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Neuroprotective Effects of Terminalia catappa L.: A Promising Natural Remedy for Alzheimer's Disease

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ABSTRACT:
Alzheimer's disease (AD) is a progressive neurodegenerative condition marked by cognitive impairment, memory deterioration, and behavioral changes. Despite advancements in understanding AD pathophysiology, existing treatments provide only symptomatic relief without halting disease progression. Natural compounds, such as those found in Terminalia catappa L. (tropical almond), have garnered attention for their neuroprotective potential. Terminalia catappa is abundant in bioactive molecules, including flavonoids, tannins, and triterpenoids, which exhibit antioxidant, anti-inflammatory, and anti-amyloidogenic properties. These attributes make Terminalia catappa a promising candidate for AD treatment. This review explores the phytochemical composition of Terminalia catappa, its mechanisms of action, and its potential therapeutic role in AD, emphasizing its ability to alleviate oxidative stress, regulate neuroinflammation, and inhibit amyloid-beta aggregation. While preclinical findings are encouraging, further clinical trials are necessary to establish its efficacy and safety in humans.

Keywords: Alzheimer's disease, Terminalia catappa, neuroprotection, oxidative stress, neuroinflammation, amyloid-beta.

I. INTRODUCTION:

Alzheimer's disease (AD) is the most prevalent form of dementia, affecting over 50 million individuals worldwide, with projections suggesting a threefold increase by 2050 due to aging populations [1]. AD is characterized by amyloid-beta plaque accumulation, neurofibrillary tangles, oxidative stress, and persistent neuroinflammation, culminating in neuronal loss and cognitive decline [2]. Current pharmacological interventions, including acetylcholinesterase inhibitors (e.g., donepezil) and NMDA receptor antagonists (e.g., memantine), primarily offer symptomatic relief and are associated with side effects [3]. These limitations have driven interest in natural products with multi-targeted mechanisms of action.Terminalia catappa L., commonly known as tropical almond, has been traditionally utilized for its anti-inflammatory, antioxidant, and hepatoprotective properties [4]. Recent studies suggest its neuroprotective benefits, particularly concerning neurodegenerative diseases like AD. This review comprehensively examines the neuroprotective potential of Terminalia catappa by analyzing its bioactive compounds, mechanisms of action, and preclinical evidence while exploring its role as a complementary therapy to existing treatments and its potential for future clinical applications.Terminalia catappa L. contains a diverse array of bioactive compounds, including flavonoids, tannins, triterpenoids, and phenolic acids, which contribute to its therapeutic potential. Flavonoids such as quercetin, kaempferol, and catechins possess potent antioxidant properties that neutralize reactive oxygen species (ROS) and mitigate oxidative stress, a key contributor to AD pathology [5]. Tannins, particularly ellagitannins, exhibit anti-inflammatory and anti-amyloidogenic activities, which may help in reducing amyloid-beta plaque formation [6]. Triterpenoids, including ursolic and oleanolic acids, regulate neuroinflammation and promote neuronal survival [7]. Additionally, phenolic acids further enhance the plant's antioxidant and neuroprotective capabilities [8]. The synergistic actions of these bioactive compounds position Terminalia catappa as a potential therapeutic agent for AD.

Therapeutic Potential of Terminalia catappa L. in Alzheimer's Disease

Antioxidant Properties:

Oxidative stress is a fundamental contributor to AD, leading to neuronal damage and cognitive decline. Terminalia catappa exhibits strong antioxidant effects by scavenging ROS and enhancing the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT) [9]. Research indicates that Terminalia catappa extracts reduce lipid peroxidation and protein oxidation, thereby

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protecting neurons from oxidative damage [10]. These antioxidant properties, primarily attributed to flavonoids and phenolic compounds, aid in preserving cellular integrity and preventing neurodegeneration [11].

Anti-inflammatory Effects:

Chronic neuroinflammation significantly contributes to neuronal loss and cognitive deficits in AD. Terminalia catappa has demonstrated strong anti-inflammatory potential by suppressing the production of pro-inflammatory cytokines such as TNF-α and IL-6 [12]. The plant's bioactive constituents, particularly tannins and triterpenoids, regulate inflammatory pathways, including NF-κB and MAPK, thereby reducing neuroinflammation and promoting neuronal survival [13]. These anti-inflammatory properties make Terminalia catappa a promising candidate for mitigating AD-associated neuroinflammation.

Anti-amyloidogenic Effects:

Amyloid-beta plaque accumulation is a primary pathological feature of AD. Terminalia catappa has shown potential in inhibiting amyloid-beta aggregation and promoting its clearance. Studies suggest that Terminalia catappa extracts decrease amyloid-beta-induced neurotoxicity and prevent fibril formation [14]. The tannins and phenolic compounds in Terminalia catappa are believed to interact with amyloid-beta peptides, preventing their aggregation [15]. These findings highlight Terminalia catappa as a valuable natural intervention for addressing amyloid pathology in AD.

Neuroprotection and Cognitive Enhancement:

Terminalia catappa has been reported to exert neuroprotective effects in animal models of AD. Treatment with Terminalia catappa extracts enhances cognitive function, memory retention, and learning abilities by reducing oxidative stress, regulating neuroinflammation, and improving synaptic plasticity [16]. Its bioactive components, particularly flavonoids and triterpenoids, facilitate the release of neurotrophic factors like brain-derived neurotrophic factor (BDNF), which supports neuronal survival and synaptic function [17]. These neuroprotective attributes suggest Terminalia catappa as a potential AD therapeutic agent.

Mechanisms of Neuroprotection by Terminalia catappa L.

The neuroprotective effects of Terminalia catappa stem from its antioxidative, anti-inflammatory, and anti-amyloidogenic actions. Flavonoids, tannins, and triterpenoids collectively counteract oxidative stress, diminish neuroinflammation, and prevent amyloid-beta aggregation [18]. Additionally, Terminalia catappa enhances synaptic plasticity and supports neuronal survival by modulating key neuroprotective pathways [19]. These multifaceted mechanisms make Terminalia catappa a promising candidate for AD treatment.

Comparative Insights: Terminalia catappa vs. Current AD Therapies

Unlike conventional AD treatments that primarily target neurotransmitter modulation, Terminalia catappa offers a broader therapeutic spectrum by addressing oxidative stress, neuroinflammation, and amyloid-beta pathology [20]. While existing pharmacological therapies provide symptomatic relief, Terminalia catappa has the potential to target underlying neurodegenerative processes, offering a holistic approach to AD management [21]. Moreover, its natural origin and favorable safety profile suggest it could serve as an adjunct or alternative to synthetic drugs, potentially reducing adverse effects and enhancing patient outcomes [22].

Challenges and Future Directions

Although preclinical studies demonstrate encouraging results, the clinical application of Terminalia catappa in AD remains in its early stages. Translating animal model findings to human trials presents challenges [23]. Variability in bioactive compound concentrations and issues with bioavailability further complicate therapeutic application [24]. Future research should focus on optimizing formulations, conducting rigorous clinical trials, and exploring novel delivery methods, such as nanoparticle-based systems, to enhance bioavailability [25]. Standardized extracts, pharmacokinetic studies, and safety assessments are crucial for integrating Terminalia catappa into AD treatment strategies [26].

II. CONCLUSION:

Terminalia catappa L. exhibits considerable potential as a neuroprotective agent for AD, owing to its antioxidative, anti-inflammatory, and anti-amyloidogenic properties.

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While promising preclinical evidence supports its efficacy, further clinical validation is essential. With continued research, Terminalia catappa could serve as a valuable complementary therapy for AD, offering a natural and multi-targeted approach to neurodegenerative disease management.

Declarations

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the author

Consent for publication

Not applicable

Availability of data and material

The data reported in this review article can be accessed in the respective references cited.

Competing interests

The author declares that they have no competing interests

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Authors' contributions

Columbus Sahu - wrote the manuscript and Prepare diagrams and referencing. Ritesh Jain Design the layout and critically revise the manuscript**.**

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Abbreviations:

AD: Alzheimer's Disease
ROS: Reactive Oxygen Species
SOD: Superoxide Dismutase
CAT: Catalase
BDNF: Brain-Derived Neurotrophic Factor
TNF-α: Tumor Necrosis Factor-alpha
IL-6: Interleukin-6
NF-κB: Nuclear Factor-kappa B
MAPK: Mitogen-Activated Protein Kinase

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