

Review

# Unlocking the Therapeutic Potential of Medicinal Plants for Alzheimer's Disease: Preclinical to Clinical Trial Insights

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**Abstract:** Alzheimer's disease (AD) is a progressive, multifactorial, and unremitting neurodegenerative disease characterized by memory loss, personality changes, and cognitive impairment. It has become more prevalent in recent years. Therefore, understanding the pathophysiology of AD and developing efficient therapeutic strategies are essential. Moreover, the progression of the disease is unaffected by the pharmaceutical approaches discovered to date. Additionally, the failure of over 200 potential drug candidates in clinical trials over the past decade suggests the complexity and difficulty of both the disease and its underlying causes. Therefore, research focused on medicinal plant-based natural products in the search for novel neuroprotective therapeutic candidates for AD is essential. Indeed, several scientific investigations have demonstrated the efficacy of many medicinal plants and their principal phytochemicals in the treatment of AD. This review article covered the pathophysiological mechanisms of AD, the necessity for natural products as anti-AD treatments, and the most recent preclinical studies revealing the function of neuroprotective medicinal plants and their bioactive compounds in the effective management of AD. In addition, the review also presents clinical trial data of promising anti-AD formulations/agents of plant origin. Revealing recent findings and highlighting the clinical trial data related to the development of new treatments for AD would promote further research in this field and pave the way for the development of more effective and safe treatments for this debilitating disease.

**Keywords:** neuroprotective; Alzheimer's disease (AD); medicinal plants; clinical trial



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## 1. Introduction

The most prevalent form of dementia worldwide is Alzheimer's disease (AD), a progressive neurological condition with a high social and caregiver cost. It is an irreversible neurodegenerative disorder marked by occasional unusual behavior, memory loss, and cognitive impairment. An increase of more than 145% in deaths attributed to AD was observed between 2000 and 2019, and it would likely be exacerbated due to the pandemic of COVID-19 [1,2]. As the world's population ages, the number of people with dementia is currently projected to become over 40 million, and this number is expected to keep growing, doubling every 20 years [3,4]. Moreover, around 58 million individuals worldwide are estimated to be suffering from AD as of 2021, which is anticipated to increase to 88 million by 2050. The survey data also reveal that approximately 6.2 million people in the United States are suffering from AD [5,6].

AD is a neuronal cell disorder that generates progressive dysfunction of neurons due to the abnormal deposition of amyloid  $\beta$  ( $A\beta$ ) and hyperphosphorylated tau proteins, genetic susceptibility, and increased oxidative stress. Eventually, this may lead to cognitive impairment and impact the function of the central and peripheral nervous systems [7,8].

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