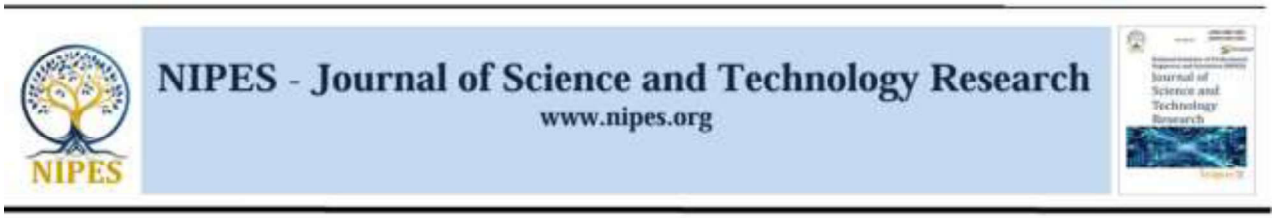
NIPES-Journal of Science and Technology, Research Vol. 7, Special Issue: Landmark University International Conference SEB4SDG 2025, pp. 733–749



Selected African Plants and their Alkaloids in the Management of Alzheimer's Diseases

Abimbola Peter Oluyori
Industrial Chemistry Programme
Department of Physical Sciences
Landmark University
Omu-Aran Kwara State, Nigeria
oluyori.abimbola@lmu.edu.ng

Adeola Tolulope Adewusi
Industrial Chemistry Programme
Department of Physical Sciences
Landmark University
Omu-Aran Kwara State, Nigeria
adewusi.adeola@lmu.edu.ng

Christiana Ajanaku
Industrial Chemistry Programme
Department of Physical Sciences
Landmark University
Omu-aran Kwara State, Nigeria
ajanaku.christiana@lmu.edu.ng

Abstract*—Alzheimer's disease is one of the most common Neurodegenerative diseases, which not only poses a serious burden on global health but also affects the quality of human life and cognitive functions. Changes in the personality, psychiatric issues, memory loss, speech and movement impairments characterize it. The precise root cause of Alzheimer's disease is yet unknown, but current drugs aim to target the β-amyloid protein, inhibit acetylcholinesterase and maintain neurotransmitter levels. However, most of these medications only manage the symptoms of Alzheimer's disease. Hence, the need for an alternative treatment that could effectively cure the disease. The therapeutic application of some medicinal plants has been found to be effective in the traditional medicine system for the treatment of various diseases. Studies revealed that many extracts from some African plants contain alkaloid bioactive compounds which showed a significant neuroprotective effect in inhibiting acetylcholinesterase enzymes and suppressing the formation of amyloid fibrils, which are major hallmarks of the disease. This present work seeks to appraise several studies on the efficacy of some selected African plant species, with a focus on the role of alkaloids in the treatment of Alzheimer's disease. Ethnopharmacological uses of these plants, their phytoconstituents and pharmacological potentials are extensively summarized.

***Keywords*— Alzheimer's disease, Alkaloids, Medicinal plants, Acetylcholinesterase inhibition, Phytochemical compounds**

https://doi.org/10.37933/nipes/7.4.2025.SI85
eISSN-2682-5821| pISSN-2734-2352

I. INTRODUCTION

Millions of individuals worldwide suffer from a diverse range of neurological conditions known as neurodegenerative diseases (NDDs). One of the most common neurological conditions is Alzheimer's Disease (AD), which accounts for 80 % of dementia cases in the elderly ones. Some of its common symptoms include progressive memory loss, learning difficulties, and a deterioration in behavior and function [1]. According to Alzheimer Disease International statistics in 2020, there are over 55 million people suffering from AD globally [2]. Although the major etiology of AD is still not known, its development is associated with the build-up of amyloid protein plaques in the brain, and this eventually results in the loss of neurons and synapses [3], [4]. During the course of AD, there is a significant loss of neurons, particularly cholinergic neurons, resulting in a decline in acetylcholine (ACh) levels [5]. Behavior, cognition, sensory, memory and/or motor function are all negatively impacted due to the loss of neurons and the breakdown of neural networks [6]. These disorders mainly impact neurons, which are the basic building blocks of the nervous system and brain. As a result, cognitive, motor, and emotional abilities gradually deteriorate.

There are currently few therapies for the treatment of AD, and most of the available treatment options only provide a temporal relief [7]. Rivastigmine, donepezil, galantamine and memantine (*Figure 1*) are some of the most approved cholinesterase inhibitors by the FDA- Food and Drug Administration- for use in AD's treatment, but further research is needed to ensure their long-term safety and tolerability [7]. Also, their usage is mostly effective during the early stages of the disease, and their administration is connected to side effects, including gastrointestinal problems [8], hence a need to search for alternative and safe options.

Alkaloids are a class of pharmacological phytochemicals and are nitrogen-containing compounds with diverse biological actions that qualify them for the potential treatment of AD. The structural features of some approved drugs for the treatment of AD contain alkaloidal moieties [9], as shown in ***Figure 1***. For

instance, Galantamine belongs to the family of isoquinoline alkaloids [10].

Hence, this study appraised some selected African plant species containing alkaloidal compounds with documented ethnopharmacological applications in the treatment of AD. The scientific investigation and confirmation of the neuroprotective capacity of these plant extracts will contribute to identifying natural compounds which may complement the current treatment options for AD.

II. Pathophysiology of Alzheimer's disease

The genetic, molecular, and cellular elements that play a major role in the pathology of AD are summarized in ***Figure 2***.

A. Aβ (Amyloid-beta) plaques

One of the major pathological characteristics of AD is the development of Aβ plaques in the extracellular space which are generated by the proteolytic cleavage of the amyloid precursor protein by Beta and gamma secretases [3]. As a result of excitotoxicity processes, calcium homeostasis failure, inflammation, and the depletion of energy and neural components, these Aβ plaques deposits are believed to cause neuronal shrinkage and death [11], [12].

B. Neurofibrillary tangles

Another common pathological characteristics of AD is the presence of neurofibrillary tangles which is due to intracellular changes. These are protein aggregates that are toxic to cells leading to neuronal death and also disrupting signaling across the cell body [13]. Neurofibrillary tangles form when tau protein builds up improperly inside neurons [14]. Microtubules are structures that help transfer chemicals and nutrients received from the cell body to the axon and dendrites and give internal support for healthy neurons [15]. In healthy neurons, tau protein usually connects with microtubules to keep them in good structure and maintain stability. However, abnormal chemical changes in AD cause tau protein to stick to other tau molecules and split from microtubules, and form threads that eventually aggregate to form tangles inside of the neurons [16]. By obstructing the transit, these tangles weaken the synaptic connection between neurons [17].

C. Decrease in level of acetylcholine

Acetylcholine (ACh) is a neurotransmitter, and its role is to relay messages from the body to the brain and again in the reverse direction – from the brain to the body. As one of the important excitatory neurotransmitters, it is involved in learning and memory as well as other cognitive functions. It is of relevant interest to discover that the central cholinergic nerve system has the ability to control the amount of ACh being produced and released in the nervous system [18]. Recent clinical data have shown that people diagnosed with AD display a substantial ACh decrease and neurodegeneration as a result of the degeneration of cholinergic neurons [19]. This specifically shows that the activity of Acetylcholine transferase is consequently reduced, and it gives a conclusion that AD patients have cholinergic system impairment [20]. One of the factors that significantly reduces the level of ACh is through an enzyme called Acetylcholinesterase (AChE), which hydrolyzes acetylcholine in producing choline as well as acetate [21].

D. Mitochondrial Dysfunction

Abnormality of signaling pathways of mitochondria could also cause the pathophysiology of AD since mitochondria are involved in many cellular and metabolic processes of the body, including neural synapses [22]. It is such a dysfunction that may lead to generating free radicals in the specified cells or cause oxidative stress and may further lead to neurodegeneration. The majority of research investigations conducted on age-related neurodegeneration suggest the central role of mitochondria and that cell death, which is mainly orchestrated by mitochondria, is prominent in neurodegeneration [23].

The main contributory factor for neurodegenerative diseases is aging, which is made worse by mitochondrial DNA mutations and oxidative stress [24]. Once the body suffers from mitochondrial dysfunction, it might easily be exposed to different pathogenic diseases, which could affect the proper functioning of the body system. Other consequences of mitochondrial abnormalities in AD include increased ROS generation, reduced ATP generation and activation of the apoptotic pathway that aggravate neuronal stress and premature cell death [25].

E. Neuroinflammation

Inflammation is an organism's response to the harm caused to the tissues by an external force such as pollution, microbial infection or chemical injury [26], and this inflammation results in cell death or damage of an organism. Neuroinflammation is a state of CNS activation in response to shifts in homeostasis due to both intrinsic and exogenous factors [27]. Studies revealed that inflammation performs a critical role in AD development. Neuroinflammation, or inflammation of the nervous system, is a complicated phenomenon that may have beneficial but harmful consequences on a range of neurological conditions [28]. Inflammation aids in damage containment, debris removal, and the start of the healing process initially, by acting as an inbuilt defensive mechanism in response to acute events like infections, trauma, or injuries, however, sustained neuroinflammation can be harmful in long-term settings since it can continue a cycle of neuronal degeneration and destruction [17]. Numerous damaging signals, including oxidative agents, redox iron, trauma, infection, tau oligomers, and Aβ, all seem to contribute to neuroinflammation [29].

The microglia cells are essential for maintaining CNS homeostasis [30]. They serve as the brain's initial line of defense and respond to abnormal situations by initiating a series of inflammatory reactions [31]. When pathogens or tissue damage are present, microglia trigger complicated immunological responses by upregulating the expression of proinflammatory mediators and toll-like receptors, thus activating the peripheral immune cells to restore tissue homeostasis [32]. Despite its neuroprotective characteristics, Microglia, when activated, can potentially worsen neuronal injury, persistent inflammatory responses, and progressive neurodegenerative disorders [33]. It

has recently come to light that activated microglia are crucial to the development of certain neurodegenerative diseases. They become active as a result of nerve damage, inflammation, or ischemia, which causes the protrusions to decrease and the cell body to grow [34]. Hence, the major cause of chronic neuro-inflammation is an overabundance of glial cells, such as microglia, becoming activated; these cells produce ROS, chemokines, and pro-inflammatory cytokines, which can exacerbate neuronal injury and cause gradual neurodegeneration [35].

III. Biological Mechanisms Contributing to the Etiology of Alzheimer's Disease

Aggregation and misfolding of proteins, excitotoxicity, oxidative stress, genetics, and environmental variables are some of the typical biological pathways that lead to Alzheimer's disease.

A. Protein Misfolding and Aggregation

The multisystem process of protein folding has important biological and molecular implications [36]. It is one of the major features common to several neurodegenerative illnesses. It appears that the aggregates are toxic cells, and the severity of NDDs increases with the degree of aggregation [37]. The most common proteins linked to the development of brain misfolded aggregates in NDDs are tau protein, TAR DNA-binding protein-43, amyloid-beta (Aβ), and alpha-synuclein [38]. Clinical research has revealed that tau protein and Aβ peptide are the primary players in the pathophysiology of AD due to their accumulation in the characteristic histopathological brain lesions, which include Aβ's senile plaques and tau protein's neurofibrillary tangles [39].

B. Oxidative Stress

Oxygen is a primary energy-producing mechanism necessary for all aerobic organisms. All living things, including brain cells engaged in tissue creation, depend on oxygen as their most essential component, but too much of it might be harmful [40]. Any disturbance in redox balance due to the generation of excessive ROS leads to oxidative stress. Due to its high oxygen need and large number of lipid cells that are sensitive to peroxidation, the brain is one of the organs that is most susceptible to the effects of ROS [41]. From earlier studies, it was postulated that oxidative stress is the underlying cause of the many neurodegenerative diseases [42]. The neurons are susceptible to oxidative stress due to their acute metabolic rate and inherently low antioxidant potential. Prolonged accumulation of ROS has been associated with neuronal cell death and dysfunction resulting from lipid peroxidation, protein oxidation and DNA damage [43], [44].

C. Genetic Factors

Most of the neurodegenerative diseases' origin has their roots in genetic disorders. Most patients with late-onset neurodegenerative diseases, including Alzheimer's, have multiple genetic susceptibility factors distributed across the genome and interactions between genetic and environmental factors [45], [46]. Early commencement of hereditary AD has been linked to mutations in Presenilin (PSEN1, & PSEN2) genes and the Amyloid precursor protein [47], [48].

D. Environmental Influences

Both human behavior and illness vulnerability may be influenced by interactions between genes and early environmental influences [49]. There are environmental variables that can increase the likelihood of acquiring neurodegenerative illnesses, including infections, exposure to neurotoxins, and lifestyle choices. One serious issue that has been connected to an increase in illness and death rates worldwide is environmental pollution. Air pollution is one of the primary causes of inflammation in the brain and lungs, which hinders the correct functioning of the central nervous system [50]. By inducing changes in blood-brain membrane permeability, neuronal inflammation, microglial cell activation, and oxidative stress, atmospheric pollutants may lead to CNS disease [51].

Similarly, serious effects of long-term exposure to heavy metal poisoning on the brain may lead to cognitive impairment and neurological disorders [52]. In line with the belief that many adult diseases have fetal origins, exposure to Lead during childhood development is an excellent example of an environmental pollutant that might operate as a risk factor to cause neurodegeneration [53]. Lead is well-known for its neurotoxic effects, although a clear correlation between its exposure and the development of AD has not been shown [54]. Lead might affect children's motor skills, IQ, speed processing, memory and cognitive abilities [54]. NDDs have also been associated with long-term exposure to transition metals, including zinc, copper, iron and manganese [55].

IV. Current Clinical Studies Against Alzheimer Disease

There are several clinical studies for early or preventative therapies based on the amyloid/tau theories as well as those that target various pathophysiologies of AD. Some approved anti-amyloid therapy includes, Lecanemab, Donanemab and Aducanumab [56]. The very effective immunoglobulin gamma 1 monoclonal antibody Aducanumab, often referred to as Aduhelm, binds to the N-terminus of Aβ fibrils and inhibits the production of amyloid [57]. Subsequent clinical trials with aducanumab showed amyloid reduction and were confirmed by an ad hoc analysis [58]. Furthermore, in terms of adverse consequences, certain research findings [59] have identified amyloid-related imaging abnormalities (ARIAs), which may be brought on by microbleeds caused by vasogenic edema of the brain. ARIAs need to be watched while treatment is being considered, and it is suggested that patients with microbleeds and probable amyloid angiopathy should not get treatment [60].

A humanized monoclonal antibody called donanemab is another therapy that might reduce amyloid deposits by identifying Aβ (3–42), which is present in amyloid plaques in aggregated form [61]. A positive decrease in the levels of

amyloid plaque was observed in 228 patients who received 10-40 mg/kg or 700-1400 mg of donanemab for 72 weeks in a clinical trial review [62]. Reduced buildup of total tau levels and less cognitive deterioration with donanemab was also observed in the patients [62]. Also, in the clinical trial conducted by [63], 6 of the 46 participants who received donanemab experienced some serious adverse events; while four of the six patients had non-drug-related events, one patient died from a myocardial infarction that was not connected to drugs, and one patient had intermittent symptomatic cerebral edema (ARIA-E).

Lecanemab, a humanized IgG1 antibody made from mAb158, binds to soluble Aβ protofibrils alone. In a clinical experiment, Lecanemab intravenous infusion dose of 10 mg/kg every 2 weeks significantly and dose-dependently reduced amyloid plaques from baseline to week 79 in 856 AD patients compared to the placebo group [56]. Some adverse effects that were reported in several AD patients from the previous clinical trials include ARIA with edema 'ARIA-E', ARIA with hemosiderin deposits 'ARIA-H', infusion-related reactions and atrial fibrillation [64], [65].

Conventional AD medications fall into two groups: N-methyl-D-aspartate receptor antagonists known as memantine, and AChE-inhibiting drugs which include donepezil, rivastigmine and galantamine [66]. AChE-inhibiting drugs increase postsynaptic activation and improve patients' cognitive and behavioral abilities [67]. Even though these medications have been used extensively, research is still being done to optimize dosage, dosage form, administration routes, and combination therapy in order to reduce side effects and maximize patient compliance.

A. Traditional use of African medicinal plants in Alzheimer's disease

The high cost of production, side effects, and low tolerability of some of the approved medications for the management of different symptoms of AD, coupled with the fact that the drugs only provide a symptomatic relief, points to the necessity for an alternative treatment option [68]. For thousands of years, nature has provided medical materials, and it has been discovered that an incredible proportion of contemporary drugs have natural origins [69]. For thousands of years, nature has provided medical ingredients, and it has been discovered that a staggering proportion of contemporary drugs have natural origins [70]. The numerous natural substances present in plants, which have long been used as traditional herbal medicines to treat a variety of ailments, including AD and certain other forms of neurodegenerative disorders, have impacted the design, discovery, and development of several innovative pharmaceuticals [71].

With its vast biodiversity resources, Africa is believed to have between 40,000 and 45,000 plant species, of which 5,000 are utilized medicinally and have been used in treating illnesses, including neurological disorders [72]. African socio-cultural legacy in traditional medicine involves therapeutic procedures that have existed for hundreds of years before modern medicine and are still widely used today, with evidence of little or no side effects [73]. Traditional medicine that has been embraced and practiced by other cultures different from the original culture is referred to as complementary or alternative medicine [74]. In many developing nations, plant materials constitute a primary source of natural medicines and are utilized to treat a variety of infectious and non-infectious ailments [75].

B. Alkaloidal compounds for Alzheimer's disease

Plants produce primary and secondary metabolites, which serve a variety of purposes. Amino acids, simple sugars, nucleic acids, and lipids are a few examples of primary metabolites, and these substances are necessary for cellular functions [76]. Plants use the secondary metabolites for unique purposes, including defense. These secondary metabolites also give plants their unique characteristics and therapeutic qualities.

Alkaloids are one of the biggest classes of bioactive compounds in natural plants. They belong to a class of basic, naturally occurring organic compound that contains one or more nitrogen atom in a heterocyclic ring [77]. Although alkaloids are mostly extracted from plants, they may also be found in fungi, animals and microbes [78]. Plants high in alkaloids, triterpenes, and flavonoids have been shown to improve cognitive function and stop acetylcholine from breaking down [79]. Among many other actions, alkaloids also demonstrated anti-neuroinflammatory, neuroprotective, antioxidant, anticancer, analgesic, antimicrobial, and antifungal properties [80], [81]. Because of their antioxidant properties, alkaloids may be able to contribute to AD treatment by addressing the oxidative stress pathway. By directly binding to neuro-receptors and/or interfering with neurotransmitter metabolism, alkaloids often function as agonists and antagonists to a range of neurotransmitters [82].

1) Natural Alkaloidal plants for Alzheimer's disease

Some African plants contain alkaloids and several other phytochemical constituents which are responsible for their biological activities. Alkaloids are bioactive compounds in many plant species, including *Adansonia digitate*, which is commonly known as Baobab [83], *Annona muricata,* commonly known as Soursop [84], etc., and these plants have reportedly shown a significant inhibition of α-amylase. The total alkaloid content of some African medicinal plants is compared with other phytochemical compounds as given in **Error! Reference source not found.**, and the total alkaloid is shown to be higher in most of the selected plants than the total phenolics and flavonoids. This suggested that the alkaloid content in the plants contributed significantly to the neuro-protective effects of the medicinal plants for the treatment of AD.

2) Synthetic Alkaloids for treatment of Alzheimer disease

In organic synthesis, alkaloids are crucial substances for producing synthetic and semi-synthetic medications that may have more biological activity than their parent molecules [85].

Galantamine is a semi-synthetic isoquinoline alkaloid, which belongs to the family of Amaryllidaceae, and it is one of the approved medications for AD treatment [5], [86]. It is derived from *Galanthus nivalis* flowers and bulbs. The synthetic pathway of Galantamine, as shown in ***Figure 3***, starts with the condensation of L-phenylalanine and L-tyrosine to form Norbelladine, which is the intermediate pathway for the synthesis of Galantamine [87].

V. Extraction and Isolation of Alkaloid compounds

A. Extraction of Alkaloid compounds

The extraction of alkaloids from African plants depends on the following factors: selected plant, the type of alkaloid to be isolated, the properties of the alkaloid, and the intended purpose. There are different techniques that could be employed for the extraction and isolation of alkaloids, and these are the traditional methods, such as solvent extraction, Soxhlet extraction, or cold maceration, and the modern methods [88]. Solvent extraction is one of the most frequently used traditional methods for the extraction of alkaloids from medicinal plants. The organic solvents commonly used for the extraction include methanol, ethanol or chloroform, and the procedure normally entails soaking the selected plant in the solvent for a particular period of time, followed by filtration and then evaporation of the solvent to collect the desired alkaloid. Soxhlet extraction is slightly different and far more efficient in this case, as the solvent flows through the plant material being extracted [89]. Maceration, or cold extraction, involves the use of plant material in which the solvent is allowed to stand with the material at room temperature for a longer time. This is less efficient than other methods but useful for heat sensitive alkaloids or small-scale extraction of the alkaloids. Even though these traditional methods are common techniques because they are easy to perform, their drawbacks include longer processing time, high energy consumption and much solvent required [90]. Targeted acid-base aided extraction techniques could result in direct extraction of alkaloidal phytochemicals which can improve the neurological outcomes of individuals with AD.

The modern methods include Microwave Assisted Extraction (MAE) and Ultrasound Assisted Extraction (UAE), and these methods have been showed to be faster, efficient are effective in terms of yield and purity [90], [91]. The choice of extraction technique is a function of the nature of the alkaloids and the level of purity desired in the extracted compound.

B. Purification and Isolation of Alkaloid compounds

Total alkaloid extracts contain mixtures of several alkaloids; hence, the isolation of a pure compound is necessary to obtain a monomer alkaloid. Several chromatographic techniques, which are column chromatography, TLC and HPLC, can be used to purify alkaloidal fractions [92]. Column chromatography is commonly used for the separation, and it can be carried out using alumina or silica gel as the stationary phase, with a suitable solvent for the separation of the individual alkaloids according to their polarity [93]. Thin-layer chromatography is employed to monitor the progress of the columns and to assay the purity of the isolated compound [94]. Selection of proper extraction solvents, the method of separation and purification of the isolated alkaloids is critically important in this process [95]. The isolated alkaloidal compounds, after purification, can be identified by mass spectrometry, Nuclear Magnetic Resonance, UV-visible, and infrared spectroscopy techniques to verify the pure compound.

Some isolated compounds from alkaloids have shown a significant neuroprotective effect against AD (***Figure 4***) [96], [97]. Carpaine and Solasodine are isolated alkaloidal compounds that have been selected as inhibitors against β-secretase, with binding energy of -9.4 kcal/mol and -9.0 kcal/mol respectively, which is better than the control drugs-galantamine and rivastigmine, with binding energy of -7.4 and -6.1 kcal/mol respectively [96]. Also, Vascinone and Vasicine are Pyrroloquinazoline alkaloids isolated from *Adhatoda vasica* leaves, which have binding energies of -6.98 and -6.62 kcal/mol respectively, and these compounds showed significant inhibition of AChE [97]. Geissoschizolline is an indole alkaloid isolated from *Geissospermum vellosii* plant, which showed a better energy affinity for AChE and BChE with binding energy of -8.4 and -9.4 kcal/mole respectively [98].

VI. Application of common African medicinal plants in the treatment of Alzheimer Disease

Many African plants (***Figure 5***) have been revealed to show a significant neuroprotective effects and higher AChE inhibitory activity, for the treatment of AD (

Table 2). These plants, particularly those belonging to the families of Fabaceae, Asteraceae, Anacardiaceae, Amaryllidaceae and Malvaceae, effectively acted as an Acetylcholinesterase (AChE) inhibitors, by helping to raise the duration and amounts of action of acetylcholine in the CNS or PNS, and preventing its usual breakdown into acetate and choline [5].

Future directions in Alzheimer disease management

The prospects of developing subsequent management procedures of AD seem bright due to recent discoveries and improved knowledge of how this disease functions. With the emergence of the disease associated with aging, research for improved treatment methods, preventive techniques, diagnostic procedures are increasing. One of the most significant areas of emphasis in the Alzheimer's treatment is the search for accurate clinical markers [99]. For example, amyloid PET (positron emission tomography) imaging and biomarkers in cerebrospinal fluid (CSF), as well as blood-based biomarkers, are assisting with identifying prevalent predictive prospective of early AD [100]. This suggests that early diagnosis of the disease makes a big difference in the change of its course.

Non-pharmacological interventions are also becoming a focus, especially as complements to pharmacotherapy. Physical activities, changes in diet, as social interaction should be encouraged to sharpen the brain and delay the effects of dementia [101]. Healthy dietary patterns and supplementation that have the benefits of antioxidants and omega-3 fatty acids are under research for their neurogenerative potential [102].

Future applications could target gene-environment interactions and diet and exercise plans suited to the unique patient.

CONCLUSION

Naturally produced alkaloids from African plants have been shown to be a potentially effective compound with significant neuroprotective activities for the treatment of AD. These bioactive compounds possess numerous pharmacological effects that target the major symptoms of AD, such as cholinergic dysfunction, reduced ACh, oxidative stress and neuroinflammation. Several African plants have been revealed to show immense AChE inhibition, neuroprotection, antioxidant and anti-inflammatory properties, thereby indicating the future prospect of these plants for the development of therapeutic agents in the treatment of AD. They could also be used to formulate effective novel medicines that target AD, with fewer side effects compared to the conventional treatment. However, more studies are required to explore the synergistic effects of these phytochemicals in combination with other phytochemicals such as phenolic compounds and flavonoids for the management of AD.

A. Tables

Table 1:Total Phytochemical Constituents of some African medicinal plants

Family	Plant species	Part used	Extraction method/ Duration	Solvent used	Total Alkaloids	Total Phenolics	Total Flavonoids	Activities	Reference
Fabaceae	*Crotalaria ochroleuca*	Leaves	Solvent extraction/24 hrs	Ethanol	4.92 ± 0.29 (49.2 ± 2.9 mg/g)*	13.72 ± 0.27 mg/g	11.00 ± 0.09 mg/g	Neuro-protective and antioxidant	[103], [104]
	Mucuna pruriens		Solvent extraction/48 hrs	Ethanol	15.03 mg/g	__	18.70 mg/g	Excellent anti-AChE activities	[105], [106]
	Senna obtusifolia	Leaves	Solvent extraction/24 hrs	Ethanol	2.83 ± 0.31 (28.3 ± 3.1 mg/g)*	27.93 ± 1.22 mg/g	14.94 ± 0.08 mg/g	Neuro-protective and antioxidant	[103], [107]
Asteraceae	*Vernonia amygdalina*	Leaves	Solvent extraction	Diethyl-ether	25.84 %	__	19.82 %	Excellent inhibition of AChE.enzymes	[108], [109]
Malvaceae	*Hibiscus cannabinus*	Leaves	Solvent extraction/ 24 hrs	Ethanol	5.04 ± 0.17 (50.4 ± 1.7 mg/g)*	25.97 ± 0.36 mg/g	14.13 ± 0.09 mg/g	AChE inhibition and antioxidant	[103], [110]
	Sida acuta	Leaves	Solvent extraction/ 48 hrs	Ethanol	5.17 ± 0.04 %	2.42 ± 0.56 %	12.49 ± 0.10 %	Cognitive enhancing activities	[111], [112]
	Corchorus olitorius	Leaves	Soxhlet / 18 hrs	Ethanol (70%)	23.4 ± 0.1 mg/g	5.28 ± 0.04 mg/g	11.68 ± 0.03 mg/g	Neuro-inflammation activity	[113], [114]
Anacardiaceae	*Lannea discolor*	Stem barks	Solvent extraction/ 72 hrs	Methanol	215.1 ± 12.45 mg/g	53.78 ± 5.13 mg/g	16.68 ± 0.11 mg/g	Excellent antioxidant	[115], [116]

	Spondias mombin	Leaves	Cold maceration/ 48 hrs	Ethanol	169.42 mg/g	218.06 mg/g	144.34 mg/g	Excellent inhibition of AChE enzymes	[117], [118]
Moringaceae	*Moringa oleifera*	Stem barks	Solvent extraction/ 72 hrs	Methanol	128.2 ± 3.42 mg/ g	26.06 ± 1.32 mg/ g	12.34 ± 1.32 mg/ g	AChE inhibition, neuroprotective and antioxidant	[115], [119]
Zingiberaceae	*Curcuma longa*	Rhizome	Solvent extraction/ 24 hrs	Methanol	0.273 ± 0.004 mg/ g	1.71 ± 0.043 mg/ g	13.90 ± 0.05 mg/ g	A potential anti-AD drug and neuroprotective effects	[120], [121]

( )* Converted values from g/100g to mg/g

Table 2: Ethno-neuropharmacological activities and Anti-neurodegenerative effects of some African plants

Family	**Species Name**	**Parts used**	**Extraction solvent / Time**	**Results**	**Reference**
Fabaceae	*Mucuna pruriens*	Seeds Leaves	Methanol / 48 hrs	A reduction in phosphorylated tau proteins level. An excellent neuroprotective effect. Excellent anti-AChE activities with IC_{50} = 508.20 µg/mL	[122] [106]
	Albizia adianthifolia	Leaf	Methanol (M), chloroform (C), ethyl acetate (EA), and N-hexane (NH),	Excellent inhibitory effect of AChE activity with IC_{50} values of; M = 11.80 ± 0.88 µg/mL C = 17.44 ± 1.74 µg/mL EA = 10.04 ± 1.67 µg/mL NH = 124.38 ± 1.51 µg/mL	[123], [124]

Asteraceae	*Dichrocephala integrifolia*	Leaf	Distilled water	Significant inhibitory effects of AChE activity. Improvement in spatial short-term and long-term memory, by counteracting memory impairment induced by scopolamine. Excellent neuroprotective effects	[125]
	Tithonia diversifolia	Leaf	Methanol	Effective inhibition of AChE activity with IC_{50} of 39.27 µg/mL Significant antioxidant activities	[126]
Anacardiaceae	*Spondias mombin*	Fruits Leaves	Ethanol / 24 hrs Ethyl acetate	Increase in cognitive performance in mice with scopolamine induced memory impairment. Excellent decrease in the activity of AChE enzymes in mice brains Excellent inhibition of AChE enzymes with % inhibition of 58.10 ± 1.08 %	[127] [118]
Amaryllidaceae	*Crinum asiaticum*	Seed	Ethanol	Significant inhibitory effect of AChE activity, and AD pathogenesis. Excellent prevention of neuronal cell death. Anti-neuroinflammation and neuroprotection	[128]
	Boophone disticha	Bulb	Methanol	Excellent Neuroprotective effects against Methyl-4-phenylpyridinium (MPP) neuro-toxicity	[129]
Scrophulariaceae/ Plantaginaceae	*Scoparia dulcis*	Plant	Ethanol	Anti-inflammatory, neuroprotective and antioxidant properties	[130]
Lamiaceae	*Ocimum gratissimum*	Leaves	Hydromethanol	Excellent improvement in cognitive functions by the inhibition of AChE	[131]
Malvaceae	*Corchorus olitorius*	Leaf	Distilled water	Significant improvement in neurodegeneration and cognitive loss by reducing neuroinflammation activity	[114]

	Cola acuminata	Leaves	Distilled water	Significant inhibition of AChE activity and enhance cholinergic function	[132]

B. Figures

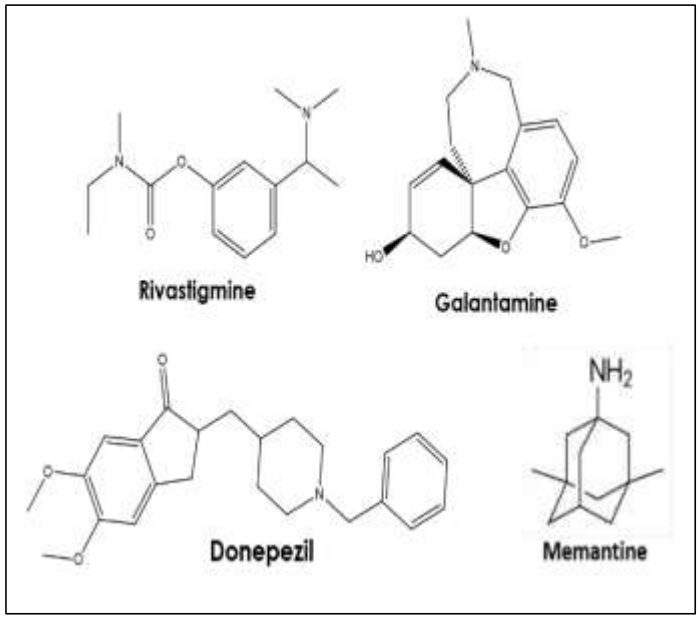


Figure 1. Structures of the approved drug that targets Alzheimer's disease

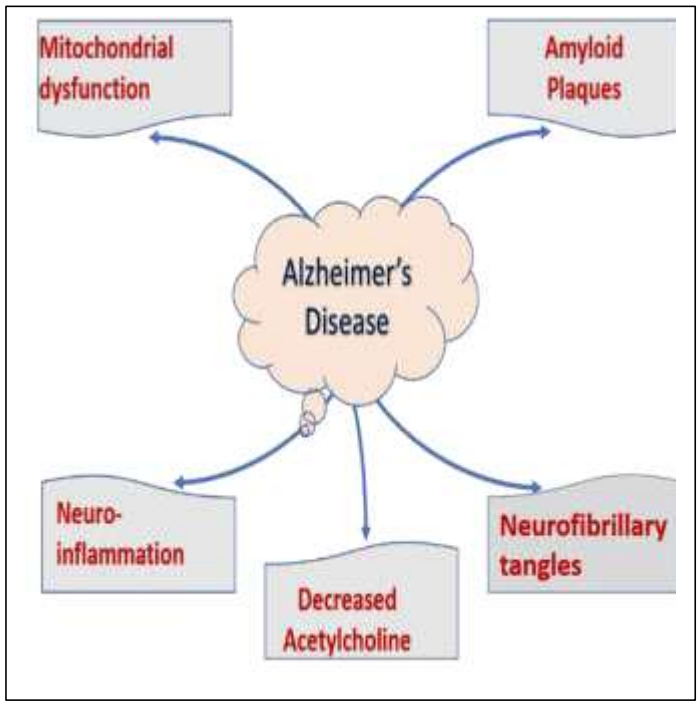


Figure 2. Major Alzheimer's disease Pathophysiology

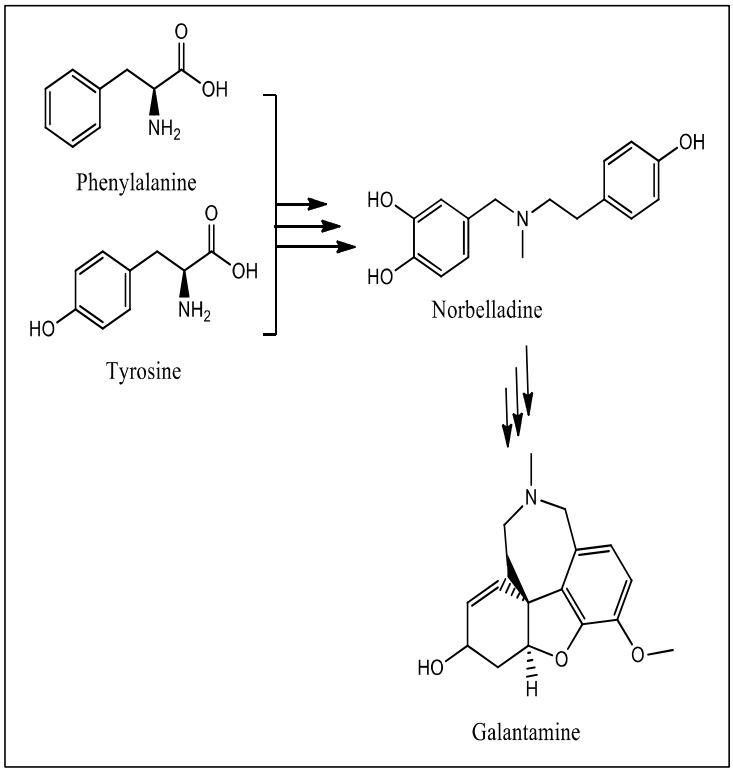


Figure 3. Synthetic pathway of Galantamine

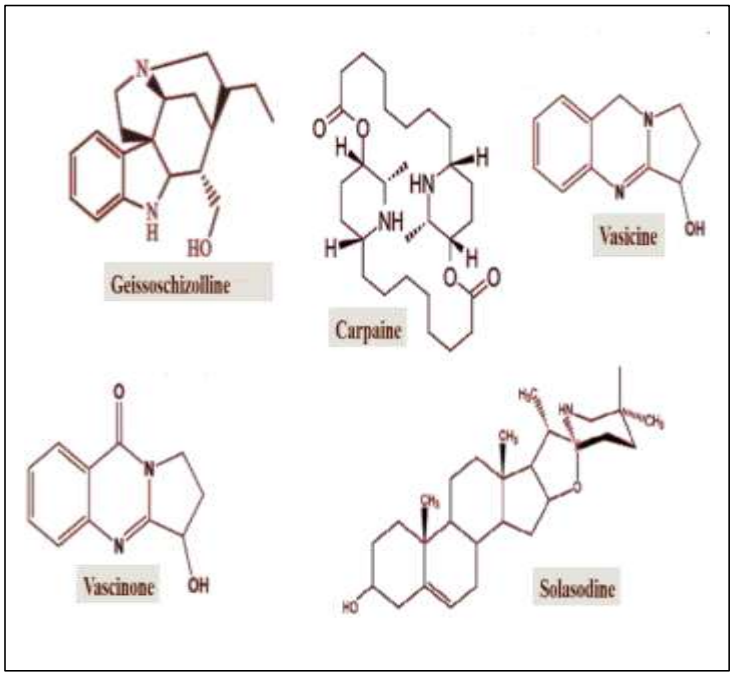


Figure 4. Isolated compounds from alkaloids

Figure 5. African medicinal plants with neuroprotective effects and ethno-neuropharmacological activities.

REFERENCES

[1] F. Durães, M. Pinto, and E. Sousa, "Old Drugs as New Treatments for Neurodegenerative Diseases.," *Pharmaceuticals (Basel)*, vol. 11, no. 2, May 2018, doi: 10.3390/ph11020044.

[2] ADI, "2020 Alzheimer's disease facts and figures," *Alzheimer's & Dementia*, vol. 16, no. 3, pp. 391–460, Mar. 2020, doi: 10.1002/alz.12068.

[3] H. Hampel *et al.*, "The Amyloid-β Pathway in Alzheimer's Disease," *Mol Psychiatry*, vol. 26, no. 10, pp. 5481–5503, Oct. 2021, doi: 10.1038/s41380-021-01249-0.

[4] O. A. Ojo *et al.*, "Deciphering the Interactions of Bioactive Compounds in Selected Traditional Medicinal Plants against Alzheimer's Diseases via Pharmacophore Modeling, Auto-QSAR, and Molecular Docking Approaches," *Molecules*, vol. 26, no. 7, p. 1996, Apr. 2021, doi: 10.3390/molecules26071996.

[5] G. Marucci, M. Buccioni, D. D. Ben, C. Lambertucci, R. Volpini, and F. Amenta, "Efficacy of acetylcholinesterase inhibitors in Alzheimer's disease," *Neuropharmacology*, vol. 190, p. 108352, Jun. 2021, doi: 10.1016/j.neuropharm.2020.108352.

[6] D. M. Wilson, M. R. Cookson, L. Van Den Bosch, H. Zetterberg, D. M. Holtzman, and I. Dewachter, "Hallmarks of neurodegenerative diseases," *Cell*, vol. 186, no. 4, pp. 693–714, Feb. 2023, doi: 10.1016/j.cell.2022.12.032.

[7] Y. Peng *et al.*, "Current and future therapeutic strategies for Alzheimer's disease: an overview of drug development bottlenecks," *Front Aging Neurosci*, vol. 15, Aug. 2023, doi: 10.3389/fnagi.2023.1206572.

[8] V. L. B. França, E. M. Bezerra, R. F. da Costa, H. F. Carvalho, V. N. Freire, and G. Matos, "Alzheimer's Disease Immunotherapy and Mimetic Peptide Design for Drug Development: Mutation Screening, Molecular Dynamics, and a Quantum Biochemistry Approach Focusing on Aducanumab::Aβ2–7 Binding Affinity," *ACS Chem Neurosci*, vol. 15, no. 19, pp. 3543–3562, Oct. 2024, doi: 10.1021/acschemneuro.4c00453.

[9] G. R. Sridhar, "Acetylcholinesterase inhibitors (Galantamine, Rivastigmine, and Donepezil)," in *NeuroPsychopharmacotherapy*, Cham: Springer International Publishing, 2021, pp. 1–13. doi: 10.1007/978-3-319-56015-1_418-1.

[10] V. Rathi, "Galantamine," in *Naturally Occurring Chemicals Against Alzheimer's Disease*, Elsevier, 2021, pp. 83–92. doi: 10.1016/B978-0-12-819212-2.00006-2.

[11] M. V. F. Silva, C. de M. G. Loures, L. C. V. Alves, L. C. de Souza, K. B. G. Borges, and M. das G. Carvalho, "Alzheimer's disease: risk factors and potentially protective measures," *J Biomed Sci*, vol. 26, no. 1, p. 33, Dec. 2019, doi: 10.1186/s12929-019-0524-y.

[12] A. P. Oluyori, A. A. Inyinbor, C. O. Aremu, O. O. Osemwegie, A. Oluwafemi, and T. A. Ogunnupebi, "Diseases Induced by Heavy Metal Exposure and their Ameliorative Phytochemicals: A Review," *Tropical Journal of Natural Product Research*, vol. 4, no. 9, pp. 479–489, Oct. 2020, doi: 10.26538/tjnpr/v4i9.1.

[13] A. E. Oxford, E. S. Stewart, and T. T. Rohn, "Clinical Trials in Alzheimer's Disease: A Hurdle in the Path of Remedy," *Int J Alzheimers Dis*, vol. 2020, pp. 1–13, Apr. 2020, doi: 10.1155/2020/5380346.

[14] S. Ahmed *et al.*, "Potential therapeutic natural products against Alzheimer's disease with Reference of Acetylcholinesterase," *Biomedicine & Pharmacotherapy*, vol. 139, p. 111609, Jul. 2021, doi: 10.1016/j.biopha.2021.111609.

[15] G. A. Mihailoff and D. E. Haines, "The Cell Biology of Neurons and Glia," in *Fundamental Neuroscience for Basic and Clinical Applications*, Elsevier, 2018, pp. 15-33.e1. doi: 10.1016/B978-0-323-39632-5.00002-5.

[16] J. Sharifi-Rad *et al.*, "Multi-Target Mechanisms of Phytochemicals in Alzheimer's Disease: Effects on Oxidative Stress, Neuroinflammation and Protein Aggregation," *J Pers Med*, vol. 12, no. 9, p. 1515, Sep. 2022, doi: 10.3390/jpm12091515.

[17] P. M. Giri, A. Banerjee, A. Ghosal, and B. Layek, "Neuroinflammation in Neurodegenerative Disorders: Current Knowledge and Therapeutic Implications," *Int J Mol Sci*, vol. 25, no. 7, p. 3995, Apr. 2024, doi: 10.3390/ijms25073995.

[18] I. Muramatsu *et al.*, "A New Aspect of Cholinergic Transmission in the Central Nervous System," in *Nicotinic Acetylcholine Receptor Signaling in Neuroprotection*, Singapore: Springer Singapore, 2018, pp. 45–58. doi: 10.1007/978-981-10-8488-1_3.

[19] Z.-R. Chen, J.-B. Huang, S.-L. Yang, and F.-F. Hong, "Role of Cholinergic Signaling in Alzheimer's Disease," *Molecules*, vol. 27, no. 6, p. 1816, Mar. 2022, doi: 10.3390/molecules27061816.

[20] N. Halder and G. Lal, "Cholinergic System and Its Therapeutic Importance in Inflammation and Autoimmunity," *Front Immunol*, vol. 12, Apr. 2021, doi: 10.3389/fimmu.2021.660342.

[21] R. Basnet, S. Khadka, B. B. Basnet, and R. Gupta, "Perspective on Acetylcholinesterase: A Potential Target for Alzheimer's Disease Intervention," *Curr Enzym Inhib*, vol. 16, no. 3, pp. 181–188, Nov. 2020, doi: 10.2174/1573408016999200801021329.

[22] R. Dhapola, P. Sarma, B. Medhi, A. Prakash, and D. H. Reddy, "Recent Advances in Molecular Pathways and Therapeutic Implications Targeting Mitochondrial Dysfunction for Alzheimer's Disease," *Mol Neurobiol*, vol. 59, no. 1, pp. 535–555, Jan. 2022, doi: 10.1007/s12035-021-02612-6.

[23] S. Xu *et al.*, "Role of Mitochondria in Neurodegenerative Diseases: From an Epigenetic Perspective," *Front Cell Dev Biol*, vol. 9, Aug. 2021, doi: 10.3389/fcell.2021.688789.

[24] F. A. Bustamante-Barrientos *et al.*, "Mitochondrial dysfunction in neurodegenerative disorders: Potential therapeutic application of mitochondrial transfer to central nervous system-residing cells," *J Transl Med*, vol. 21, no. 1, p. 613, Sep. 2023, doi: 10.1186/s12967-023-04493-w.

[25] A. Misrani, S. Tabassum, and L. Yang, "Mitochondrial Dysfunction and Oxidative Stress in Alzheimer's Disease," *Front Aging Neurosci*, vol. 13, Feb. 2021, doi: 10.3389/fnagi.2021.617588.

[26] E. E. Elgorashi and L. J. McGaw, "African plants with in vitro anti-inflammatory activities: A review," *South African Journal of Botany*, vol. 126, pp. 142–169, Nov. 2019, doi: 10.1016/j.sajb.2019.06.034.

[27] I. O. Owemidu, A. M. Ajayi, and S. A. Onasanwo, "Anti-neuroinflammatory properties of Waltheria americana L. leaf

in experimental animals," *Phytomedicine Plus*, vol. 2, no. 1, p. 100217, Feb. 2022, doi: 10.1016/j.phyplu.2022.100217.

[28] A. Adamu, S. Li, F. Gao, and G. Xue, "The role of neuroinflammation in neurodegenerative diseases: current understanding and future therapeutic targets," *Front Aging Neurosci*, vol. 16, Apr. 2024, doi: 10.3389/fnagi.2024.1347987.

[29] L. Guzman-Martinez, R. B. Maccioni, V. Andrade, L. P. Navarrete, M. G. Pastor, and N. Ramos-Escobar, "Neuroinflammation as a Common Feature of Neurodegenerative Disorders," *Front Pharmacol*, vol. 10, Sep. 2019, doi: 10.3389/fphar.2019.01008.

[30] G. Gelders, V. Baekelandt, and A. Van der Perren, "Linking Neuroinflammation and Neurodegeneration in Parkinson's Disease," *J Immunol Res*, vol. 2018, pp. 1–12, 2018, doi: 10.1155/2018/4784268.

[31] W. Zhang *et al.*, "Microglia-associated neuroinflammation is a potential therapeutic target for ischemic stroke.," *Neural Regen Res*, vol. 16, no. 1, pp. 6–11, Jan. 2021, doi: 10.4103/1673-5374.286954.

[32] J. Qin, Z. Ma, X. Chen, and S. Shu, "Microglia activation in central nervous system disorders: A review of recent mechanistic investigations and development efforts," *Front Neurol*, vol. 14, Mar. 2023, doi: 10.3389/fneur.2023.1103416.

[33] C. A. Butler, A. S. Popescu, E. J. A. Kitchener, D. H. Allendorf, M. Puigdellívol, and G. C. Brown, "Microglial phagocytosis of neurons in neurodegeneration, and its regulation," *J Neurochem*, vol. 158, no. 3, pp. 621–639, Aug. 2021, doi: 10.1111/jnc.15327.

[34] K. Nakaso, "Roles of Microglia in Neurodegenerative Diseases," *Yonago Acta Med*, vol. 67, no. 1, p. 2024.02.001, 2024, doi: 10.33160/yam.2024.02.001.

[35] W. Zhang, D. Xiao, Q. Mao, and H. Xia, "Role of neuroinflammation in neurodegeneration development," *Signal Transduct Target Ther*, vol. 8, no. 1, p. 267, Jul. 2023, doi: 10.1038/s41392-023-01486-5.

[36] J. Gandhi *et al.*, "Protein misfolding and aggregation in neurodegenerative diseases: a review of pathogeneses, novel detection strategies, and potential therapeutics," *Rev Neurosci*, vol. 30, no. 4, pp. 339–358, May 2019, doi: 10.1515/revneuro-2016-0035.

[37] O. Koszła and P. Sołek, "Misfolding and aggregation in neurodegenerative diseases: protein quality control machinery as potential therapeutic clearance pathways," *Cell Communication and Signaling*, vol. 22, no. 1, p. 421, Aug. 2024, doi: 10.1186/s12964-024-01791-8.

[38] C. Soto and S. Pritzkow, "Protein misfolding, aggregation, and conformational strains in neurodegenerative diseases.," *Nat Neurosci*, vol. 21, no. 10, pp. 1332–1340, Oct. 2018, doi: 10.1038/s41593-018-0235-9.

[39] W. Gulisano *et al.*, "Role of Amyloid-β and Tau Proteins in Alzheimer's Disease: Confuting the Amyloid Cascade.," *J Alzheimers Dis*, vol. 64, no. s1, pp. S611–S631, 2018, doi: 10.3233/JAD-179935.

[40] A. Singh, R. Kukreti, L. Saso, and S. Kukreti, "Oxidative Stress: A Key Modulator in Neurodegenerative Diseases," *Molecules*, vol. 24, no. 8, p. 1583, Apr. 2019, doi: 10.3390/molecules24081583.

[41] M. Sharifi-Rad *et al.*, "Lifestyle, Oxidative Stress, and Antioxidants: Back and Forth in the Pathophysiology of Chronic Diseases," *Front Physiol*, vol. 11, Jul. 2020, doi: 10.3389/fphys.2020.00694.

[42] E. O. Olufunmilayo, M. B. Gerke-Duncan, and R. M. D. Holsinger, "Oxidative Stress and Antioxidants in Neurodegenerative Disorders," *Antioxidants*, vol. 12, no. 2, p. 517, Feb. 2023, doi: 10.3390/antiox12020517.

[43] S. Afzal, A. S. Abdul Manap, A. Attiq, I. Albokhadaim, M. Kandeel, and S. M. Alhojaily, "From imbalance to impairment: the central role of reactive oxygen species in oxidative stress-induced disorders and therapeutic exploration.," *Front Pharmacol*, vol. 14, p. 1269581, 2023, doi: 10.3389/fphar.2023.1269581.

[44] G. O. Egharevba *et al.*, "Antidiabetic, antioxidant and antimicrobial activities of extracts of Tephrosia bracteolata leaves," *Heliyon*, vol. 5, no. 8, p. e02275, Aug. 2019, doi: 10.1016/j.heliyon.2019.e02275.

[45] N. S. Ogonowski, L. M. García-Marín, A. S. Fernando, V. Flores-Ocampo, and M. E. Rentería, "Impact of genetic predisposition to late-onset neurodegenerative diseases on early life outcomes and brain structure," *Transl Psychiatry*, vol. 14, no. 1, p. 185, Apr. 2024, doi: 10.1038/s41398-024-02898-9.

[46] J.-C. García and R.-H. Bustos, "The Genetic Diagnosis of Neurodegenerative Diseases and Therapeutic Perspectives," *Brain Sci*, vol. 8, no. 12, p. 222, Dec. 2018, doi: 10.3390/brainsci8120222.

[47] M. Quan, S. Cao, Q. Wang, S. Wang, and J. Jia, "Genetic Phenotypes of Alzheimer's Disease: Mechanisms and Potential Therapy," *Phenomics*, vol. 3, no. 4, pp. 333–349, Aug. 2023, doi: 10.1007/s43657-023-00098-x.

[48] V. Van Giau, E. Bagyinszky, Y. S. Yang, Y. C. Youn, S. S. A. An, and S. Y. Kim, "Genetic analyses of early-onset Alzheimer's disease using next generation sequencing," *Sci Rep*, vol. 9, no. 1, p. 8368, Jun. 2019, doi: 10.1038/s41598-019-44848-2.

[49] G. Esposito, A. Azhari, and J. L. Borelli, "Gene × Environment Interaction in Developmental Disorders: Where Do We Stand and What's Next?," *Front Psychol*, vol. 9, Oct. 2018, doi: 10.3389/fpsyg.2018.02036.

[50] H. Kim, W.-H. Kim, Y.-Y. Kim, and H.-Y. Park, "Air Pollution and Central Nervous System Disease: A Review of the Impact of Fine Particulate Matter on Neurological Disorders," *Front Public Health*, vol. 8, Dec. 2020, doi: 10.3389/fpubh.2020.575330.

[51] M. Nabi and N. Tabassum, "Role of Environmental Toxicants on Neurodegenerative Disorders," *Frontiers in Toxicology*, vol. 4, May 2022, doi: 10.3389/ftox.2022.837579.

[52] R. H. Althomali *et al.*, "Exposure to heavy metals and neurocognitive function in adults: a systematic review," *Environ Sci Eur*, vol. 36, no. 1, p. 18, Jan. 2024, doi: 10.1186/s12302-024-00843-7.

[53] A. C. Olufemi, A. Mji, and M. S. Mukhola, "Potential Health Risks of Lead Exposure from Early Life through Later Life: Implications for Public Health Education.," *Int J Environ Res Public Health*, vol. 19, no. 23, Nov. 2022, doi: 10.3390/ijerph192316006.

[54] D. Ramírez Ortega *et al.*, "Cognitive Impairment Induced by Lead Exposure during Lifespan: Mechanisms of Lead Neurotoxicity," *Toxics*, vol. 9, no. 2, p. 23, Jan. 2021, doi: 10.3390/toxics9020023.

[55] H. Wang, F. Yang, S. Zhang, R. Xin, and Y. Sun, "Genetic and environmental factors in Alzheimer's and Parkinson's diseases and promising therapeutic intervention via fecal microbiota transplantation," *NPJ Parkinsons Dis*, vol. 7, no. 1, p. 70, Aug. 2021, doi: 10.1038/s41531-021-00213-7.

[56] L.-K. Huang, Y.-C. Kuan, H.-W. Lin, and C.-J. Hu, "Clinical trials of new drugs for Alzheimer disease: a 2020–2023 update," *J Biomed Sci*, vol. 30, no. 1, p. 83, Oct. 2023, doi: 10.1186/s12929-023-00976-6.

[57] J. Moini, A. Logalbo, and J. G. Schnellmann, "Pharmacology of Alzheimer's disease," in *Neuropsychopharmacology*, Elsevier, 2023, pp. 275–286. doi: 10.1016/B978-0-323-95974-2.00003-7.

[58] K. Wojtunik-Kulesza, M. Rudkowska, and A. Orzeł-Sajdłowska, "Aducanumab—Hope or Disappointment for Alzheimer's Disease," *Int J Mol Sci*, vol. 24, no. 5, p. 4367, Feb. 2023, doi: 10.3390/ijms24054367.

[59] S. Budd Haeberlein *et al.*, "Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease," *J Prev Alzheimers Dis*, 2022, doi: 10.14283/jpad.2022.30.

[60] M.-K. Sin, E. Zamrini, A. Ahmed, K. Nho, and I. Hajjar, "Anti-Amyloid Therapy, AD, and ARIA: Untangling the Role of CAA.," *J Clin Med*, vol. 12, no. 21, Oct. 2023, doi: 10.3390/jcm12216792.

[61] T. A. Bayer, "Pyroglutamate Aβ cascade as drug target in Alzheimer's disease," *Mol Psychiatry*, vol. 27, no. 4, pp. 1880–1885, Apr. 2022, doi: 10.1038/s41380-021-01409-2.

[62] A. Rashad *et al.*, "Donanemab for Alzheimer's Disease: A Systematic Review of Clinical Trials.," *Healthcare (Basel)*, vol. 11, no. 1, Dec. 2022, doi: 10.3390/healthcare11010032.

[63] S. L. Lowe *et al.*, "Donanemab (LY3002813) Phase 1b Study in Alzheimer's Disease: Rapid and Sustained Reduction of Brain Amyloid Measured by Florbetapir F18 Imaging," *Journal of Prevention of Alzheimer's Disease*, pp. 1–11, 2021, doi: 10.14283/jpad.2021.56.

[64] L. S. Honig *et al.*, "Updated safety results from phase 3 lecanemab study in early Alzheimer's disease," *Alzheimers Res Ther*, vol. 16, no. 1, p. 105, May 2024, doi: 10.1186/s13195-024-01441-8.

[65] Y. Qiao, Y. Chi, Q. Zhang, and Y. Ma, "Safety and efficacy of lecanemab for Alzheimer's disease: a systematic review and meta-analysis of randomized clinical trials," *Front Aging Neurosci*, vol. 15, May 2023, doi: 10.3389/fnagi.2023.1169499.

[66] D.-D. Li, Y.-H. Zhang, W. Zhang, and P. Zhao, "Meta-Analysis of Randomized Controlled Trials on the Efficacy and Safety of Donepezil, Galantamine, Rivastigmine, and Memantine for the Treatment of Alzheimer's Disease," *Front Neurosci*, vol. 13, May 2019, doi: 10.3389/fnins.2019.00472.

[67] G. Marucci, M. Buccioni, D. D. Ben, C. Lambertucci, R. Volpini, and F. Amenta, "Efficacy of acetylcholinesterase inhibitors in Alzheimer's disease," *Neuropharmacology*, vol. 190, p. 108352, Jun. 2021, doi: 10.1016/j.neuropharm.2020.108352.

[68] R. N. L. Lamptey, B. Chaulagain, R. Trivedi, A. Gothwal, B. Layek, and J. Singh, "A Review of the Common Neurodegenerative Disorders: Current Therapeutic Approaches and the Potential Role of Nanotherapeutics," *Int J Mol Sci*, vol. 23, no. 3, p. 1851, Feb. 2022, doi: 10.3390/ijms23031851.

[69] N. Chaachouay and L. Zidane, "Plant-Derived Natural Products: A Source for Drug Discovery and Development," *Drugs and Drug Candidates*, vol. 3, no. 1, pp. 184–207, Feb. 2024, doi: 10.3390/ddc3010011.

[70] N. Chaachouay and L. Zidane, "Plant-Derived Natural Products: A Source for Drug Discovery and Development," *Drugs and Drug Candidates*, vol. 3, no. 1, pp. 184–207, Feb. 2024, doi: 10.3390/ddc3010011.

[71] N. Nasim, I. S. Sandeep, and S. Mohanty, "Plant-derived natural products for drug discovery: current approaches and prospects," *The Nucleus*, vol. 65, no. 3, pp. 399–411, Dec. 2022, doi: 10.1007/s13237-022-00405-3.

[72] E. Mshelia Halilu, "Cultivation and Conservation of African Medicinal Plants for Pharmaceutical Research and Socio-Economic Development," in *Medicinal Plants*, IntechOpen, 2022. doi: 10.5772/intechopen.102637.

[73] V. N. L. C. Motamarri, H. Gebremariam Baye, H. Saad Ali, and F. Belayneh Usamo, "Traditional African Medicine," in *Natural Medicinal Plants*, IntechOpen, 2022. doi: 10.5772/intechopen.96576.

[74] S. Goswami, A. Ali, M. E. Prasad, and P. Singh, "Pharmacological significance of Catharanthus roseus in cancer management: A review," *Pharmacological Research - Modern Chinese Medicine*, vol. 11, p. 100444, Jun. 2024, doi: 10.1016/j.prmcm.2024.100444.

[75] I. B. Abubakar *et al.*, "Traditional medicinal plants used for treating emerging and re-emerging viral diseases in northern Nigeria," *Eur J Integr Med*, vol. 49, p. 102094, Jan. 2022, doi: 10.1016/j.eujim.2021.102094.

[76] I. P. Ejidike *et al.*, "Phytochemical Constituents of Biological Prominence from Medicinal Plants as Therapeutic agents in Disease Treatment," *Anchor University Journal of Science and Technology*, vol. 2, no. 2, pp. 89–114, 2022.

[77] M.-J. U. Ferreira, "Alkaloids in Future Drug Discovery," *Molecules*, vol. 27, no. 4, p. 1347, Feb. 2022, doi: 10.3390/molecules27041347.

[78] P. Dey *et al.*, "Analysis of alkaloids (indole alkaloids, isoquinoline alkaloids, tropane alkaloids)," in *Recent Advances in Natural Products Analysis*, Elsevier, 2020, pp. 505–567. doi: 10.1016/B978-0-12-816455-6.00015-9.

[79] D. O. Kennedy, "Phytochemicals for Improving Aspects of Cognitive Function and Psychological State Potentially Relevant to Sports Performance," *Sports Medicine*, vol. 49, no. S1, pp. 39–58, Feb. 2019, doi: 10.1007/s40279-018-1007-0.

[80] B. Aryal *et al.*, "Potential Therapeutic Applications of Plant-Derived Alkaloids against Inflammatory and Neurodegenerative Diseases," *Evidence-Based Complementary and Alternative Medicine*, vol. 2022, pp. 1–18, Mar. 2022, doi: 10.1155/2022/7299778.

[81] R. Bai *et al.*, "Discovery of natural anti-inflammatory alkaloids: Potential leads for the drug discovery for the treatment of inflammation," *Eur J Med Chem*, vol. 213, p. 113165, Mar. 2021, doi: 10.1016/j.ejmech.2021.113165.

[82] G. Hussain *et al.*, "Role of Plant Derived Alkaloids and Their Mechanism in Neurodegenerative Disorders," *Int J Biol Sci*, vol. 14, no. 3, pp. 341–357, 2018, doi: 10.7150/ijbs.23247.

[83] M. L. Silva, K. Rita, M. A. Bernardo, M. F. de Mesquita, A. M. Pintão, and M. Moncada, "Adansonia digitata L. (Baobab) Bioactive Compounds, Biological Activities, and the Potential Effect on Glycemia: A Narrative Review.,"

Nutrients, vol. 15, no. 9, May 2023, doi: 10.3390/nu15092170.

[84] M. T. Nguyen *et al.*, "Determination of the phytochemical screening, total polyphenols, flavonoids content, and antioxidant activity of soursop leaves (Annona muricata Linn.)," *IOP Conf Ser Mater Sci Eng*, vol. 736, no. 6, p. 062011, Jan. 2020, doi: 10.1088/1757-899X/736/6/062011.

[85] S.-K. Daley and G. A. Cordell, "Alkaloids in Contemporary Drug Discovery to Meet Global Disease Needs.," *Molecules*, vol. 26, no. 13, Jun. 2021, doi: 10.3390/molecules26133800.

[86] G. S. Santos, S. B. P. Sinoti, F. T. C. de Almeida, D. Silveira, L. A. Simeoni, and K. K. P. Gomes-Copeland, "Use of galantamine in the treatment of Alzheimer's disease and strategies to optimize its biosynthesis using the in vitro culture technique," *Plant Cell, Tissue and Organ Culture (PCTOC)*, vol. 143, no. 1, pp. 13–29, Oct. 2020, doi: 10.1007/s11240-020-01911-5.

[87] H. Kaur *et al.*, "Harnessing plant biotechnology-based strategies for in vitro galanthamine (GAL) biosynthesis: a potent drug against Alzheimer's disease," *Plant Cell, Tissue and Organ Culture (PCTOC)*, vol. 149, no. 1–2, pp. 81–103, May 2022, doi: 10.1007/s11240-022-02229-0.

[88] C. Bitwell, S. Sen Indra, C. Luke, and M. K. Kakoma, "A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants," *Sci Afr*, vol. 19, p. e01585, Mar. 2023, doi: 10.1016/j.sciaf.2023.e01585.

[89] M. A. López-Bascón and M. D. Luque de Castro, "Soxhlet Extraction," in *Liquid-Phase Extraction*, Elsevier, 2020, pp. 327–354. doi: 10.1016/B978-0-12-816911-7.00011-6.

[90] L. Shen *et al.*, "A comprehensive review of ultrasonic assisted extraction (UAE) for bioactive components: Principles, advantages, equipment, and combined technologies," *Ultrason Sonochem*, vol. 101, p. 106646, Dec. 2023, doi: 10.1016/j.ultsonch.2023.106646.

[91] C. C. Pei, T. S. Hsien, F. C. Hsuan, H. L. Hsuan, C. C. Chi, and L. M. Yi, "Microwave- and Ultrasound-Assisted Extraction of Pectin Yield and Physicochemical Properties from Lemon Peel," *J Agric Food Res*, vol. 15, p. 101009, Mar. 2024, doi: 10.1016/j.jafr.2024.101009.

[92] A. Abubakar and M. Haque, "Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes," *J Pharm Bioallied Sci*, vol. 12, no. 1, p. 1, 2020, doi: 10.4103/jpbs.JPBS_175_19.

[93] W. Feng, M. Li, Z. Hao, and J. Zhang, "Analytical Methods of Isolation and Identification," in *Phytochemicals in Human Health*, IntechOpen, 2020. doi: 10.5772/intechopen.88122.

[94] S. Nazar, M. A. Hussain, A. Khan, G. Muhammad, and S. N. A. Bukhari, "Alkaloid-rich plant Tylophora indica; current trends in isolation strategies, chemical profiling and medicinal applications," *Arabian Journal of Chemistry*, vol. 13, no. 8, pp. 6348–6365, Aug. 2020, doi: 10.1016/j.arabjc.2020.05.037.

[95] M. M. Phukan *et al.*, "Alkaloids and terpenoids: Synthesis, classification, isolation and purification, reactions, and applications," in *Handbook of Biomolecules*, Elsevier, 2023, pp. 177–213. doi: 10.1016/B978-0-323-91684-4.00017-7.

[96] I. A. Onifade *et al.*, "In silico study of selected alkaloids as dual inhibitors of β and γ-Secretases for Alzheimer's disease," Sep. 14, 2024. doi: 10.1101/2024.09.10.612359.

[97] K. Bhanukiran *et al.*, "Vasicinone, a pyrroloquinazoline alkaloid from Adhatoda vasica Nees enhances memory and cognition by inhibiting cholinesterases in Alzheimer's disease," *Phytomedicine Plus*, vol. 3, no. 2, p. 100439, May 2023, doi: 10.1016/j.phyplu.2023.100439.

[98] J. A. Lima *et al.*, "Geissoschizoline, a promising alkaloid for Alzheimer's disease: Inhibition of human cholinesterases, anti-inflammatory effects and molecular docking," *Bioorg Chem*, vol. 104, p. 104215, Nov. 2020, doi: 10.1016/j.bioorg.2020.104215.

[99] M. Dulewicz, A. Kulczyńska-Przybik, P. Mroczko, J. Kornhuber, P. Lewczuk, and B. Mroczko, "Biomarkers for the Diagnosis of Alzheimer's Disease in Clinical Practice: The Role of CSF Biomarkers during the Evolution of Diagnostic Criteria.," *Int J Mol Sci*, vol. 23, no. 15, Aug. 2022, doi: 10.3390/ijms23158598.

[100] J. E. Georgakas, M. D. Howe, L. I. Thompson, N. M. Riera, and M. C. Riddle, "Biomarkers of Alzheimer's disease: Past, present and future clinical use," *Biomark Neuropsychiatry*, vol. 8, p. 100063, Jun. 2023, doi: 10.1016/j.bionps.2023.100063.

[101] M. N. Key and A. N. Szabo-Reed, "Impact of Diet and Exercise Interventions on Cognition and Brain Health in Older Adults: A Narrative Review," *Nutrients*, vol. 15, no. 11, p. 2495, May 2023, doi: 10.3390/nu15112495.

[102] L. J. Dominguez *et al.*, "Nutrition, Physical Activity, and Other Lifestyle Factors in the Prevention of Cognitive Decline and Dementia," *Nutrients*, vol. 13, no. 11, p. 4080, Nov. 2021, doi: 10.3390/nu13114080.

[103] A. Nyero, G. U. Anywar, I. Achaye, and G. M. Malinga, "Phytochemical composition and antioxidant activities of some wild edible plants locally consumed by rural communities in northern Uganda.," *Front Nutr*, vol. 10, p. 1070031, 2023, doi: 10.3389/fnut.2023.1070031.

[104] O. C. Aworh, "From lesser‐known to super vegetables: the growing profile of African traditional leafy vegetables in promoting food security and wellness," *J Sci Food Agric*, vol. 98, no. 10, pp. 3609–3613, Aug. 2018, doi: 10.1002/jsfa.8902.

[105] O. A. Ushie, S. I. Iyen, F. E. Abeng, T. I. Azuaga, U. C. Okpaegbe, and E. F. Aikhoje, "Quantification of Alkaloids, Flavonoids and Saponins in Physalis angulata and Mucuna pruriens," *FRsCS*, vol. 1, no. 2, pp. 86–89, 2019.

[106] I. Fatima *et al.*, "Evaluation of potential inhibitory effects on acetylcholinesterase, pancreatic lipase, and cancer cell lines using raw leaves extracts of three fabaceae species," *Heliyon*, vol. 9, no. 5, p. e15909, May 2023, doi: 10.1016/j.heliyon.2023.e15909.

[107] J. Kwon *et al.*, "Phenolic constituents isolated from Senna tora sprouts and their neuroprotective effects against glutamate-induced oxidative stress in HT22 and R28 cells," *Bioorg Chem*, vol. 114, p. 105112, Sep. 2021, doi: 10.1016/j.bioorg.2021.105112.

[108] A. Bukunmi Aborisade, "Phytochemical and Proximate Analysis of Some Medicinal Leaves," *Clin Med Res (N Y)*, vol. 6, no. 6, p. 209, 2017, doi: 10.11648/j.cmr.20170606.16.

[109] J. O. Oladele, O. M. Oyeleke, O. T. Oladele, and M. Olaniyan, "Neuroprotective mechanism of Vernonia amygdalina in a rat model of neurodegenerative diseases," *Toxicol Rep*, vol. 7, pp. 1223–1232, 2020, doi: 10.1016/j.toxrep.2020.09.005.

[110] R. R. Nhouma *et al.*, "Neuroprotective, behavioral and biochemical effects of aqueous extract of Hibiscus cannabinus L. on aluminum chloride induced Alzheimer's disease in male Wistar rats," *Academia Journal of Medicinal Plants*, vol. 9, no. 8, pp. 118–134, 2021, doi: 10.15413/ajmp.2021.0109.

[111] K. C. Edward, D. U. Chijioke, and C. G. Friday, "Phytochemical Screening and Antibacterial Activities of Ethanolic and Aqueous Leaf Extracts of Alchornea cordifolia and Sida acuta on Organisms Isolated from Meat," *Nigerian Journal of Microbiology*, vol. 37, no. 1, pp. 6558–6569, 2023.

[112] J. Singh, P. K. Nayak, A. K. Kushwaha, D. N. S. Gautam, and M. K. Nandi, "Neuroprotective role of Sida acuta Burm. f. in scopolamine-induced memory impairment rat model," *Journal of Drug Research in Ayurvedic Sciences*, vol. 8, no. 1, pp. 65–73, Jan. 2023, doi: 10.4103/jdras.jdras_74_22.

[113] N. M. Hussien, S. E. Labib, R. A. El-Massry, and H. T. M. Hefnawy, "PHYTOCHEMICAL STUDIES AND ANTIOXIDANT ACTIVITY OF LEAVES EXTRACTS OF Corchorus olitorius L. (MOLOKHIA)," *Zagazig J. Agric. Res.*, vol. 44, no. 6, pp. 2231–2239, 2017.

[114] R. Wagdy, R. M. Abdelkader, A. H. El-Khatib, M. W. Linscheid, N. Hamdi, and H. Handoussa, "Neuromodulatory Activity of Dietary Phenolics Derived from Corchorus olitorius L.," *J Food Sci*, vol. 84, no. 5, pp. 1012–1022, May 2019, doi: 10.1111/1750-3841.14587.

[115] B. Mwamatope, D. Tembo, E. Kampira, C. Maliwichi-Nyirenda, and V. Ndolo, "Seasonal Variation of Phytochemicals in Four Selected Medicinal Plants," *Pharmacog Res.*, vol. 13, no. 4, pp. 218–26, 2021.

[116] A. Maroyi, "LANNEA DISCOLOR: ITS BOTANY, ETHNOMEDICINAL USES, PHYTOCHEMISTRY, AND PHARMACOLOGICAL PROPERTIES," *Asian Journal of Pharmaceutical and Clinical Research*, vol. 11, no. 10, p. 49, Oct. 2018, doi: 10.22159/ajpcr.2018.v11i10.27523.

[117] U. S. Eze, C. Obi, and A. O. James, "Quantification of Phytochemical Constituents of Ethanol Yellow Spondias mombin Leaf Extract in Ogba/Ebgema/Ndoni Local Government Area of Rivers State, Nigeria," *J. Appl. Sci. Environ. Manage*, vol. 28, no. 8, pp. 2557–2574, 2024, doi: https://dx.doi.org/10.4314/jasem.v28i8.34.

[118] T. Elufioye, E. Obuotor, J. Agbedahunsi, and S. Adesanya, "Anticholinesterase constituents from the leaves of Spondias mombin L. (Anacardiaceae)," *Biologics*, vol. Volume 11, pp. 107–114, Aug. 2017, doi: 10.2147/BTT.S136011.

[119] W. Arozal, E. Purwoningsih, H. J. Lee, A. J. Barinda, and A. Munim, "Effects of Moringa oleifera in Two Independents Formulation and as Neuroprotective Agent Against Scopolamine-Induced Memory Impairment in Mice," *Front Nutr*, vol. 9, Mar. 2022, doi: 10.3389/fnut.2022.799127.

[120] P. Van Tan, "The Determination of Total Alkaloid, Polyphenol, Flavonoid and Saponin Contents of Pogang gan (Curcuma sp.)," *Int J Biol*, vol. 10, no. 4, p. 42, Sep. 2018, doi: 10.5539/ijb.v10n4p42.

[121] S. Shao, X. Ye, W. Su, and Y. Wang, "Curcumin alleviates Alzheimer's disease by inhibiting inflammatory response, oxidative stress and activating the AMPK pathway," *J Chem Neuroanat*, vol. 134, p. 102363, Dec. 2023, doi: 10.1016/J.JCHEMNEU.2023.102363.

[122] P. P. Parvatikar *et al.*, "Effect of Mucuna pruriens on brain NMDA receptor and tau protein gene expression in cerebral ischemic rats," *Front Physiol*, vol. 14, Feb. 2023, doi: 10.3389/fphys.2023.1092032.

[123] M. A. Sonibare, I. O. Ayoola, and T. O. Elufioye, "Antioxidant and acetylcholinesterase inhibitory activities of leaf extract and fractions of Albizia adianthifolia (Schumach) W.F. Wright," *J Basic Clin Physiol Pharmacol*, vol. 28, no. 2, pp. 143–148, Mar. 2017, doi: 10.1515/jbcpp-2015-0054.

[124] S. Ahmed *et al.*, "Potential therapeutic natural products against Alzheimer's disease with Reference of Acetylcholinesterase," *Biomedicine & Pharmacotherapy*, vol. 139, p. 111609, Jul. 2021, doi: 10.1016/j.biopha.2021.111609.

[125] N. E. Kouémou *et al.*, "Nootropic and Neuroprotective Effects of Dichrocephala integrifolia on Scopolamine Mouse Model of Alzheimer's Disease," *Front Pharmacol*, vol. 8, Nov. 2017, doi: 10.3389/fphar.2017.00847.

[126] O. A. Ojo *et al.*, "HPLC-DAD fingerprinting analysis, antioxidant activities of Tithonia diversifolia (Hemsl.) A. Gray leaves and its inhibition of key enzymes linked to Alzheimer's disease," *Toxicol Rep*, vol. 5, pp. 585–592, 2018, doi: 10.1016/j.toxrep.2018.05.003.

[127] A. M. Ajayi, B. Ben-Azu, J. C. Godson, and S. Umukoro, "Effect of Spondias Mombin Fruit Extract on Scopolamine-induced Memory Impairment and Oxidative Stress in Mice Brain," *J Herbs Spices Med Plants*, vol. 27, no. 1, pp. 24–36, Jan. 2021, doi: 10.1080/10496475.2020.1777613.

[128] H.-S. Lim, Y. Kim, Y. J. Kim, E. Sohn, J.-H. Kim, and S.-J. Jeong, "The Effects of Crinum asiaticum var. japonicum Baker Seeds on Neuroprotection and Antineuroinflammation in Neuronal Cell Lines," *Nat Prod Commun*, vol. 15, no. 10, Oct. 2020, doi: 10.1177/1934578X20965465.

[129] T. S. Kangwa, D. C. Hiss, A. A. Hussein, O. E. Ekpo, and S. I. Omoruyi, "In vitro neuroprotective effects of boophone disticha, brunsvigia bosmaniae and strumaria truncata extracts in SH-SY5Y cells," *South African Journal of Botany*, vol. 166, pp. 512–524, Mar. 2024, doi: 10.1016/j.sajb.2024.01.062.

[130] T. Raghunathan, S. Srinivasan, and S. Jamuna, "Neuroprotective Effect of Ethanolic Extract of Scoparia dulcis on Acrylamide-Induced Neurotoxicity in Zebrafish Model," *Appl Biochem Biotechnol*, vol. 196, no. 7, pp. 3992–4007, Jul. 2024, doi: 10.1007/s12010-023-04733-1.

[131] M. A. Folawiyo, A. J. Ajibare, M. Adefisayo, Adebukola, and A. R. Adeleye, Gbenga Sunday Adedamola, "The cognitive-enhancing activity of hydromethanolic leaf extract of Ocimum gratissimum in mice," *J Pharmacogn Phytochem*, vol. 9, no. 3, pp. 393–397, 2020.

[132] A. Asuku, M. Ayinla, T. Olajide, Z. Yakub, and B. Owoyele, "Cola acuminata Mitigates Cognitive Deficit and Oxidative Stress in Mercury Chloride-induced Neurotoxicity in Male Wistar Rats," *NIgerian Journal of Neuroscience*, vol. 14, no. 2, pp. 33–40, Dec. 2023, doi: 10.47081/njn2023.14.2/001.