

Ethnopharmacological Study of Keumiki Leaf (*Glochidion* spp) as a Candidate Therapy for Degenerative Diseases

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Abstract.

*Degenerative diseases, particularly neurodegenerative disorders, pose significant global health challenges. Traditional medicine systems offer valuable leads for novel therapeutic development. This ethnopharmacological study investigated Keumiki leaf (*Glochidion* spp), a traditional medicinal plant from Aceh Province, Indonesia, as a therapeutic candidate for degenerative diseases. Comprehensive ethnobotanical surveys revealed high recognition (89.3%) of Keumiki for treating cognitive impairment, inflammatory conditions, and age-related disorders. Phytochemical analysis demonstrated rich composition with total phenolic content of 347.0 ± 4.12 mg GAE/g and total flavonoid content of 163.2 ± 2.78 mg QE/g in ethanol extract. Antioxidant assays revealed potent activity with DPPH IC_{50} of $23.45 \mu\text{g/mL}$, comparable to standard antioxidants. Molecular mechanism studies using Western blot and RT-PCR demonstrated significant activation of the Nrf2/HO-1 antioxidant pathway (2.3-fold and 1.8-fold increases, respectively) and suppression of pro-inflammatory pathways, including downregulation of NF- κ B, TNF- α , IL-1 β , and IL-6. Strong correlations between phytochemical content and biological activities ($r > 0.87$) suggest phenolic and flavonoid compounds as primary contributors to therapeutic effects. This integrated ethnopharmacological approach validates traditional knowledge and provides scientific evidence supporting *Glochidion* spp as a promising therapeutic candidate for degenerative diseases through dual antioxidant and anti-inflammatory mechanisms.*

Keywords: *Glochidion* spp, ethnopharmacology, degenerative diseases, antioxidant activity and traditional medicine.

I. INTRODUCTION

Degenerative diseases, particularly neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease, pose increasing global health challenges as populations age worldwide. The pathophysiology of these conditions involves complex interactions of oxidative stress, neuroinflammation, protein aggregation, and mitochondrial dysfunction. Current therapeutic approaches primarily provide symptomatic relief without addressing these underlying pathological mechanisms, highlighting an urgent need for novel therapeutic interventions that can target multiple disease pathways simultaneously.

Traditional medicine systems have historically provided valuable leads for modern drug discovery, with many contemporary pharmaceuticals originating from ethnopharmacological knowledge. Indonesia, with its exceptional biodiversity comprising over 25,000 plant species, has maintained centuries-old medicinal plant traditions. The traditional Indonesian medicine system, Jamu, was recognized as a UNESCO Intangible Cultural Heritage in 2023, emphasizing its cultural and scientific significance. Recent advances in ethnopharmacological research have highlighted the importance of natural antioxidants in neuroprotection, with polyphenolic compounds showing particular promise for mitigating oxidative stress-induced neuronal damage through activation of the Nrf2/HO-1 pathway, a master regulator of cellular antioxidant defense systems.

In Aceh Province, Indonesia, traditional communities have historically utilized Keumiki plants (*Glochidion* spp) for treating age-related and cognitive disorders. Recent ethnobotanical studies have documented the persistence of traditional knowledge regarding medicinal plant use in the region. However, comprehensive ethnopharmacological investigation of Keumiki in Aceh Province remains limited, with no prior systematic evaluation of its phytochemical composition, antioxidant capacity, or molecular mechanisms of action. This study addresses this knowledge gap by investigating the

ethnopharmacological applications, phytochemical composition, antioxidant capacity, and molecular mechanisms of Acehese *Glochidion* spp as a therapeutic candidate for degenerative diseases.

II. RESULTS AND DISCUSSION

Ethnopharmacological Investigation.

Comprehensive literature review and traditional knowledge documentation revealed high recognition (89.3%) of Keumiki as a medicinal plant with diverse therapeutic applications in Acehese traditional medicine. The plant is traditionally used for cognitive impairment and memory enhancement, inflammatory conditions and joint pain, digestive disorders and gastrointestinal problems, dermatological applications for wound healing, conditions of asthenia and general fatigue, and respiratory system disorders. Decoction preparation represents 78.4% of documented methods, achieved by boiling fresh or dried leaves for internal use. Topical application as paste or poultice is used for external applications. The high consensus among traditional practitioners validates the plant's medicinal significance and provides a foundation for scientific investigation. Taxonomic identification was confirmed through morphological analysis and verification with Herbarium Bogoriense, with voucher specimens deposited for future reference.

Phytochemical Composition. Successive extraction using solvents of increasing polarity (n-hexane, ethyl acetate, methanol, and ethanol) revealed that ethanol extract exhibited the highest yield (15.73%), total phenolic content (347.0 ± 4.12 mg GAE/g), and total flavonoid content (163.2 ± 2.78 mg QE/g). The high phenolic and flavonoid content is comparable to other medicinal plants with established antioxidant properties and supports the therapeutic potential of *Glochidion* spp. Qualitative phytochemical screening confirmed the presence of multiple bioactive compound classes including alkaloids, flavonoids, saponins, tannins, and triterpenoids. Advanced spectroscopic analysis using Nuclear Magnetic Resonance ($^1\text{H-NMR}$ and $^{13}\text{C-NMR}$), Liquid Chromatography-Mass Spectrometry (LC-MS/MS), and Fourier Transform Infrared Spectroscopy (FTIR) successfully identified characteristic triterpenoid compounds, multiple phenolic compounds, flavonoid glycosides, and triterpenoid saponins. These compounds have been previously reported to possess neuroprotective properties in related plant species.

Antioxidant Activities. The ethanol extract demonstrated potent and multi-faceted antioxidant capacity through three complementary assays. DPPH radical scavenging assay revealed an IC_{50} value of $23.45 \mu\text{g/mL}$, which compares favorably with established antioxidants such as ascorbic acid and indicates significant free radical scavenging capacity. The ABTS radical scavenging assay confirmed the extract's ability to neutralize different types of free radicals, with results showing substantial Trolox equivalent antioxidant capacity. Ferric reducing antioxidant power (FRAP) assay demonstrated significant electron-donating capacity, indicating the extract's ability to reduce ferric ions and thereby prevent oxidative chain reactions. These results collectively demonstrate that *Glochidion* spp possesses robust antioxidant activity through multiple mechanisms, including direct free radical scavenging and metal chelation, which are critical for therapeutic applications in oxidative stress-related degenerative diseases.

Molecular Mechanisms. Western blot and RT-PCR analyses revealed that *Glochidion* spp extract modulates key cellular defense pathways at both protein and gene expression levels. Specifically, treatment with the extract resulted in significant activation of the Nrf2/HO-1 pathway, a master regulator of cellular antioxidant defense systems. Western blot analysis showed increased protein expression of Nrf2 (2.3-fold increase) and its downstream target HO-1 (1.8-fold increase), indicating enhanced transcription of antioxidant response elements. Concurrently, NF- κ B activation was significantly suppressed (0.4-fold of control), suggesting anti-inflammatory effects. Gene expression analysis by RT-PCR confirmed these findings, showing upregulation of antioxidant defense genes (Nrf2: 2.1-fold, HO-1: 1.7-fold) and significant downregulation of pro-inflammatory genes including TNF- α (0.3-fold), IL-1 β (0.4-fold), and IL-6 (0.3-fold). These molecular changes indicate that

Glochidion spp extract can simultaneously enhance endogenous antioxidant defenses while suppressing inflammatory responses, providing a dual mechanism of action relevant for degenerative disease treatment. Pearson's correlation analysis revealed strong positive correlations between phytochemical content and biological activities: total phenolic content correlated with DPPH activity ($r = 0.943$), total flavonoid content with ABTS activity ($r = 0.891$), and total phenolic content with FRAP values ($r = 0.876$), suggesting that phenolic and flavonoid compounds are primarily responsible for the observed antioxidant activities.

III. DISCUSSION.

The convergence of traditional knowledge, phytochemical diversity, and demonstrated biological activities positions Glochidion spp favorably for clinical development. Traditional decoction methods likely optimize extraction of water-soluble bioactive compounds, validating traditional knowledge. Nrf2/HO-1 pathway activation is particularly relevant for neuroprotection, as this pathway enhances endogenous antioxidant enzyme systems. Concurrent NF- κ B suppression and reduced pro-inflammatory cytokines suggest Glochidion spp can address both oxidative stress and neuroinflammation, key pathological mechanisms in neurodegenerative disorders. Strong correlations between phytochemical content and antioxidant activity provide foundation for standardization and quality control protocols essential for clinical translation.

IV. CONCLUSION

This ethnopharmacological investigation provides compelling evidence for Glochidion spp as a therapeutic candidate for degenerative diseases. Key findings include: (1) extensive traditional knowledge (89.3% recognition) supporting therapeutic use for cognitive disorders; (2) rich phytochemical composition with 347.0 mg GAE/g total phenolics and 163.2 mg QE/g total flavonoids; (3) potent antioxidant activities (DPPH $IC_{50} = 23.45 \mu\text{g/mL}$) comparable to standard antioxidants; and (4) Nrf2/HO-1 pathway activation (2.3-fold and 1.8-fold respectively) with suppression of pro-inflammatory gene expression, providing dual antioxidant and anti-inflammatory effects.

The integration of traditional knowledge with modern analytical methods validates ethnopharmacological approaches in drug discovery. Future research priorities include: (1) bioavailability and pharmacokinetic studies; (2) in vivo efficacy evaluation in animal models; (3) isolation of specific bioactive compounds; (4) development of standardized formulations; and (5) clinical trial design. This research represents a sustainable model respecting cultural heritage while contributing to global health solutions.

V. ACKNOWLEDGMENTS

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VI. DISCLOSURE STATEMENT

The authors report no conflicts of interest.

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