aggregation and inhibiting further interaction with monomers.[88,89] Moreover, the glutathione derivative of withanolide A-CR-777, yielded from the bioconversion of ashwagandha extract, showed neuroprotective effects against neuronal injury by increasing cell survival, improving neurite network, and reducing α-Syn expression.[90] Hence, these findings suggest that ashwagandha may inhibit the formation of Aβ 42 deposits in AD.[91] In addition, ashwagandha plays a modulatory role in neuroinflammation, as chronic brain inflammation contributes to neurodegeneration and impairs cognitive function.[92] Ashwagandha's modulatory role in inflammatory responses is mediated by inhibiting pro-inflammatory cytokines and reducing microglial activation.[93]

Another notable mechanism by which ashwagandha may potentially mitigate AD-like pathologies is the promotion of neuronal growth and neurogenesis. The presence of withanolide A, a component of active withanolides, has been reported to promote neuronal differentiation and dendrite growth, thereby enhancing neurogenesis. Kuboyama *et al.*[94] reported that dendritic growth in human neuroblastoma cells was enhanced by withanolide A, significantly associated with improved neuronal function and development. The neurogenic effect is highly relevant in addressing AD-like pathologies, including neuronal loss and impairment in synaptic plasticity. Despite the availability of preclinical and *in vitro* studies on Ashwagandha's neuroprotective effects, the evidence from clinical trials is limited. However, there are notable findings from pilot studies. Choudhary *et al.*[85] reported improvements in cognitive and motor performance among patients administered with ashwagandha extracts, suggesting its role in improving cognitive function in AD treatment. There is a need for more longitudinal clinical studies to establish its optimal dosages. Recently, withanolide A was also reported to cross the blood–brain barrier following intranasal administration, aiding its penetration into the cortex and cerebellum.[95] However, there is a need for more studies to assess other affected brain regions in AD patients and compare noticeable effects and mechanisms in the regions to fully elucidate the mechanistic effect of ashwagandha in the treatment of AD.

3.8. Moringa

M. oleifera, also known as moringa, is a medicinal plant commonly used in African herbal medicine for medicinal and cooking purposes due to its nutritional benefits and medicinal properties.[96] The medicinal plant contains various bioactive compounds, such as quercetin, isothiocyanates, kaempferol, essential vitamins, and minerals that contribute to its antioxidant and anti-inflammatory properties.[97] These compounds have specific modulatory roles in major mechanisms affected in AD.[98] The antioxidants in moringa scavenge free radicals and exhibit neuroprotection against oxidative damage.[99] There is documented evidence for the role of moringa phytochemicals, such as polyphenols, flavonoids (including quercetin, kaempferol, and isoquercitrin), and phenolic acids (including chlorogenic, ferulic, and gallic acids), in enhancing the antioxidative system and upregulating endogenous antioxidant enzymes.[100-103] Among other compounds, the β-carotene has been reported to promote neuronal growth and enhance cellular antioxidant defenses by activating the Nrf2/Keap1 pathway, resulting in increased nuclear translocation of Nrf2 and subsequent expression of antioxidant response element-dependent genes.[104,105]

The inflammatory modulatory role of moringa lies in its effects on cytokines and signaling pathways involved in AD progression.[106] In cytokine modulation, moringa significantly downregulates pro-inflammatory cytokines (including tumor necrosis factor [TNF]-α, interleukin[IL]-6, and IL-1β), which are notably elevated markers in AD and throughout its progression.[107] Other inflammatory signaling pathways mediated by bioactive compounds from moringa include the NF-κB and mitogen-activated protein kinase pathways.[108,109] In the NF-κB pathway, bioactive compounds, such as isoquercetin, contribute to the inactivation of NF-κB, inhibition of translocation to the nucleus, and subsequent transcription of inflammatory genes by inhibiting phosphorylation of IκB-α.[109,110] Consequently, the production of inflammatory mediators, such as cyclooxygenase-2 (COX-2) and prostaglandin E2, that contribute to AD neuroinflammatory features, is halted.[110] An isolated component of the n-butanol moringa seed extract, β-sitosterol; helps balance Th1 and Th2 cytokines; and mediates chronic inflammation, a hallmark of AD.[111]

Tajuddin and Rahman[112] reported the cognitive-enhancing effects of moringa extract in rat models of AD to mitigate oxidative stress and enhance the cholinergic pathway. The cholinergic pathway is a key pathway in learning and memory, and enhanced cholinergic activity is a significant marker for restoring learning and memory impairments, which are symptoms of AD.[113] AChE, the enzyme responsible for acetylcholine breakdown during synaptic transmission, is reported to be inhibited by moringa, thereby increasing acetylcholine levels and improving memory.[114] However, there is a dearth of research on designing a well-standardized, bioavailable moringa formulation for AChE inhibition as a treatment for AD.[115] Furthermore, moringa has been reported to promote synaptic plasticity and neuronal growth that are essential for reversing neurodegenerative processes observed in AD.[116] Moringa also inhibits β-site APP cleaving enzyme 1, consequently reducing production of Aβ in the brain.[117] In addition to its potential to reduce Aβ plaque formation, moringa has been shown to enhance neprilysin expression, facilitating the clearance of Aβ from the brain.[118,115] The dual action represents a biological benchmark in reference to the cognitive improvements observed in various animal models, as reported in Fauziah *et al.*,[119] highlighting its potential as a therapeutic option for AD. However, extensive research is needed to establish the standardized dose based on efficacy and safety in humans, especially in a longitudinal setting.

3.9. Cancer bush

S. frutescens, also known as cancer bush, is another African medicinal plant widely used in traditional medicine in Southern Africa.[120] Its bioactive compounds, including L-canavanine, pinitol, and gamma-aminobutyric acid (GABA), are recognized for their anti-inflammatory, antioxidant, and anti-cancer properties.[121,122] The neuroprotective effects are mainly based on its modulatory role against oxidative stress and inflammation involved in the pathophysiology of neurodegenerative diseases.[123] An *in vitro* study reported that the cancer bush exhibited antioxidant activity and effectively scavenged ROS.[124] Its anti-inflammatory effects are notable, as it inhibits pro-inflammatory cytokines and modulates inflammatory pathways, such as NF-kB, to protect the brain against chronic inflammation and associated damage.[125] Greef and Kunert[126] reported the immunomodulatory effects of L-canavanine and its therapeutic potential in neurodegenerative conditions. However, there remains a significant gap in clinical research, especially in AD studies, as there is a dearth of large-scale human trials to verify the efficacy and safety of cancer bush toward AD treatment and prevention. The majority of existing studies are pilot studies, such as Johnson *et al.*'s[127] randomized double-blinded-controlled study where adult healthy rats were administered with 400 mg/kg capsules constituted of cancer bush leaf extract (twice daily), and reported no significant differences in vitals, blood, and biomarkers, even with increased appetite.[127] Hence, there is a need to formulate clinical trials based on existing pilot studies to uncover the potential of cancer bush as a treatment for AD. Limited AD-specific clinical data for cancer bush highlights the need for further trials. The molecular mechanisms by which the bioactive compounds act are also not yet fully understood. Understanding of its pharmacokinetics and bioavailability is necessary for clinical translation. Hence, there is a need for more research in that area to explore the long-term effects and safety in humans. Comparing the cascade of effects from other neuroprotective agents could support the investigation and development of a relatively effective dose of cancer bush and its advantages over established treatments.

3.10. Gotu kola

C. asiatica, commonly known as gotu kola, is a perennial plant used in traditional medicine based on its major bioactive triterpenoids, including asiaticoside, asiatic acid, and madecassoside.[128] Gotu kola's neuroprotective effects are observed through improved cognitive function through several mechanisms, including neuroinflammation modulation, neuronal growth promotion, and oxidative stress reduction. Asiaticoside is a major triterpenoid with the potential to promote dendritic arborization and neurogenesis. Notably, Rao *et al.*[129] reported that asiaticoside administered at doses of 10–40 mg/kg body weight to aged rats led to improved memory and learning through aided dendritic growth in hippocampal neurons. The antioxidant properties of madecassoside and asiatic acid are also asserted to be based on scavenging free radicals and inhibiting oxidative pathways.[130] The bioactive compounds in gotu kola with anti-inflammatory properties act by inhibiting inflammatory cytokines and suppressing NF-kB activation. Studies have reported the role of gotu kola extracts in reducing the pro-inflammatory cytokine levels, such as TNF-α and IL-6, which are contributory markers in neuroinflammation.[131] Rao *et al.*[132] administered aged rats with a methanolic extract of gotu kola at doses ranging from 10 to 40 mg/kg body weight and observed several features, including cognitive improvement, dendritic arborization in the neurons of the hippocampus, and enhanced learning and memory function. Wattanathorn *et al.*[133] conducted a double-blind, placebo-controlled clinical trial involving healthy elderly participants, administering gotu kola extract at a dose of 500 mg daily for 8 weeks. Participants receiving the extract showed improvements in cognitive

performance, including memory and attention, as well as improved mood, compared to those receiving a placebo.[133] The extraction methods for gotu kola vary across studies, with methanol and ethanol commonly used as solvents to extract the active compounds, which are then concentrated and administered to animal models.[134] For clinical trials, standardized extracts were prepared through solvent extraction, followed by filtration and concentration, to ensure consistent active compound concentrations.[133] There is a growing body of research evidence in clinical trials using gotu kola to improve cognitive and memory function, mood, anxiety, and overall brain function.[129,135-142] However, there are relatively few trials specifically focused on AD recently; hence, more large-scale studies are needed to establish efficacy in the treatment of AD and its safety. Gray *et al.*[143] also highlighted the issue of the lack of standardization in the studies, with variability in study quality and relevance, but the positive background knowledge is that there is no adverse effect associated with gotu kola in the human studies conducted.

3.11. Sage

Another common African medicinal plant is *S. officinalis*, also known as sage. It is used in traditional medicine and for cooking purposes. According to phytochemical analyses, the major bioactive compounds in sage include rosmarinic acid, carnosic acid, and essential oils, which contribute significantly to its therapeutic effects against ailments.[144] Rosmarinic acid, a well-studied compound in sage, exhibits anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines (including TNF-α, IL-1β, and IL-6), downregulating the expression of adhesion molecules, and modulating inflammatory pathways regulated by enzymes such as COX-2, thereby reducing neuroinflammation.[145-147] Notably, rosmarinic acid from sage has been shown to downregulate matrix metalloproteinase-9, a protein involved in tissue remodeling and neuroinflammation. To corroborate the findings on anti-inflammatory response, Wei *et al.*[148] reported that rosmarinic acid down-regulated NOD-, LRR-, and pyrin domain-containing protein 3 inflammasome, TLR4, and CD14 involved in the innate neuro-immune response.

There is also research evidence for sage's antioxidant mechanism, which neutralizes free radicals and reduces oxidative stress damage to neurons.[149] Another major compound present in sage is carnosic acid, which has been reported to have notable neuroprotective effects through its antioxidant activity, activating cellular defense mechanisms against oxidative stress. Huang *et al.*[150] have demonstrated that carnosic acid inhibited Aβ plaque formation in AD. Sage also contains essential oils, such as monoterpenes, 1,8-cineole, and thujone, which contributed significantly to its cholinesterase-inhibitory activity. Inhibition of AChE by sage extracts has been associated with increased acetylcholine levels, which support cognitive function and memory.[151]

Given the potential of sage to improve cognitive performance, Tildesley *et al.*[152] conducted a randomized, double-blind, placebo-controlled trial, in which participants received a standardized sage extract, and findings showed significantly improved cognitive performance and mood in healthy older adults.[152] Participants also showed enhanced memory recall, attention, and overall cognitive function compared to those receiving a placebo. Another study by Akhondzadeh *et al.*[153] investigated the effects of sage in patients with mild to moderate AD through a randomized, double-blind, placebo-controlled study, administering sage extract to participants for 4 months. The study findings showed a cognitive-enhancing function of sage and a reduction in anxiety and depression levels.[153] Sage extract is typically administered at standardized doses in clinical studies to ensure consistent concentrations of the active compound. Tildesley *et al.*[152] administered 300 mg of sage extract daily and used steam distillation and solvent extraction methods to effectively concentrate the essential oils and active compounds. In Akhondzadeh *et al.*,[153] the dosage of sage extract was 600 mg daily, divided into two doses, and the extract was prepared using hydroalcoholic extraction methods to preserve the bioactive compounds.[153]

3.12. Brahmi

Brahmi is another notable medicinal plant used in traditional medicine due to its active compounds, particularly the bacosides A and B, which exhibit antioxidant, anti-inflammatory, and neuroprotective activity.[154] Several studies have also reported the role of brahmi in promoting synaptic plasticity through the increased magnitude of long-term potentiation, aiding cholinergic system function, and promoting dendritic growth.[155,156] Kongkeaw *et al.*'s[157] meta-analysis of data from randomized control trials reported that brahmi improved memory, cognition, and overall cognitive function in 437 eligible subjects.[157] The findings are corroborated by Pase *et al.*,[158] highlighting its efficacy for memory retrieval among healthy adults. Furthermore, Raghav *et al.*[159] reported the effect of brahmi in improving attention and cognitive processing in children diagnosed with attention-deficit/hyperactivity disorder, emphasizing its possible application in varying age groups.[159] The anxiolytic effects of brahmi have also been assessed in a double-blind, placebo-controlled study by Stough *et al.*,[160] where brahmi supplements administered for 12 weeks significantly reduced the anxiety levels and improved cognitive performance among healthy older adults.[160] Calabrese

et al.[161] also reported the role of Bacopa in improving mood, emotional well-being, and cognitive function.[161] The extraction procedures adopted in these studies vary; however, the standardized extracts are typically within the 40–50% bacosides range. The dose range in the clinical trial is 300–450 mg/day, and cognitive performance is reported after consistent use for at least 12 weeks. More research is needed to fully elucidate the mechanisms through which brahmi exerts its effects and to determine the safety and efficacy from a longitudinal perspective, particularly in cognitively impaired individuals.

3.13. Bitter kola

G. kola is a plant native to West and Central Africa, and also known as bitter kola.[162] Bitter kola and its seeds have been used in traditional medicine to treat various ailments, including fever, diarrhea, and cold.[162] The major phytoconstituents in bitter kola are kolaviron, garcinianin, kolanone, gakolanone, garcinoic acid, garcinal, garcifuran A and B, garcipyran A, biflavonoids, and xanthones; some of which are not present in other plants.[162] Kolaviron, a biflavonoid complex present in bitter kola, has been extensively studied based on its antioxidant effects in reducing ROS.[163,164] Farombi and Nwaokeafor[165] reported several mechanisms associated with kolaviron's role in antioxidant systems, including directly scavenging free radicals, inhibiting lipid peroxidation (indicated by downregulated MDA levels and conjugated diene formation in kolaviron-treated rats), and chelating metal ions (such as iron and copper ions), thereby protecting lipoproteins and cellular membranes from oxidative damage.[165] Kolaviron has also been reported to modulate inflammatory pathways, contributing to its neuroprotective effects, as Farombi *et al.*[163] reported its neuroprotective effects against cognitive deficit and oxidative stress damage in AD rat models. The anti-inflammatory properties are associated with reduced microglial activation and the inhibition of pro-inflammatory cytokine release. Numerous studies have examined the role of kolaviron against various neurotoxic agents, and it has shown potential to ameliorate memory deficits, improve learning, and attenuate AD-like symptoms and Aβ pathology in animal models.[166-170] Although there are limited clinical trials investigating the effects of bitter kola on cognitive function, the robust research evidence from preclinical studies and the plant's traditional use highlight its potential benefits in maintaining brain health. It has also been used for other ailments across various body systems, including cardiovascular health, liver protection, and antimicrobial activity, but the question is to determine the specific dose needed to achieve expected outcomes in humans. The history of traditional use and findings from animal models suggest that bitter kola could play a significant role in complementary and alternative medicine for brain health. However, recent findings from Thomas *et al.*,[171] using kola nut extract administered at high dose and long duration, showed inhibition of hippocampus-dependent learning and memory and hippocampal neurogenesis. The adverse effects observed in the animal model emphasize the dose-dependent duality and the need for careful consideration when elucidating the therapeutic effects of bitter kola, as well as cautious interpretation. Furthermore, this emphasizes the need for more studies to understand the molecular implications across doses and to translate preclinical findings into clinical settings to formulate standardized, safe, and effective doses in mitigating AD.

3.14. Rooibos

Another indigenous African plant, commonly found in South Africa, is *A. linearis*, also known as rooibos, mainly consumed as an herbal tea (caffeine-free tisane).[172] Rooibos is rich in polyphenolic compounds, including aspalathin, nothofagin, and a wide array of flavonoids, which modulate oxidative stress and inflammation in the brain.[173] Flavonoids, such as aspalathin, quercetin, and nothofagin, possess antioxidative activity in scavenging free radicals, corroborating their role in inhibiting oxidative processes and complementing neuroprotection against cellular damage.[174,175] Rooibos is believed to modulate inflammatory pathways by inhibiting the production of pro-inflammatory cytokines and reducing the activation of microglial cells. Ulicná *et al.*[176] reported the protective capacity of rooibos extract against oxidative stress and improved cognitive function in an AD rat model. Although limited, studies have demonstrated the mediating role of polyphenols in rooibos in amyloidogenic pathways, including γ-secretase activity, thereby reducing Aβ peptide formation.[177] Flavonoids present in rooibos attenuate Aβ plaque deposition in animal models and act as an anxiolytic through GABAergic neurotransmission.[177] This was observed in the pentylenetetrazole-induced seizure model, where green rooibos extract exhibited anxiolytic effects and prevented intracellular ROS accumulation in zebrafish larvae, rescuing GABA receptor signaling.[178] These studies highlight the potential in mitigating cognitive deficits associated with AD by protecting against oxidative damage. While the pre-clinical evidence is promising, there remains a need for clinical studies. However, the findings from preclinical studies and the traditional use of rooibos in South Africa suggest its potential to prevent or delay AD onset.

3.15. Bitter leaf

V. amygdalina, also known as bitter leaf, is extensively utilized in traditional African medicine. It contains bioactive

compounds, such as vernodalin, vernomygdin, and various flavonoids. Bitter leaf's neuroprotective capacity centers on its role in safeguarding neuronal health and altering the progression of AD through mechanisms associated with the antioxidant system, AChE suppression, oxidative stress reduction, anti-inflammatory activity, and neurobehavioral restorative effects.[179,180] Vernodalin and vernomygdin have been shown to effectively scavenge free radicals, reducing oxidative stress within the brain, preserving neuronal integrity, and preventing the cascade of damage that causes cognitive decline.[179-181] Part of these antioxidant activities is linked to flavonoids and sesquiterpene lactones, such as vernodalin and vernomygdin in bitter leaf.[181] Bitter leaf exhibits significant anti-inflammatory effects by dampening this inflammatory response,[182-184] which is necessary for neuroprotection against inflammatory damage. Onasanwo *et al.*[182] reported that its anti-inflammatory and antinociceptive role in the rat model was through limiting leukocyte migration and reducing lipid peroxidation, thereby protecting tissue against inflammation. It also has a role in microglial activation, as Adelodun *et al.*[184] reported that bitter leaf treatment attenuated hippocampal neurotoxicity in the CA1 region of the hippocampus through its anti-neuroinflammatory effects in protecting against neuronal damage. Odu *et al.*[185] demonstrated its significant effect against scopolamine-induced cognitive deficits and oxidative damage in an AD rat model and reported its role similarly to donepezil in counteracting the cognitive impairments associated with AD.[185] The extensive use of bitter leaf in traditional medicine, along with its well-documented antioxidant and anti-inflammatory properties, suggests future applications in brain health to delay or prevent the progression of neurodegenerative conditions, such as AD.[179]

3.16. Ginger

Another commonly used African medicinal plant in traditional medicine is ginger, a flowering plant with a rhizome that is also used as a spice. It contains compounds, such as gingerol, shogaol, and paradol, that collectively contribute to its potential in promoting brain health. Gingerol, a well-studied antioxidant, and shogaol, a compound with anti-inflammatory effects through modulation of inflammatory pathways, together help mitigate neuroinflammation observed in AD patients.[186-189] Ginger modulates cholinergic activity by increasing acetylcholine levels, thereby improving cognitive performance.[190,191] Karam *et al.*[192] investigated the effects of ginger extract in an AD rat model and reported significant protection against cognitive deficits and oxidative damage compared to the control group, suggesting its therapeutic role in mitigating AD. This pre-clinical finding is corroborated by Zeng *et al.*,[194] who showed that ginger root extracts ameliorated behavioral dysfunction, with ginger-administered groups showing reduced levels of NF-κB, IL-1β, and MDA, indicative of its potential in mitigating AD.[194] Saenghong *et al.*[193] investigated the ginger supplementation effects (800 mg once daily) on cognitive function in middle-aged healthy women and highlighted its positive effect on cognitive performance and the brain. Although extensive clinical research is needed, these findings support the potential role of ginger in supporting cognitive health and preventing age-related cognitive decline.

3.17. Holy basil

Another notable medicinal plant is *O. sanctum*, widely recognized as holy basil or tulsi, used in Ayurvedic practices and African medicine. It contains major compounds, such as eugenol, ursolic acid, and rosmarinic acid.[195] Eugenol, a major constituent of holy basil, has antioxidant properties that help mitigate oxidative stress through scavenging free radicals.[196] The anti-inflammatory activity of ursolic acid against inflammation in neurodegenerative diseases has also been reported.[197] Rosmarinic acid exerts its neuroprotective effects by modulating inflammatory pathways and supporting synaptic plasticity, which are necessary for cognitive function.[198] Venu *et al.*[199] examined the effect of 200 mg/kg body weight of holy basil extract on AD rats for a duration of 28 days and reported cognitive improvement and reductions in oxidative stress markers.[199] Pal *et al.*[200] investigated the effects of holy basil at 150 mg/kg body weight in a rat model and observed amelioration of memory deficits and improved neurotransmitter levels.[200] Singh and Singh[201] reviewed various herbal remedies, including holy basil, and highlighted its traditional use for enhancing brain function. Although clinical evidence is sparse, the historical use of medicinal plants in traditional medicine aligns with the findings from preclinical studies.

3.18. Green tea

C. sinensis, another common medicinal plant also known as green tea, holds a long history in traditional medicine and is derived from its leaves. The observed positive effects are attributed to its rich content of polyphenolic compounds, especially catechins, such as epigallocatechin gallate (EGCG).[202] EGCG and other catechins in green tea neutralize free radicals, thereby reducing oxidative stress.[202] Furthermore, EGCG modulates inflammatory pathways by inhibiting pro-inflammatory cytokines.[203] Green tea compounds promote synaptic plasticity by increasing BDNF levels and enhancing cognitive function for learning and memory.[204] A previous study using an

AD cell model demonstrated the neuroprotective effects of EGCG and revealed that it effectively protects against Aβ-induced neurotoxicity.[205] EGCG reduces oxidative stress and prevents aggregation of Aβ plaques, suggesting the therapeutic benefits of green tea consumption in counteracting the development and progression of AD.[205] Kuriyama *et al.*[206] reported a strong association of regular green tea consumption with improved cognitive function and a reduced risk of cognitive decline in older adults.[206] Participants who regularly consumed green tea demonstrated better cognitive performance than those who did not, suggesting a possible role for green tea in delaying age-related cognitive decline.[206]

3.19. Stonebreaker

P. amarus, also known as stonebreaker or *ewe olobe* in Yoruba, is very common and widely used in African traditional medicine due to its array of health benefits.[207] Stonebreaker contains compounds, such as phyllanthin, hypophyllanthin, and flavonoids, with notable antioxidant, anti-inflammatory, and hepatoprotective properties, collectively suggesting its therapeutic potential.[208] The major phytochemical constituents of stonebreaker include the lignans, phyllanthin and hypophyllanthin, which have been associated with antioxidant effects and may help mitigate oxidative stress relevant to neurodegeneration.[208] Flavonoids also play a significant role in reducing oxidative damage and inflammation by inhibiting the production of ROS and pro-inflammatory cytokines.[209] Stonebreaker extract at a specific dose range modulates inflammatory pathways by suppressing NF-κB and mitigating inflammatory responses in rat models.[210] Rajeshkumar *et al.*[211] highlighted the plant's ability to alleviate cognitive deficits and oxidative damage in an AD rat model, based on assessed learning and memory capabilities and preservation of neuronal integrity.[211] Corroborating Rajeshkumar *et al.*[211] findings, Enogieru *et al.*[210] explored the neuroprotective and ameliorative effects of stonebreaker and demonstrated that stonebreaker extract provided significant protection against neurotoxicity induced by oxidative stress and inflammation, translating into improved cognitive function and reduced neuronal damage. Similarly, Iteire *et al.*[207] highlighted the antioxidative role of stonebreaker against potassium dichromate-induced neurotoxicity in rats. These culminating findings highlight the plant's potential as a promising therapeutic option in managing and preventing neurodegenerative diseases.[210] The clinical trials investigating the effects of stonebreaker on cognitive function, specifically AD, remain sparse. Although there is pre-clinical research evidence, there is a need for longitudinal clinical studies to assess its safety and the effective dose range in humans.

4. Future directions

There is a need to engage in application and research to address some of the identified gaps in ensuring notable progress in utilizing these plants in AD treatment. First, there is a need to standardize herbal extracts, considering associated factors that can cause variability, to ensure consistent and accurate concentrations of bioactive compounds in research methodology. During clinical trials, this will help ensure rigorous quality control measures in validating the efficacy and safety of these treatments. While preclinical studies have shown promising results, more extensive, well-designed clinical trials are needed to confirm the effectiveness of these herbal treatments in large human populations. Key parameters, including optimal dosages, treatment durations, and potential side effects, should be considered. As a future research direction, more studies (preclinical-to-clinical) should adopt a combination of herbal treatment with conventional AD treatment regimens at optimal safety dosages to enhance treatment efficacy and AD management. More importantly, there is a need to engage local communities and experienced users, who commonly use these plants for traditional medicine, to understand the cultural, spiritual, and ethical factors to be considered in the research design and development of treatments. Strengthening collaboration between traditional healers and researchers and respecting the perspectives of these indigenous people can aid the acceptance and well-aligned cultural use of these therapies.

In addition, creating ethical frameworks and guidelines that protect intellectual property rights and indigenous knowledge is critical for bridging the trust gap and aligning interests. These measures will safeguard African communities and the interests of traditional practitioners who possess this knowledge, thereby preventing the exploitation and misappropriation of their heritage. Several countries and organizations have initiated these processes by establishing guidelines for ethical research in traditional medicine that emphasizes benefit-sharing, informed consent, community involvement, and respect for cultural practices. We recommend implementing these guidelines in regions where they do not exist, as incorporating them into the research design will not only enhance the relevance of the findings but also provide a broader perspective that supports the integration of traditional therapies into healthcare. As these progress, there is a need to develop easy-to-understand regulatory guidelines for end-users and consumers on the use of herbal medicine for AD treatment, encompassing requests for approval of herbal treatments for safety and efficacy, and preserving intellectual property rights.

5. Conclusion

The African medicinal plants discussed in this review demonstrate several mechanisms for mitigating AD-associated pathologies, including cognitive enhancement, neuroprotection, and the reduction of AD-associated pathologies, such as Aβ plaques and tau hyperphosphorylation. Despite these promising results, the application of these herbal treatments in clinical settings remains limited. Regulatory challenges, variability in bioactive compound concentrations, standardized dosage, and the need for further rigorous clinical trials are significant hurdles that may need to be overcome. Nonetheless, the unique phytochemical properties of these plants offer a viable option to develop alternative therapies for AD, especially in regions where these medicinal plants are culturally accepted and readily available. To advance the field and address the limitations, there is a need for extensive clinical trials, development of frameworks and regulations, and consideration of contextual factors to incorporate culturally accepted and accessible therapies into research and healthcare applications. This will require further cooperation among researchers, policymakers, community residents, and traditional healers to fully harness the potential of African medicinal plants for the treatment of AD.

Acknowledgments

None.

Funding

None.

Conflict of interest

The authors declare that they have no competing interests.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

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