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SELECTED INDONESIAN MEDICINAL PLANTS FOR THE MANAGEMENT OF ALZHEIMER'S DISEASE – A REVIEW

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ABSTRACT

Psychological issues significantly exacerbate numerous neurodegenerative disorders, including Alzheimer's disease. Alzheimer's disease, the most common form of dementia, affects health and well-being. Researchers are currently searching for novel neuroprotective compound candidates derived from natural ingredients and empirically demonstrated to have pharmacological effects on Alzheimer's disease. Researchers are implementing this as a substitute for Alzheimer's disease medications, which currently have numerous hazardous adverse effects. Several native Indonesian medicinal plants, such as *Zingiber officinale*, *Andrographis paniculata*, *Apium graveolens*, *Kaempferia galanga*, *Psidium guajava*, *Curcuma longa*, and *Morinda citrifolia*, have been shown to protect neurons in different ways by scientists. Consequently, this review article explores the potential of numerous indigenous Indonesian medicinal plants that exhibit pharmacological effects on Alzheimer's disease.

KEYWORDS: Alzheimer's disease, *Zingiber officinale*, *Andrographis paniculata*, *Apium graveolens*, *Kaempferia galanga*, *Psidium guajava*, *Curcuma longa*, *Morinda citrifolia*.

INTRODUCTION

Neurodegenerative diseases are defined as the loss of function and eventual death of nerve cells in the brain or peripheral nervous system. Neurological conditions, estimated to affect one in three people at some point in their lives, rank as the second largest cause of death and a major source of disability.[1] Dementia is the primary focus of most available prevalence data, as it is the most common cause of neurodegenerative diseases. However, besides the most common neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, and stroke, there are also various other neurological diseases such as Parkinson's disease, motor neuron disease, Huntington's disease, spinocerebellar ataxia, and spinal muscular atrophy.[2] Anatomic (functional systems), cellular (nerve groups), protein susceptibility (structural changes, biochemical modifications, and changes in physiological function), and genetic changes all influence how the disease develops. Persistent neuroinflammation is a common occurrence, and the pathogenesis of neurological disease is often complex, with all of these factors interrelated and perpetuating each other.[3] While successful drugs remain undiscovered, current therapeutic options for neurological diseases largely provide symptomatic support for patients and caregivers. Early diagnosis is critical for treatment planning and can help improve long-term support for patients and their families.[4] A recent review on the use of herbal medicines for the treatment of neurodegenerative diseases has been investigated.[5]

The use of medicinal plants in the treatment of various diseases has increased worldwide because they are considered much safer than synthetic drugs.[6,7] Researchers continue to explore active compounds from natural ingredients, especially medicinal plants, which people have traditionally used to treat hyperuricemia in various countries.[8,9] The aim is to find new compounds for the treatment of Alzheimer's disease that have mild side effects with low toxicity, so they do not harm patients.[10,11] Consequently, this review article explores the potential of numerous indigenous Indonesian medicinal plants that exhibit pharmacological effects on Alzheimer's disease.

Zingiber officinale

Zingiber officinale is a spice commonly used for culinary and medicinal purposes for centuries. People have long used *Z. officinale*, a medicinal plant belonging to the *Zingiberaceae* family, for antimicrobial, antidiabetic, nephroprotective, hepatoprotective, anti-inflammatory,

anticancer, and immunomodulatory treatment.[12] In the Ellman test, administration of *Z. officinale* was reported to have anti-Alzheimer's effects by inhibiting acetyl- and butyrylcholinesterase with an IC_{50} value of 41 µg/mL.[13]

Andrographis paniculata
Andrographis paniculata Nees., known as bitter, is a medicinal plant that is empirically used as a medicine for respiratory diseases, diabetes, cancer, obesity, skin infections, herpes, dysentery, fever, sore throat, urinary tract infections, diarrhea, and to reduce inflammation.[14] Administering *A. paniculata* at doses of 200, 400, and 600 mg/kg has neuroprotective effects against cognitive dysfunction by regulating p62-Kelch-like ECH-associated protein 1 (Keap1)-Nuclear factor E2 related factor 2 (Nrf2) and activating autophagy in a mouse model of cognitive deficits induced by aluminum chloride and D-galactose.[15]

Apium graveolens
Apium graveolens is a plant belonging to the *Umbelliferae* family. *A. graveolens* seeds contain various substances, such as essential oils, flavonoids, coumarin, and linoleic acid. People have long used *A. graveolens* seeds to treat arthritis and gout, as well as to reduce muscle spasms, calm nerves, and reduce inflammation.[16] The active ingredient in *A. graveolens*, L-3-n-butylphthalide (L-NBP), has been shown to improve synaptic function, lower Aβ plaque burden, oxidative stress, and microglial activation at a dose of 15 for 3 months in an Alzheimer's mouse model.[17]

Kaempferia galanga
Kaempferia galanga is an herbal plant known for its rhizomes, which are used in traditional medicine and as a cooking spice. This plant has green leaves and flowers that grow above the ground. Various traditional medicines use the fragrant rhizome of *K. galanga* due to its reported anti-inflammatory, antimicrobial, and antioxidant properties.[18] Administration of *K. galanga* was reported to have anti-Alzheimer's effects by inhibiting acetylcholinesterase with an IC_{50} value of 21.94 µg/mL.[19]

Psidium guajava
Psidium guajava, usually known as guava, is a medicinal plant that has been used traditionally for a long time in tropical countries, including Indonesia. The *Myrtaceae* family includes *P. guajava*, a plant known for its anti-inflammatory, analgesic, anti-diabetic, anti-hypertensive, anti-microbial, antioxidant, antibacterial, and antitumor properties.[20,21] Researchers found that giving 200 µg/mL of *P. guajava* could help fight Alzheimer's by blocking acetylcholinesterase in the brain.[22]

Curcuma longa
Curcuma longa is a medicinal plant belonging to the *Zingiberaceae* family. Asia, particularly India and China, widely cultivates this plant. *C. longa* is a sterile plant that does not produce any seeds. This plant grows 3-5 feet tall, and the flowers are yellow. The rhizome is a thick and fleshy underground stem.[23] People have widely reported *C. longa* as a medicinal plant that can help control inflammation and pain. This effect occurs because this plant contains at least three natural polyphenols, namely curcumin, demethoxycurcumin, and bisdemethoxycurcumin, which are known as curcuminoids.[24,25] It was found that giving *C. longa* to people with Alzheimer's prevented the buildup of amyloid-β protein and the inflammation that comes from it. It also stopped β-secretase and acetylcholinesterase from working, with an IC_{50} of 0.25 µg/mL.[26]

Morinda citrifolia
Morinda citrifolia is commonly used in popular medicine in Indonesia. Traditional medicinal practices use many parts of the *M. citrifolia* tree, including the roots, leaves, and seeds. Researchers have reported various properties of this plant, such as immunostimulatory, antitumor, antidiabetic, anti-obesity, antibacterial and antiseptic, antifungal, antiviral, leishmanicide, anti-inflammatory, antinociceptive and analgesic, antioxidant, neuroprotective, wound healing, antiallergic, antiangiogenic, antiemetic and anti-nausea, anti-gastric ulcer and esophagitis, anthelmintic, antimutagenic, antipsychotic, anxiolytic, photoprotective, and periodontal tissue regeneration activity.[27] The administration of *M. citrifolia* has anti-Alzheimer's effects by inhibiting acetylcholinesterase at concentrations of 400 and 800 µg/mL.[28]

CONCLUSION
Indonesia possesses a variety of medicinal plants with potential properties for developing alternative medicines to treat various Alzheimer's diseases. Empirical evidence and scientific testing have proven the effectiveness of these plants in treating various Alzheimer's diseases. These plants contain active compounds that have neuroprotective properties and different working mechanisms, making it impossible to separate them from each other. Researchers hope to enhance Alzheimer's disease treatment through research on medicinal plants.

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