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Utiliization of Natural Compound from Pegagan (*Centella asiatica* (L.) Urb.) and Their Potential Role in the Health Sector

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Abstract: *Centella asiatica*, also known as Gotu Kola, is a medicinal plant widely used in traditional medicine. This abstract discusses its various health benefits supported by scientific research, including wound healing, cognitive enhancement, and anxiety reduction. It also explores its potential in treating skin conditions, venous insufficiency, and improving circulation. Further research is needed to fully understand its mechanisms of action and optimize its therapeutic applications. *Centella asiatica* (*C. asiatica*), commonly known as Gotu Kola, is a herbaceous plant extensively used in traditional Asian medicine for centuries. This review summarizes the scientifically validated health benefits of *C. asiatica* based on available research, primarily from Scopus-indexed publications. The plant's bioactive compounds, including triterpenoid saponins (asiaticoside, madecassoside, asiatic acid, and madecassic acid), contribute to its diverse pharmacological activities. *C. asiatica* exhibits significant wound healing properties by promoting collagen synthesis, angiogenesis, and fibroblast proliferation. Furthermore, studies suggest its potential in enhancing cognitive function, reducing anxiety, and improving memory. Its efficacy in treating skin conditions like eczema and psoriasis, as well as venous insufficiency and microcirculation, has also been reported. While promising, further research is needed to elucidate the precise mechanisms of action, determine optimal dosages, and explore potential synergistic effects with other therapeutic agents for various health conditions. This review aims to provide a comprehensive overview of the evidence-based health benefits of *C. asiatica*, highlighting its potential as a valuable natural remedy in modern medicine.

Keywords: Bioactive; *Centella asiatica*; Medicial plants; Pegagan; Phytochemicals; Toxicity

Introduction

Centella asiatica, commonly known as Gotu Kola, is a perennial herbaceous plant belonging to the Apiaceae family, native to tropical and subtropical regions of the world, particularly in Asia (Nikolich-Zugih et al., 2016). Traditionally, it has been utilized in various cultures for its medicinal properties, with historical references dating back to ancient Ayurvedic and Traditional Chinese Medicine practices (Dartigues, 2022). The plant is renowned for its diverse pharmacological effects, which include wound healing, anti-inflammatory, antioxidant, and neuroprotective properties (Jana, 2022).

Recent scientific investigations have begun to validate these traditional uses, revealing the presence of bioactive compounds such as triterpenoids, flavonoids, and phenolic acids, which contribute to its therapeutic potential (Mascarelo, 2023). Studies have demonstrated that *C. asiatica* can enhance collagen synthesis, promote angiogenesis, and accelerate wound healing, making it a valuable agent in dermatological applications (Abdoli, 2022). Additionally, its cognitive-enhancing effects have

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garnered attention, with research indicating potential benefits in memory improvement and anxiety reduction Chobe, 2020).

Despite the growing body of evidence supporting the health benefits of *C. asiatica*, there remains a need for further exploration to fully elucidate its mechanisms of action and therapeutic applications (Kazeminia, 2020). This introduction aims to provide an overview of the significance of *Centella asiatica* in health and medicine, highlighting its traditional uses, active constituents, and the scientific research that underpins its efficacy. As interest in natural remedies continues to rise, *C. asiatica* stands out as a promising candidate for further investigation in the field of herbal medicine and pharmacology.

Originally categorized within the Hydrocotyloideae subfamily under the genus Hydrocotyle, *Centella asiatica* (L.) Urb. Now belongs to the Apiaceae family's Mackinlayoideae subfamily. Before this reclassification, scientists recognized this species as Hydrocotyle asiatica by Hydrocotyle nomenclature (Nicolas & Plunkett, 2009). This plant is known by different local names across countries, with the most common being "Asian Pennywort", "Penny-wort", and "Gotu kola" (Tambaro, 2023).

The *Centella asiatica* plant is often called the "Magic Potion" due to its significant role in traditional medicine across various regions, including China and ancient Africa (Borras, 2021). *Centella asiatica* is a creeping herb that thrives in diverse soil conditions, such as sandy or humus-rich environments (Bandomo, 2021). The edible foliage of this species exhibits a distinctive yellowish-green hue, featuring slender petioles and thin, oval-shaped blades. Through its interconnected stolons, ranging from green to reddish colouration, *C. asiatica* spreads laterally across the ground. This species thrives across numerous tropical and subtropical territories worldwide (Al-Nahain et al., 2019). While initially native to Southeast Asian regions and Pacific Island communities, the plant now flourishes in various nations, such as South Africa, Mexico, and Ecuador (Sun, 2020).

Beyond its culinary application as a leafy vegetable in salads (Bandara, 2022). *Centella asiatica* has gained significant recognition in healthcare due to its versatile therapeutic properties (Apu et al., 2010). In Ayurvedic medicine, *C. asiatica* serves as a remedy for various neurological disorders, including Alzheimer's, dementia, anxiety, and depression (Arumugam et al., 2011). Contemporary scientific investigations are exploring its extensive healing capabilities and analyzing the biological activity of its phytochemical constituents. Traditional Indian Ayurvedic medicine has long regarded *C. asiatica* as an all-encompassing medicinal plant, utilized for millennia to address various health conditions ranging from minor ailments to severe disorders (Bryant, 1983). Research has documented numerous therapeutic benefits (Figure 1), encompassing its capacity to shield neural tissue, regenerate nerves, regulate immune function, combat depression, boost memory, protect digestive organs, support heart health, defend against radiation, fight cancer, inhibit microbes, accelerate wound recovery, reduce inflammation, manage diabetes, and neutralize free radicals (Aziz et al., 2007; Bisht et al., 2013).

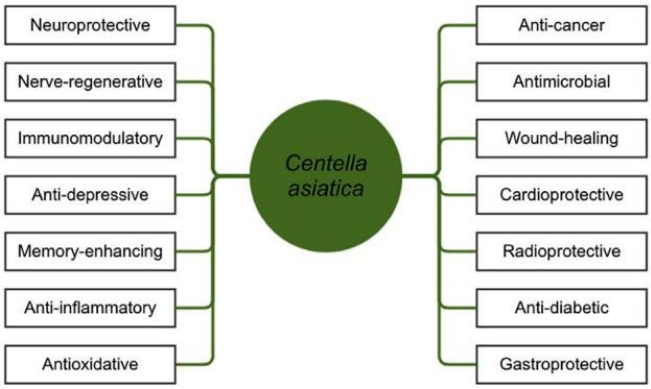

Figure 1. Pharmacological properties of *Centella asiatica* (Bisht et al., 2013)

Method

This review article aims to synthesize the existing literature on *Centella asiatica*, focusing on its pharmacological properties, traditional uses, and potential therapeutic applications. A systematic literature search was conducted to identify relevant studies published.

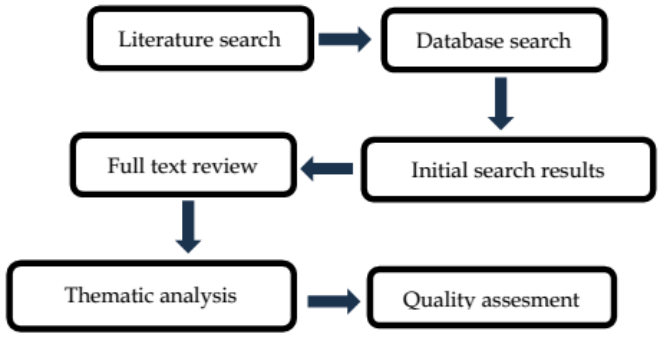

Figure 2. Research flow

Result and Discussion

Utilization of Centella Asiatica in Traditional Medicine

Since ancient times, *Centella asiatica* has served both as a therapeutic agent and food source. The plant's consumption in cooking correlates strongly with its therapeutic properties recognized by indigenous

communities. As documented in numerous historical healing practices (Apu et al., 2010), *Centella asiatica* holds significance as an ethnomedicinal species (Puttarak, 2017).

For centuries, *Centella asiatica* has served medicinal purposes throughout India and Southeast Asia. Historical documentation shows its inclusion in the ancient Sanskrit medical compendium (Ayurveda) dating back to 500 AD. The plant, known in Sanskrit as "manduk-parni," appears in the ancient medical manuscript "Sushruta Samhita" from 1200 BC. During the 19th century, the Indian Pharmacopoeia formally recognized *Centella asiatica* as a therapeutic agent for multiple conditions, including wound management, dermatological disorders (such as leprosy, lupus, varicose ulcers, eczema, and psoriasis), gastrointestinal issues, febrile conditions, amenorrhea, and female genital tract ailments (Aziz et al., 2007). Historical documentation demonstrates that *Centella asiatica* has been integral to traditional healing practices. Indigenous practitioners across Java and Indonesian archipelago have employed this herb for medicinal applications, particularly in managing leprosy on distant islands. Within the framework of Indian Ayurveda, *Centella asiatica* holds significance as a versatile therapeutic agent, with its applications in Ayurvedic practices spanning millennia for addressing various health conditions, from minor to persistent disorders (Arumugam et al., 2011).

Historical records show that *Centella asiatica* played a significant role in Ayurvedic healing practices, where its above-ground components were employed to address numerous conditions including dermatological disorders, syphilis, rheumatism, psychological ailments, epilepsy, hysteria, fluid loss, and leprosy (Al-Nahain et al., 2019). Documentation of this medicinal plant appears in Shennong's classical Chinese herbal compendium dating back two millennia (Arribas-Lopez, 2022). Chinese therapeutic applications encompassed the management of pyrexia, dysentery, urological infections, and hepatic disorders (Wanasuntrowong, 2012). Throughout Southeast Asian therapeutic traditions, practitioners utilized this botanical specimen to enhance urinary function, combat exhaustion, manage gastrointestinal issues, treat ocular conditions, reduce inflammation, ease respiratory distress, and regulate cardiovascular pressure (Bhandari et al., 2013). Research conducted by Rohini et al. (2022) documented multiple therapeutic applications of this plant, including its effectiveness against fever, abdominal discomfort, scrophula (a tuberculosis variant), and syphilis. Their investigation highlighted the plant's dual role as an organophosphate pesticide antidote and nutritional supplement across North America. The plant's medicinal value extends to Madagascar, where it serves as a leprosy treatment, while communities in Java and the Malay Peninsula utilize it for wound healing and addressing cognitive impairment (Kothiyal et al., 2021). The study identified three distinct varieties of *Centella asiatica*, each originating from specific geographical regions (Table 1).

Table 1. Findings on *Centella asiatica* Varieties (Brinkhaus, 2000)

Varieties	Morphology	Geographic position
Centella Asiatica L. var. tipical	The leaves are finely hairy and elliptical in shape with tightly crinkled edges	Madagaskar, South Asia
Centella Asiatica L. var. Abyssinica	The hairy leaves are denser and have softer leaf edges	Tropical region and equator
Centella Asiatica L. var. floridana	The leaves are more elongated and broader compared to other varieties	Africa, America to Argentina, and the tropical regions of Oceania

Phytochemistry of Centella asiatica

Research investigations have documented that *Centella asiatica* encompasses over 70 distinct phytochemicals. The plant's biochemical profile exhibits abundant quantities of triterpenes, flavonoids, essential oils, alkaloids, and amino acids. As documented in Table 2, the primary phytochemical constituents of *Centella asiatica* have been extensively cataloged in scientific literature. The plant demonstrates remarkable chemical diversity, incorporating multiple compound families: various terpene classes (monoterpenes, sesquiterpenes, diterpenes, triterpenes, tetraterpenes), phenolic substances (flavonoids, tannins), alkaloids, carbohydrates, vitamins, minerals, and amino acids (Bryant, 1983).

The tabulated data demonstrates how phytochemical profiles fluctuate based on multiple factors, including regional distribution, weather patterns, plant variants, and laboratory procedures utilized. Research findings reveal that *Centella asiatica* exhibits a rich array of chemical components, with variations linked to the plant's geographical origins. Investigations documented in scientific publications have examined the bioactive elements of *Centella asiatica* throughout diverse Asian territories (China, India, Indonesia, Malaysia, and Sri Lanka), uncovering multiple distinct compounds (Devkota & Jha, 2009;

Nicolas & Plunkett, 2009; Kothiyal et al., 2021; Ding et al., 2022).

Studies have shown that environmental factors and geographical sources influence metabolite production patterns (Oyenihi et al., 2023), with analyses of *Centella asiatica* specimens across Chinese regions revealing distinct variations in triterpene concentrations (Chanana, 2016). As a primary constituent of *Centella asiatica*, triterpenoids encompass numerous structural variants, with biosynthetic studies demonstrating the pathway's capacity to generate thousands of distinct triterpen derivatives (Orhan, 2012).

Table 2. Phytochemical Compounds of *Centella asiatica* (Bisht et al., 2013)

Main group	Constituent
Triterpene acids	Asiatic acid, Madasiatic acid, Madecassic acid, Thankunic acid, Indocentoic acid, Euscaphic acid, Terminolic acid, Isothankunic acid, Bayogenin, Centic acid, Betulinic acid, Cenellic acid, Brahmic acid, Idocentic acid
Triterpene sugar esters	Asiaticoside, Asiaticoside A, Asiaticoside B, Asiaticoside C, Asiaticoside D, Asiaticoside E, Asiaticoside F, Braminoside, Brahmoside, Brahminoside, Thankuniside, Isothankuniside, Centellasaponin A, Centellasapogenol, Sceffoleoside A, Centellasaponin B, Centellasaponin C, Centellasaponin D, Centelloside, Madecassoside
Triterpene steroids	Stigmasterol, Sitosterol
Essential oils	β-Caryophyllene, Terpene Acetate, Terpinene Pinene, α-Humulene, Biclyclogermacrene, Germacrene B, Elemene, Famesol, Myrcene
Flavonoids (polyphenols)	Quercetin glycoside, Kaempferol, Astragalin, Catechin, Rutin, Naringin
Sesquiterpenes	Bicycloelemene, Trans-farnesene, Ermacrene
Vitamins	Ascorbic acid, Nicotinic acid, β-carotene
Minerals	Calcium, Phosphorus, Iron, Potassium, Magnesium, Manganese, Zinc, Sodium, Copper
Amino acids	Alanine and serine (major), Aminobutyrate, Aspartate, Glutamate, Histidline, Lysine, Threonine, Arginine, Leucine, Iso-leucine, Valine, Methionine, Tyrosine, Mesoinositol, Centellose, Arabinogalactan
Other constituents	Hydrocotylin (an alkaloid), Vallerine (a bitter compound), Phytosterols (e.g. Campesterol, Stosterol, Stigmasterol), Resin, 14 different polyacetylenes

Triterpenoid Compounds

Among the key bioactive compounds in *Centella asiatica* (Jo et al., 2023), centalloids - a classification of pentacyclic triterpenoid saponins - function as crucial secondary metabolites driving its therapeutic properties. These compounds play a vital role in mediating plant-environment relationships. Research by Nicolas et al. (2009) demonstrates that such metabolites function as protective agents through various mechanisms, encompassing phytoalexins, phytoanticipins, anti-feedants, attractants, and pest pheromones, ultimately contributing to human wellness. Natural sources of terpenes and their terpenoid variants have demonstrated significant advantages for human health maintenance. The formation of terpenes occurs through biosynthetic polymerization of 2-methylbutadiene (isoprene units), resulting in their characteristic cyclic configuration. These compounds exhibit a fundamental molecular structure of C_5H_8. The categorization of terpenes depends on their isoprene unit count (C5), ranging from hemiterpenes (C5) to complex polyterpenes. The classification system encompasses several groups: hemiterpenes with a single unit, monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), sesterterpenes (C25), triterpenes (C30), carotenoids (C40), and polyterpenes containing multiple extended isoprene chains (Kunjumon et al., 2022).

Research literature categorizes sterols and triterpenes as members of the triterpenoid compound family. These substances exist predominantly as glycosides, specifically saponins, which concentrate heavily within numerous plant species. The classification of saponins depends on their aglycone structural arrangement. Within the category of triterpenoid saponins, one finds triterpen aglycones featuring a pentacyclic configuration with a C30 structural base. In *Centella asiatica*, triterpenes demonstrate two distinct variations, distinguished by methyl substitution patterns at positions C19 and C20, identified as oleanane and ursane (Figure 3). Among the triterpenes found in *Centella asiatica*, the most significant compounds include madecassic acid, asiaticoside, and their associated triterpen sapogenins - specifically

madecassic acid and asiatic acid (Figure 4) (Muller et al., 2013).

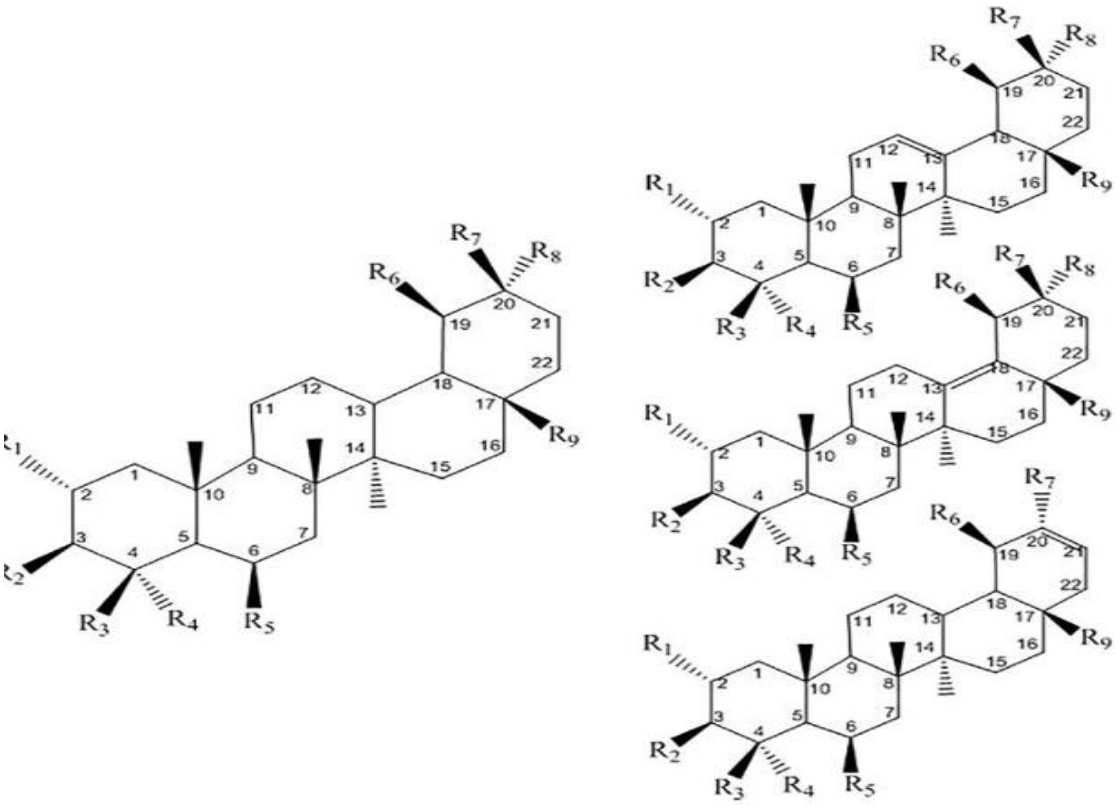

Figure 3. Basic structure of pentacyclic triterpen metabolites of centella: ursane type (R6, R7 = methyl) or oleanane type (R7, R8 = methyl) with double bonds occurring at C12-C13, C13-C18, or C20-C21

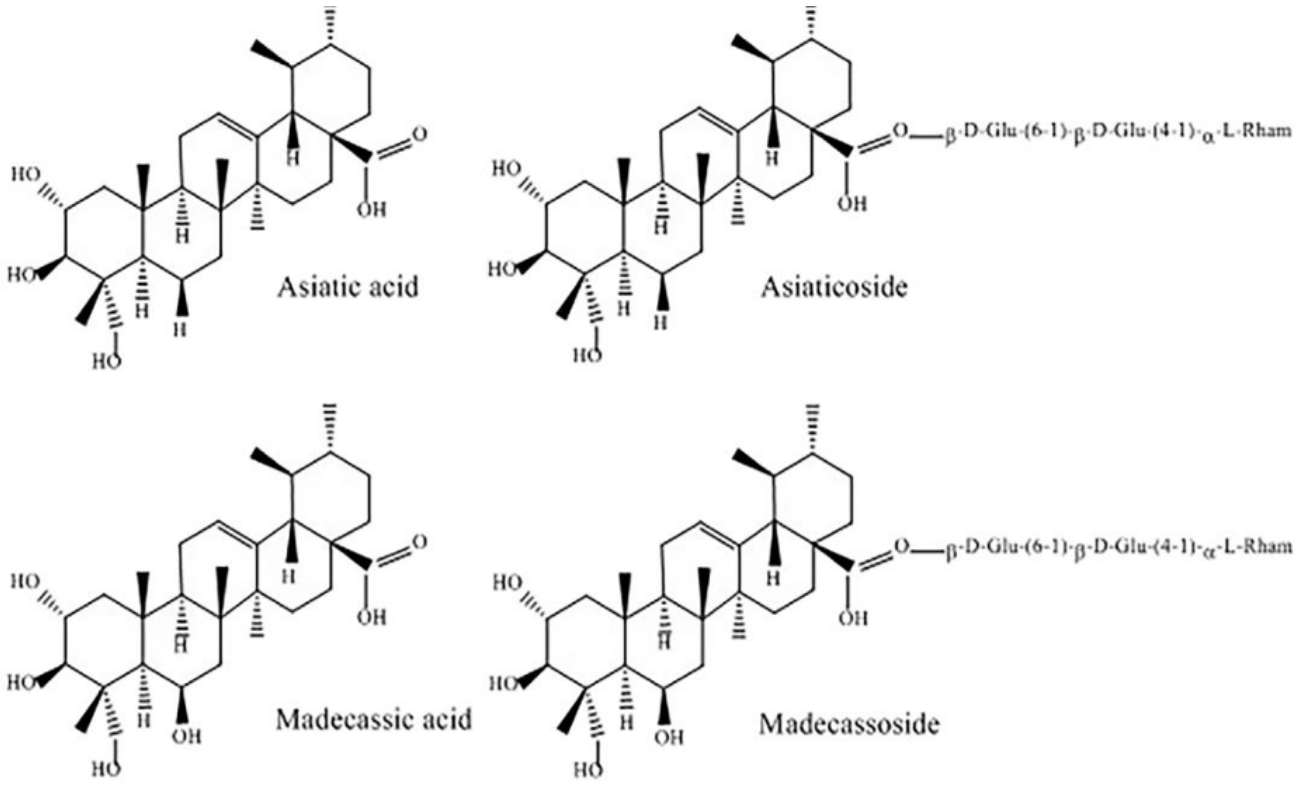

Figure 4. The most dominant triterpenoid structures in *Centella asiatica* (Devkota & Jha, 2009)

Utilization in Health Fields

Neuroscientists have increasingly focused on neuroprotective strategies in recent years as neurological conditions affecting the central and peripheral nervous system become more common. While researchers attributed these disorders primarily to free radical damage, subsequent investigations revealed multiple disease-specific pathological mechanisms (Othman et al., 2023).

A major neurocognitive disorder known as dementia primarily affects older populations. It is characterized by impairments in cognitive capabilities (encompassing mental processes like memory, verbal communication, reasoning, and decision-making) and challenges in executing everyday tasks (including household management and independent living). Studies have shown that numerous individuals with dementia display cerebral irregularities stemming from various causes (Rohini & Smitha, 2022).

As the primary contributor to dementia cases globally, Alzheimer's disease (AD) represents a steadily advancing neurological deterioration that impacts roughly 47 million individuals and typically results in mortality within nine years of initial detection. The condition predominantly manifests in individuals exceeding age 65, with advanced age remaining the principal factor for developing this disorder. Multiple hypotheses elucidate the intricate disease mechanism, encompassing the cholinergic, amyloid cascade, and tau theories, which operate through distinct biochemical processes. The disease initiation stems from key factors, including oxidative damage, free radical activity, inflammation, and immune system dysfunction (Sabaragamuwa et al., 2018).

Research suggests that *Centella asiatica* is an acetylcholinesterase (AChE) inhibitor, representing one of its primary pathways in combating Alzheimer's disease. In vitro experiments have examined this plant's capacity to inhibit AChE activity. When researchers analyzed hydroalcoholic extracts of *Centella asiatica* obtained through a 48-hour room-temperature immersion of dried plant material in an ethanol-water solution (95:5), they observed AChE enzyme inhibition, recording an IC50 measurement of 106.55 ± 9.96 µg/mL (Seong et al., 2023).

An investigation evaluated various *Centella asiatica* preparations: ethanol-derived extracts from Turkish and Indian sources (utilizing 75% ethanol extraction of plant powder over three days) alongside standardized Chinese extracts (containing primarily asiaticoside and madecassoside) (Truong et al., 2024). Results demonstrated that exclusively the Chinese standardized *Centella asiatica* extract achieved AChE inhibition, measuring 48.28 ± 1.64% at 200 µg/mL concentration. Interestingly, while the Turkish and Indian extracts demonstrated butyrylcholinesterase inhibitory effects, the Chinese standardized extract lacked this property. Additional investigations examined AChE inhibition by comparing India-sourced commercial dry *Centella asiatica* extracts against fresh preparations. Researchers utilized Soxhlet extraction with absolute ethanol to obtain fresh extracts from the dried plant material. Analysis revealed that these fresh preparations demonstrated lower inhibition rates (27.09 ± 0.39%) than their commercial counterparts (39-40%), though stability testing showed only slight potency loss across six months. Notably, when investigating AChE inhibitory properties among 80 TCM herbs, scientists found that *Centella asiatica* extracts (using methanol, dichloromethane, and raw water as solvents) displayed no substantial activity. Their methodology involved a six-hour reflux boiling of fresh plant material. Current literature reveals sparse data regarding AChE inhibitory capabilities of different *Centella asiatica* preparations, suggesting additional investigation is warranted (Singh et al., 2014).

Antioxidant Activity of Centella asiatica

The emergence of oxidative stress occurs when there is a disruption in the equilibrium between bodily antioxidant defense mechanisms and free radical production. Research has established oxidative stress as a crucial element contributing to Alzheimer's disease development. According to the oxidative stress theory, the central nervous system (CNS) experiences greater molecular damage from Reactive Oxygen Species (ROS) and free radicals compared to other body organs, primarily because it contains elevated levels of oxidizable fatty acids, requires more oxygen, and possesses fewer conventional antioxidant defenses (Yang et al., 2023).

Research suggests that managing oxidative stress represents a strategy for improving cognitive function, with multiple interventions under investigation. Experimental findings revealed that extended administration of *Centella asiatica* extracts spanning 25 days diminished colchicine-induced memory deficits and oxidative injury and counteracted elevated AChE activity (Xie et al., 2024).

Research findings demonstrated that *Centella asiatica* extracts mitigated cognitive decline, enzyme activity, and D-glucose-induced oxidative stress (Nicolas & Plunkett, 2009). A subsequent investigation analyzing *Centella asiatica* leaf powder confirmed its impact on brain oxidative indicators. The findings highlighted *Centella asiatica's* potential as a neuroprotective agent capable of regulating oxidative imbalances stemming from internal factors and neural

toxicity. When administered orally (300 mg/kg body weight/day for 60 days), *Centella asiatica* extract significantly improved brain antioxidant status by lowering LPO and elevating PCO levels. These outcomes established *Centella asiatica's* role in safeguarding ageing rat brains from oxidative deterioration. Furthermore, experimental research with rodents demonstrated that regular *Centella asiatica* extract intake modified H_2O_2-triggered oxidative stress throughh antioxidant defense mechanisms (Devkota & Jha, 2009; Ding et al., 2022; Bryant, 1983).

Therapeutic Use as an Anti-inflammatory Agent

When tissues and cells sustain damage from pathogens, chemical exposure, or physical trauma, the body initiates an inflammatory response as a protective mechanism. Persistent inflammatory conditions, marked by uncontrolled inflammatory processes, contribute to various long-term health disorders, such as cancer, heart disease, diabetes, arthritis, and neurological deterioration. Nature's botanical realm has evolved numerous phytochemical compounds that possess anti-inflammatory properties (Kothiyal et al., 2021).

Research indicates that *Centella asiatica* demonstrates inflammation-reducing properties attributed to its terpenoid and flavonoid compounds. Researchers validated these anti-inflammatory characteristics through in vitro analysis using the Human Red Blood Cell (HRBC) membrane stabilization technique. Additional investigations revealed that the triterpenoid compound madecassic acid, derived from *Centella asiatica*, displayed notable anti-inflammatory capabilities surpassing those of its related compound madecassoside (Ding et al., 2022).

Safety, Toxicity, and Drug Interactions

Safety assessments of *Centella asiatica* formulations demonstrate minimal risks, as pharmacovigilance monitoring reveals no significant adverse reactions. Though rare, some individuals experience digestive discomfort and nausea after consuming *Centella asiatica* supplements orally. For over three decades, European markets have successfully distributed approved products with processed *Centella asiatica* extract.

Research examining medication interactions plays a vital role in determining how safely *Centella asiatica* can be consumed as either food, supplements, or alongside prescribed medicines. Research utilizing recombinant human cytochrome P450 assessments examined asiaticoside and madecassoside, two key triterpenes found in *Centella asiatica*, demonstrating their capacity to interact with medications by inhibiting human cytochrome P450 enzymes. Located predominantly in hepatic tissue, cytochrome P450 (CYP) enzymes facilitate drug breakdown, which makes any alteration in their function particularly relevant when analyzing medication interactions (Nicolas & Plunkett, 2009). Research findings demonstrated that asiaticoside and madecassoside exhibited inhibitory activity against CYP2C19 and CYP3A4 among six tested isoforms. The observed suppression by these triterpenes remained modest when evaluated against IC50 measurements of established selective inhibitors. These results indicate potential interactions between asiaticoside and madecassoside with pharmaceutical compounds processed by CYP2C19 and CYP3A4 (Bandara, 2022).

Research suggests that *Centella asiatica* preparations might induce liver toxicity, especially when combined with other hepatotoxic medicines, though robust research validating this concern remains scarce. The herb demonstrates possible interactions with diuretic compounds, producing combined effects. Studies also point to *Centella asiatica's* promise as an anxiety treatment through its calming characteristics (Devkota & Jha, 2009).

Conclusion

The conclusion states that *Centella asiatica* has attracted significant attention and a variety of therapeutic properties.

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Author Contributions

R.L.D.: Writing – original draft, visualization, conceptualization; R.Y.: Writing - review and editing; Y.: Writing - review and conceptualization.

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Conflicts of Interest

The review article's authors confirm the absence of any conflicting interests that might affect their preparation of this manuscript.

References

Abdoli, N., Salari, N., Darvishi, N., Jafarpour, S., Solaymani, M., Mohammadi, M., & Shohaimi, S. (2022). The global prevalence of major depressive disorder (MDD) among the elderly: A systematic review and meta-analysis. *Neuroscience and*

Biobehavioral Reviews, *132*(1), 1067–1073. https://doi.org/10.1016/j.neubiorev.2021.10.041

Al-Nahain, A., Jahan, R., Rahman, T., Nurunnabi, M., & Rahmatullah, M. (2015). Centella asiatica: From Ethnomedicinal Uses to the Possibility of New Drug Discovery. In *Therapeutic Medicinal Plants* (pp. 38–56). CRC Press. https://doi.org/10.1201/b19773-3

Apu, A. S., Muhit, M. A., Tareq, S. M., Pathan, A. H., Jamaluddin, A. T. M., & Ahmed, M. (2010). Antimicrobial activity and brine shrimp lethality bioassay of the leaves extract of Dillenia indica linn. *Journal of Young Pharmacists*, *2*(1), 50–53. https://doi.org/10.4103/0975-1483.62213

Arribas-López, E., Zand, N., Ojo, O., Snowden, M. J., & Kochhar, T. (2022). A Systematic Review of the Effect of Centella asiatica on Wound Healing. *International Journal of Environmental Research and Public Health*, *19*(6), 122–132. https://doi.org/10.3390/ijerph19063266

Arumugam, T., Ayyanar, M., Koil Pillai, Y. J., & Sekar, T. (2011). Phytochemical screening and antibacterial activity of leaf and callus extracts of Centella asiatica. *Bangladesh Journal of Pharmacology*, *6*(1), 55–60. https://doi.org/10.3329/bjp.v6i1.8555

Aziz, Z. A., Davey, M. R., Power, J. B., Anthony, P., Smith, R. M., & Lowe, K. C. (2007). Production of asiaticoside and madecassoside in Centella asiatica in vitro and in vivo. *Biologia Plantarum*, *51*(1), 34–42. https://doi.org/10.1007/s10535-007-0008-x

Bandara, M. S., Lee, L. E., & Thomas, J. E. (2022). Gotu Kola (Centella asiatica L.): An Under-Utilized Herbs. *The American Journal of Plant Science and Biotehnology*, *1*(1). Retrieved from http://globalsciencebooks.info/Online/GSBOnline/images/2011/AmJPSB_5(SI2)/AmJPSB_5(SI2)20-31o.pdf

Bandomo, G. V., Cadalso, A. E. R., Caridad, R. de la, MuñozI, R., Turiño, E. R. A., Jiménez, V. S. R., & Abril, R. E. F. (2021). Medicinal Plants, Precautions for Their Use in the Elderly. *Journal of Pharmacy and Pharmacology*, *9*(4), 149–159. https://doi.org/10.17265/2328-2150/2021.04.004

Bhandari, A. K., Negi, J. S., Baunthiyal, M., Bisht, V. K., & Singh, N. (2013). A quick bud breaking response of a surface model for rapid clonal propagation in Centella asiatica (L.). *International Journal of Biotechnology and Molecular Biology Research*, *4*(6), 93–97. https://doi.org/10.5897/ijbmbr2013.0167

Bisht, V. K., Kandari, L. S., Negi, J. S., Bhandari, a K., & Sundriyal, R. C. (2013). Traditional use of medicinal plants in district Chamoli, Uttarakhand, India. *Journal of Medicinal Plants Research*, *7*(15), 918–929. Retrieved from https://shorturl.at/rZ1jZ

Borrás, S., Martínez-Solís, I., & Ríos, J. L. (2021). Medicinal Plants for Insomnia Related to Anxiety: An Updated Review. *Planta Medica*, *87*(10–11), 738–753. https://doi.org/10.1055/a-1510-9826

Brinkhaus, B., Lindner, M., Schuppan, D., & Hahn, E. G. (2000). Chemical, pharmacological and clinical profile of the East Asian medical plant Centella asiatica. *Phytomedicine*, *7*(5), 427–448. https://doi.org/10.1016/S0944-7113(00)80065-3

Bryant, J. P., Chapin, F. S., & Klein, D. R. (1983). Carbon/Nutrient Balance of Boreal Plants in Relation to Vertebrate Herbivory. *Oikos*, *40*(3), 357. https://doi.org/10.2307/3544308

Chanana, P., & Kumar, A. (2016). Possible Involvement of Nitric Oxide Modulatory Mechanisms in the Neuroprotective Effect of Centella asiatica Against Sleep Deprivation Induced Anxiety Like Behaviour, Oxidative Damage and Neuroinflammation. *Phytotherapy Research*, *30*(4), 671–680. https://doi.org/10.1002/ptr.5582

Chobe, S., Chobe, M., Metri, K., Patra, S. K., & Nagaratna, R. (2020). Impact of Yoga on cognition and mental health among elderly: A systematic review. *Complementary Therapies in Medicine*, *52*(1), 103–111. https://doi.org/10.1016/j.ctim.2020.102421

Dartigues, J. F., Le Bourdonnec, K., Tabue-Teguo, M., Le Goff, M., Helmer, C., Avila-Funes, J. A., Coureau, G., Feart, C., Pérès, K., Genuer, R., Letenneur, L., Amieva, H., & Proust-Lima, C. (2022). Co-Occurrence of Geriatric Syndromes and Diseases in the General Population: Assessment of the Dimensions of Aging. *Journal of Nutrition, Health and Aging*, *26*(1), 37–45. https://doi.org/10.1007/s12603-021-1722-3

Devkota, A., & Jha, P. (2009). Variation in growth of Centella asiatica along different soil composition. *Botany Research International*, *2*(1), 55–60. Retrieved from http://www.idosi.org/bri/2(1)09/10.pdf

Ding, B., Niu, W., Wang, S., Zhang, F., Wang, H., Chen, X., Chen, S., Ma, S., Kang, W., Wang, M., Li, L., Xiao, W., Guo, Z., & Wang, Y. (2022). Centella asiatica (L.) Urb. attenuates cardiac hypertrophy and improves heart function through multi-level mechanisms revealed by systems pharmacology. *Journal of Ethnopharmacology*, *291*, 115106. https://doi.org/10.1016/j.jep.2022.115106

Jana, A., & Chattopadhyay, A. (2022). Prevalence and potential determinants of chronic disease among elderly in India: Rural-urban perspectives. *PLoS ONE*, *17*(3 March), 93–99. https://doi.org/10.1371/journal.pone.0264937

Jo, Y. H., Yeon, S. W., Ahn, J. H., Turk, A., Liu, Q., Kim, M.-O., Hwang, B. Y., Park, S.-Y., & Lee, M. K.

(2023). Polyacetylenes from the adventitious roots of Centella asiatica with glucose uptake stimulatory activity. *Journal of Biotechnology*, *368*, 53–59. https://doi.org/10.1016/j.jbiotec.2023.04.006

Kazeminia, M., Salari, N., Vaisi-Raygani, A., Jalali, R., Abdi, A., Mohammadi, M., Daneshkhah, A., Hosseinian-Far, M., & Shohaimi, S. (2020). The effect of exercise on anxiety in the elderly worldwide: a systematic review and meta-analysis. *Health and Quality of Life Outcomes*, *18*(1), 363–372. https://doi.org/10.1186/s12955-020-01609-4

Kothiyal, S. C., Saklani, S., & Mathur, A. (2021). Study on nutritional and phytochemical profile of seven edible food supplements of Uttarakhand (Garhwal Himalaya). *Vegetos*, *34*(3), 678–683. https://doi.org/10.1007/s42535-021-00241-x

Kunjumon, R., Johnson, A. J., & Baby, S. (2022). Centella asiatica: Secondary metabolites, biological activities and biomass sources. *Phytomedicine Plus*, *2*(1), 100176. https://doi.org/10.1016/j.phyplu.2021.100176

Mascarelo, A., Alves, A. L. S., Hahn, S. R., Doring, M., & Portella, M. R. (2023). Incidence and risk factors for polypharmacy among elderly people assisted by primary health care in Brazil. *BMC Geriatrics*, *23*(1), 606–612. https://doi.org/10.1186/s12877-023-04195-4

Müller, V., Albert, A., Barbro Winkler, J., Lankes, C., Noga, G., & Hunsche, M. (2013). Ecologically relevant UV-B dose combined with high PAR intensity distinctly affect plant growth and accumulation of secondary metabolites in leaves of Centella asiatica L. Urban. *Journal of Photochemistry and Photobiology B: Biology*, *127*(1), 161–169. https://doi.org/10.1016/j.jphotobiol.2013.08.014

Nicolas, A. N., & Plunkett, G. M. (2009). The demise of subfamily Hydrocotyloideae (Apiaceae) and the re-alignment of its genera across the entire order Apiales. *Molecular Phylogenetics and Evolution*, *53*(1), 134–151. https://doi.org/10.1016/j.ympev.2009.06.010

Nikolich-Žugich, J., Goldman, D. P., Cohen, P. R., Cortese, D., Fontana, L., Kennedy, B. K., Mohler, M. J., Olshansky, S. J., Perls, T., Perry, D., Richardson, A., Ritchie, C., Wertheimer, A. M., Faragher, R. G. A., & Fain, M. J. (2016). Preparing for an aging world: Engaging biogerontologists, geriatricians, and the society. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, *71*(4), 435–444. https://doi.org/10.1093/gerona/glv164

Orhan, I. E. (2012). Centella asiatica (L.) Urban: From traditional medicine to modern medicine with neuroprotective potential. *Evidence-Based Complementary and Alternative Medicine*, *2012*, 946259. https://doi.org/10.1155/2012/946259

Othman, Z. S., Maskat, M. Y., Mobarak, N. N., Khalid, R. M., Zahari, S. M. S. N. S., & Hassan, N. H. (2023). Utilization of triethylammonium hydrogen sulphate-mediated solvent for optimization of asiaticoside extraction and antioxidant capacity of Centella asiatica (L.). *Journal of King Saud University-Science*, *35*(8). https://doi.org/10.1016/j.jksus.2023.102863

Oyenihi, A. B., George, T. T., Oyenihi, O. R., Obilana, A. O., & Opperman, M. (2023). Three decades of research on Centella asiatica: Insights and future trends from bibliometric analysis. *Journal of Herbal Medicine*, *39*, 100662. https://doi.org/10.1016/j.hermed.2023.100662

Puttarak, P., Dilokthornsakul, P., Saokaew, S., Dhippayom, T., Kongkaew, C., Sruamsiri, R., Chuthaputti, A., & Chaiyakunapruk, N. (2017). Effects of Centella asiatica (L.) Urb. on cognitive function and mood related outcomes: A Systematic Review and Meta-analysis. *Scientific Reports*, *7*(1), 234–244. https://doi.org/10.1038/s41598-017-09823-9

Rohini, M. R., & Smitha, G. R. (2022). Studying the effect of morphotype and harvest season on yield and quality of Indian genotypes of Centella asiatica: A potential medicinal herb cum underutilized green leafy vegetable. *South African Journal of Botany*, *145*(1), 275–283. https://doi.org/10.1016/j.sajb.2021.11.024

Sabaragamuwa, R., Perera, C. O., & Fedrizzi, B. (2018). Centella asiatica (Gotu kola) as a neuroprotectant and its potential role in healthy ageing. *Trends in Food Science and Technology*, *79*, 88–97. https://doi.org/10.1016/j.tifs.2018.07.024

Seong, E., Heo, H., Sang Jeong, H., Lee, H., & Lee, J. (2023). Enhancement of bioactive compounds and biological activities of Centella asiatica through ultrasound treatment. *Ultrasonics Sonochemistry*, *94*, 106353. https://doi.org/10.1016/j.ultsonch.2023.106353

Singh, S., Singh, D. R., Banu, V. S., & Avinash, N. (2014). Functional constituents (micronutrients and phytochemicals) and antioxidant activity of Centella asiatica (L.) Urban leaves. *Industrial Crops and Products*, *61*, 115–119. https://doi.org/10.1016/j.indcrop.2014.06.045

Sofianti, M., Sunandar, A., & Qurbaniah, M. (2024). Development of Encyclopedia Learning Media Based on Local Vegetables as An Innovative Biology Learning Resource. *Jurnal Hasil Penelitian Dan Kajian Kepustakaan Di Bidang Pendidikan,*

Pengajaran Dan Pembelajaran, *10*(3), 1024–1031. Retrieved from https://e-journal.undikma.ac.id/index.php/jurnalkependidikan/article/view/12674/6236

Sun, B., Wu, L., Wu, Y., Zhang, C., Qin, L., Hayashi, M., Kudo, M., Gao, M., & Liu, T. (2020). Therapeutic Potential of Centella asiatica and Its Triterpenes: A Review. *Frontiers in Pharmacology*, *11*(1), 16–23. https://doi.org/10.3389/fphar.2020.568032

Tambaro, S., Mitra, S., Gera, R., Linderoth, B., Wahlberg, L. U., Darreh-Shori, T., Behbahani, H., Nilsson, P., & Eriksdotter, M. (2023). Feasibility and therapeutical potential of local intracerebral encapsulated cell biodelivery of BDNF to AppNL−G−F knock-in Alzheimer mice. *Alzheimer's Research and Therapy*, *15*(1), 137–145. https://doi.org/10.1186/s13195-023-01282-x

Truong, H. T. H., Ho, N. T. H., Ho, H. N., Nguyen, B. L. Q., Le, M. H. D., & Duong, T. T. (2024). Morphological, phytochemical and genetic characterization of Centella asiatica accessions collected throughout Vietnam and Laos. *Saudi Journal of Biological Sciences*, *31*(1), 103895. https://doi.org/10.1016/j.sjbs.2023.103895

Wanasuntronwong, A., Tantisira, M. H., Tantisira, B., & Watanabe, H. (2012). Anxiolytic effects of standardized extract of Centella asiatica (ECa 233) after chronic immobilization stress in mice. *Journal of Ethnopharmacology*, *143*(2), 579–585. https://doi.org/10.1016/j.jep.2012.07.010

Xie, M., Jiang, Z., Lin, X., & Wei, X. (2024). Application of plant extracts cosmetics in the field of anti-aging. *Journal of Dermatologic Science and Cosmetic Technology*, *1*(2), 100014. https://doi.org/10.1016/j.jdsct.2024.100014

Yang, L., Marney, L., Magana, A. A., Choi, J., Wright, K., Mcferrin, J., Gray, N. E., Soumyanath, A., Stevens, J. F., & Maier, C. S. (2023). Quantification of caffeoylquinic acids and triterpenes as targeted bioactive compounds of Centella Asiatica in extracts and formulations by liquid chromatography mass spectrometry. *Journal of Chromatography Open*, *4*, 100091. https://doi.org/10.1016/j.jcoa.2023.100091