Title: Alkaloids as drug leads in Alzheimer's treatment: Mechanistic and therapeutic insights

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Abstract: Alzheimer's disease (AD) has few effective treatment options and continues to be a major global health concern. AD is a neurodegenerative disease that typically affects elderly people. Alkaloids have potential sources for novel drug discovery due to their diverse chemical structures and pharmacological activities. Alkaloids, natural products with heterocyclic nitrogen-containing structures, are considered potential treatments for AD. This review explores the neuroprotective properties of alkaloids in AD, focusing on their ability to regulate pathways such as amyloid-beta aggregation, oxidative stress, synaptic dysfunction, tau hyperphosphorylation, and neuroinflammation. The FDA has approved alkaloids such as acetylcholinesterase inhibitors like galantamine and rivastigmine. This article explores AD's origins, current market medications, and clinical applications of alkaloids in AD therapy. This review explores the development of alkaloid-based drugs for AD, focusing on pharmacokinetics, blood–brain barrier penetration, and potential adverse effects. Future research should focus on the clinical evaluation of promising alkaloids, developing recently discovered alkaloids, and the ongoing search for novel alkaloids for medical treatment. A pharmaceutical option containing an alkaloid may potentially slow down the progression of AD while enhancing its symptoms. This review highlights the potential of alkaloids as valuable drug leads in treating AD, providing a comprehensive understanding of their mechanisms of action and therapeutic implications.

Keywords: Alzheimer’s disease Alkaloids Neuroprotection Acetylcholinesterase inhibitors Blood–brain barrier penetration

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