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From traditional healing to contemporary therapeutics: Phytochemistry, pharmacology, and herbal formulations of *Centella asiatica*

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ABSTRACT

Centella asiatica is a herbaceous plant of the Apiaceae family has been extensively used in traditional medicine for centuries to treat a wide range of illnesses. *C. asiatica* shows many pharmacological effects, such as antibacterial, anticancer, wound healing, neuroprotective, immunomodulatory, anti-inflammatory, hepatoprotective, insecticidal, and antioxidant properties. Phytochemicals like triterpenes and their glycosides, such as triterpenoid saponins, triterpene acids, and triterpenoid steroids, are the primary constituents of *C. asiatica*. Because of its many health advantages, *C. asiatica* is currently sold as an oral supplement and a cosmetic ingredient. The current review discusses the pharmacological properties of bioactive substances and the phytochemical analysis of plant extracts based on the literature to comprehend the mechanisms underlying the compounds' therapeutic potential. The article also describes the formulations of pharmaceutical products, their traditional uses, interactions, safety issues. This review critically evaluates current evidence and highlights research gaps and future potential applications in medicine.

1. INTRODUCTION

Medicinal plants are commonly used to treat a variety of diseases. For centuries, humans have utilized natural resources such as plants and animals as remedies for their ailments, a practice that has laid the foundation for the development of modern medicines. Malaysia, in particular, is a Southeast Asian country rich in flora and fauna. It is a multiracial nation with cultures and customs deeply influenced by several ethnic groups, primarily Malay, Indian, and Chinese. As a result, Malaysian plants have been utilized across these different cultures and customs (Liew et al., 2020). Most Malaysian ethnic groups believe that herbal products, unlike modern pharmaceuticals, are free from hazardous chemicals and adverse effects (Kim &

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Lean, 2013). Malaysia is also one of the 12 megadiverse nations in the world, exhibiting an exceptionally high level of endemism. A lot of its herbaceous plants, along with other species, are rare, because at least 25% of its tree flora can only be found in this region. Approximately 2,000 species of medicinal plants are known to offer health benefits in Malaysia (Bakar et al., 2018).

Centella asiatica (*C. asiatica*), locally known as pegaga, is a perennial plant that thrives in swampy areas across tropical and subtropical climates in India, Southeast Asia, and Malaysia. It grows predominantly in and around water, bearing small, oval fruit and small**,** fan-shaped green leaves. Its flowers range from white to light purple or pink. While the entire plant is utilized in medicine (Gohil et al., 2010), the majority of studies frequently use the stems and leaves as experimental samples to investigate its biological activities. The leaf morphology is shown in Fig. 1. According to Hamzah (2013), *pegaga* easily reproduces asexually via stolons. Zainal Abidin and Kamaruddin (2005) stated that planting *pegaga* 20 cm apart between rows and 20 cm between plants within a row is advised to ensure healthy growth. Sandy loam soil featuring high levels of organic matter and good water infiltration is optimal for its cultivation. Furthermore, Khobragade (2017) observed that while the plant can survive in soil with a pH range from 6.0 to 9.0, it exhibits substantial growth at a specific pH of 8.3.

Fig 1. The leaf morphology of *Centella asiatica*

2. TRADITIONAL USES

C. asiatica has been extensively used in traditional medicine, with the history of 2,000 years in Chinese herbal therapy and 3,000 years in Indian Ayurvedic medicine, respectively. This is known as Mandukaparni in Ayurvedic medicine and has been used to treat a variety of diseases such as elephantiasis, kidney diseases, bronchitis, asthma, and leprosy. In Chinese herbal medicine, it is primarily applied to treat leucorrhoea and toxic fever. Historically, populations in the Kra Peninsula and Java Island utilized this plant to heal wounds both internally and externally. Traditional practitioners also employed it to manage emotional disorders, such as depression, that may be linked to physiological functions. By the mid-20th century, *C. asiatica* ethanolic extract was used to treat leprosy (Samuel et al., 2022). In Malaysia, *pegaga* serves as a side dish within the Malay community, a cooling drink within the Chinese community, and as

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a tonic within the Indian community. It is commonly consumed fresh as a raw vegetable (*ulam* or salad), especially among the local Malay and Javanese populations. Among Thai and Chinese communities, it is believed to reduce "inner heat" and assist in the healing of aphthous ulcers. In India, it is a key component in the traditional summer drink *thandaayyee* and is highly valued as a brain tonic (Hashim, 2011). The Malay community also uses the leaves in herbal teas for the treatment of leprosy and rheumatism. The leaves of *pegaga* that are heated until crisp, or juice mixed with food, are administered to alleviate diarrhea in children. Additionally, *pegaga* leaves are widely believed to offer restorative benefits for postpartum mothers.

3. PHYTOCHEMISTRY

C. asiatica contains a wide range of phytoconstituents, mainly triterpenoids, flavonoids, phenolic acids, and vitamins. Its major compounds include asiaticoside, asiatic acid, madecassoside, madecassic acid, centelloside, quercetin, kaempferol, chlorogenic acid, rutin, ferulic acid, coumarin, and ascorbic acid. These bioactive compounds contribute significantly to its antioxidant, anti-inflammatory, wound-healing, and neuroprotective properties (Gray et al., 2018; Sun et al., 2020). According to a study by Kotagiri and Chaitanya (2017), leaf extracts contain higher concentrations of secondary metabolites than stem extracts, including tannins, phenols, flavonoids, saponins, anthraquinones, lignins, terpenes, and alkaloids. Another study by Polash et al. (2017) similarly showed that leaf extracts contain more tannins, flavonoids, saponins, phenols, and glycosides than stem extracts. The important chemical constituents are depicted in Fig. 2.

Over the decades, the phytochemistry of *C. asiatica* and its extraction methods have been extensively studied. Rafi et al. (2018) developed a reliable method for identifying and classifying *C. asiatica* based on cultivation age. They concurrently examined four triterpenes (madecassoside, asiaticoside, madecassic acid, and asiatic acid) from the methanol extract of *C. asiatica* using high-performance liquid chromatography (HPLC). The concentration of these triterpenes varied among *C. asiatica* samples depending on whether they were collected 3, 4, or 5 months after planting. Monton et al. (2019) optimized *C. asiatica* dynamic maceration using response surface methodology (RSM) to achieve high content of asiatic acid, madecassic acid, asiaticoside, and madecassoside. The content of the four centelloids was observed, and its correlation with the two factors, which are extraction temperature and extraction time, was studied. The simultaneous greatest content of four centelloids was attained at both high and low temperature/time. Mohammad Azmin and Mat Nor (2020) investigated the chemical fingerprints of six bioactive components of *C. asiatica* in ethanolic and aqueous ethanol extracts: kaempferol, quercetin, luteolin, gallic acid, rutin, and catechin. Through maceration extraction and subsequent HPLC analysis, they determined that kaempferol was the predominant bioactive ingredient, with a concentration of 373.2 mg/g dry powder in the 100% ethanolic extract. According to Idris et al. (2020), optimal parameters for the extraction process were determined using the Taguchi method on *C. asiatica*, which included factors such as microwave power, extraction time, vacuum pressure, and stirring rate. The highest concentration of extracted asiaticoside was 158.8 µg/mL. On comparison between traditional methods of extraction and those of modern times, Mohapatra et al. (2021) found microwave-assisted extraction using methanol to be the best method. This method allowed identification of eight compounds in *C. asiatica*, namely, asiaticoside, madecassoside, rutin, quercetin, kaempferol, madecassic acid, asiatic acid, and chlorogenic acid. Abu Bakar et al. (2022) have studied the antioxidant activity, total phenolic content (TPC), and

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bioactive constituents of various types of *C. asiatica*, such as *Pegaga Kampung*, *Pegaga Nyonya*, Pegaga Salad, and Pegaga Thailand. Out of all these varieties, the Pegaga Kampung showed TPC (9.22 mg GAE/g) and asiaticoside concentration (0.259 mg/g), thus signifying better antioxidant potential.

Furthermore, Kumari et al. (2022) optimized the ultrasound-assisted extraction process for asiaticoside from *C. asiatica* leaves employing RSM and Artificial Neural Networks (ANNs) in order to design effective prediction models. The asiaticoside was quantified using a mobile phase composed of butanol, ethyl acetate, and water (4:1:5). Based on their results, the predicted yield was highly comparable to the experimentally determined yield. Yuan et al. (2023) used tandem mass spectrometry in conjunction with high-performance liquid chromatography (HPLC-MS/MS) o develop a novel and quick approach for identifying four bioactive components of *C. asiatica* extracted using a supramolecular solvent (SUPRAS). Hydrogen bond interactions and dispersion were the driving reasons behind the herb extraction process in the SUPRAS. With HPLC-MS/MS, the innovative SUPRAS approach has shown itself to be sensitive, effective, and environmentally friendly.

For the first time, betaine-based natural deep eutectic solvents (NADES) were utilized in the ultrasound-assisted extraction (UAE) of asiaticoside from *C. asiatica* by Mohd Fuad and Mohd Nadzir (2023). A betaine-levulinic acid (Bet-Lev) at a molar ratio of 1:2 and a water content of 30% w/w was found to be the most effective solvent for extracting asiaticoside. An extraction yield of 229.92 ± 1.67 mg/g was obtained by using optimized extraction parameters including extraction time of 32 minutes, extraction temperature of 36°C, ultrasonic power of 140 W, and L/S ratio of 49 mL/g. The impact of ultrasonic treatment for varying durations on the bioactive components and biological activities of *C. asiatica* leaves was examined by Seong et al. (2023). The accumulation of stress indicators was significantly increased by ultrasound elicitation, especially for ten minutes, which resulted in increased phenolic-triggering enzyme activities. When compared to leaves that were not treated, the accumulation of secondary metabolites and antioxidant activities were also noticeably enhanced. The phytochemicals present in different extracts of *C. asiatica* are shown in Table 1.

Alqahtani et al. (2015) investigated how the primary triterpenoid and phenolic component concentrations in *C. asiatica* are affected by the harvesting time. Australian *C. asiatica* was harvested over several months from a specific location. Using HPLC-DAD analysis, the main triterpenes, flavonoid compounds, and chlorogenic acid were quantitatively identified. The findings showed that the highest yield of the target triterpenoids is obtained when *C. asiatica* is harvested in the summer. In another study, Quyen et al. (2020) evaluated the phytochemical profile, TPC, TFC, and antioxidant activities of *C. asiatica* leaves. The ethanolic extract shows TPC and TFC were 2.14 ± 0.29 mg GAE/g and 23.03±2.89 mg QE/g, respectively. The extraction methods using ethanolic and water resulted in varied TPC: 2.14 ± 0.29 (mg GAE/g) and 2.82 ± 1.68 (mg GAE/g), respectively (Quyen et al., 2020). Minarti et al. (2021) stated that the aerial parts of *C. asiatica* possess antidiabetic effects. Bioassay-guided fractionation was employed to identify the bioactive crude fractions demonstrating α-glucosidase inhibitory activity. The *C. asiatica* ethyl acetate fraction exhibited the highest TPC and TFC, measuring 14.41 ± 0.02 mg GAE/g extract and 48.43 ± 0.05 mg QE/g extract, respectively.

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Table 1. Comparison of different extraction, analytical methods and identified compounds of *C. asiatica.*

Extraction methods	Solvent extracts	Analytical methods	Key compounds	References
Ultrasonication	70% ethanol	Potentiostat/ galvanostat	Chlorogenic acid, kaempferol.	Leite et al. (2018)
Maceration	70% ethanol	LC-MS/ GC-MS	Asiaticoside, madecassic acid, asiatic acid.	Zakaria et al. (2019)
Maceration	Methanolic extract	LC-MS	Alkaloid Flavonoid Glycosides Coumarin, lignans, Phenolic acid Phytosterols Stigmasterol Lipids Saturated Fatty Acid	Ondeko et al. (2020)
		GC-MS	Alkaloid, Flavonoid Glycosides, Coumarin, Lignans, Todolactol A, Phenolic Acid, Phytosterols, Saturated Fatty Acid Stilbenes Triterpene Glycoside	
Microwave assisted extraction	Ethanol solution	HPLC	Asiatic acid, madecassic acid, asiaticoside and madecassoside.	Yingngam et al. (2020)
Microwave assisted extraction	80% ethanol	RSM	Madecassoside (7.332 ± 0.386% w/w), asiaticoside (4.560 ± 0.153% w/w), madecassic acid (0.357 ± 0.013% w/w), and asiatic acid (0.209 ± 0.025% w/w).	Thong-on et al. (2021)
Ultrasound assisted extraction			Madecassoside (2.262 ± 0.046% w/w), asiaticoside (1.325 ± 0.062% w/w), madecassic acid (0.082 ± 0.009% w/w) and asiatic acid (0.052 ± 0.007% w/w)	
Ultrasound assisted extraction	Methanol extract	UHPLC-MS/MS	Chlorogenic acid, madecassoside, asiaticosside, madecassic acid, asiatic acid.	Sabaragamuwa et al. (2022)
-	Centevita® (hydroalcoholic solvents extract)	LC-MS	Quercetin 3-O- glucuronide, Madecassoside, Centellasaponin B, Isoterminoloside, Isoasiaticoside, Asiaticoside, Quercetin, Centella saponin C, Kaempferol, Isorhamnetin, Asiaticoside C, Asiaticoside F, Terminolic, Madecassic acid, Asiatic acid.etc.	Masi et al. (2022)
Reflux	Methanol extract	HPLC	4′-hydroxyl-7-methoxyl-6-prenyl-3-O-trans-p-coumaroyl-flavonol, (2R,3R,2″S)-3-furanoyl- brosimacutin E, (-)-epigallocatechin 3-O-p-coumaroate, pinobanksin-3-propanoate, kaempferol, pachypodol, coryaurone A.	Zheng et al. (2022)

https://doi.org/10.24191/IJPNaCS.v9i1.09

Sonication	Ethanol and methanol mixture	FT-ICR MS	Caffeic acid, Glucose, Quinic acid, Ferulic acid, Sedoheptulose, Kaempferol, Epicatechin, Quercetin, Chlorogenic acid, Kaempferol-3-O-glucoside, Asiatic acid, Kaempferol 3-O-acetyl-glucoside, Raffinose, Madecassic acid, Asiaticoside, Madecassoside	Islam et al. (2022)
Maceration	Methanol	LC-MS	Alkaloid, Stilbenes, Resveratol 3-O-glucoside, Triterpene Glycoside	Kandasamy et al. (2023)

4. PHARMACOLOGICAL PROPERTIES

The various phytochemicals found in *C. asiatica* have led to numerous medical applications for this plant. For example, madecassoside, asiatic acid, and asiaticoside are antioxidants that neutralize free radicals and minimize oxidative damage (Bandopadhyay et al., 2023). This property is beneficial in preventing the onset of neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease. Furthermore, the phytochemicals found in this herb inhibit the formation of pro-inflammatory cytokines and enhance neuronal survival, thereby protecting the central nervous system from harm. Elevated levels of monoamine neurotransmitters n this herbal plant can cause antidepressant-like effects.

Madecassoside has been linked to vitiligo as a potentially effective treatment (Ling et al., 2017). It has also been shown to significantly shield the skin against inflammatory acne. Additionally, asiaticoside promotes angiogenesis during skin wound regeneration, which improves burn wound healing (Hou et al., 2016). Madecassoside and asiaticoside contribute to improved wound healing and a reduction in keloid scarring (Park, 2021). When these substances are applied topically, hyperpigmentation, photoaging of the skin, cellulite, striae, and periocular wrinkles all improve. Madecassoside has demonstrated both medicinal and cosmetic benefits, significantly improving skin hydration and moisturization both *in vitro* and *in vivo* (Bandopadhyay et al., 2023). It has been established that madecassoside significantly reduces the production of pro-inflammatory cytokines, such as TLR2 and IL-1β, which are secreted by *Propionibacterium acnes* (*P. acnes*) in stimulated THP-1 human monocytic cells (Park, 2021) . Additional characteristics, such as cardioprotective benefits, have also been reported. Numerous investigations have revealed that asiatic acid, a major *C. asiatica* triterpene, protects cardiomyocytes by modulating key signaling pathways that are implicated in the etiology of myocardial ischemia and cardiac hypertrophy (Yi et al., 2022). Moreover, asiatic acid reduces intracellular calcium ion levels, inhibits the overproduction of reactive oxygen species, and improves mitochondrial membrane potential to mitigate mitochondrial dysfunction (Huang et al., 2016). The antimicrobial activities of *C. asiatica* have also been documented against a variety of bacteria, including *Vibrio cholerae*, *Shigella* species, *Bacillus subtilis*, *Proteus vulgaris*, and *Staphylococcus aureus*. Even against bacteria like *B. cereus* and *Listeria monocytogenes* that can withstand extreme osmotic stress, *C. asiatica* demonstrated potent antibacterial properties (Sieberi et al., 2020).

Diabetes mellitus (DM) is a metabolic condition in which the insulin hormone fails to properly regulate carbohydrate, protein, and fat metabolism, raising fasting and postprandial blood glucose levels. Retinopathy, neuropathy, nephropathy, atherosclerotic coronary artery disease, and peripheral

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atherosclerotic vascular disease are the main chronic complications associated with diabetes. *C. asiatica* may exert antidiabetic effects by suppressing inflammatory processes, increasing glutathione and catalase levels, and lowering reactive oxygen species (Setyaningsih et al., 2021). Moreover, it binds to the 5′ upstream element of the peroxisome proliferator response, thereby activating peroxisome proliferator-activated receptor **γ** (PPARγ). Although the precise mechanism remains to be fully clarified, this process enhances insulin sensitivity. The various reported biological activities of *C. asiatica* are summarized in Table 2.

5. TOXICOLOGY STUDIES

Apart from the efficacy and quality of drugs, safety is also one of the three aspects of effective medicines regulation (World Health Organization [WHO], 2003). In addition to conventional drug products, herbal and traditional medicines must meet strict safety requirements before they are marketed. In general, toxicity studies are meant to assess the adverse effects of a substance on a living organism (Prasesti & Kurniati, 2022). From toxicological data, researchers can generate dose-response curves to ascertain the optimal dosage suitable for human consumption (Chinedu, 2013).

Pingale (2008) studied the acute toxicity of *C. asiatica* at oral doses of 3, 5, and 7 g/kg body weight (bw). Swiss mice were given a single dose of the entire plant powder in the form of an aqueous slurry. According to the study's findings, the animals in all dose groups did not exhibit any changes in bw, food intake, or water consumption. The fact that no mortality was noted even at the maximum dosage of 7 g/kg bw indicates that the plant powder has no discernible toxic effects on mice (Pingale, 2008). Oruganti et al. (2010) evaluated the safety of *C. asiatica* in albino rats following oral dosing for 30 days. The apoptotic index and serum indicators (alanine aminotransferase [ALT], aspartate aminotransferase [AST], blood urea nitrogen [BUN], and creatinine) significantly increased at the highest dose. Cell viability counts significantly decreased in the treatment groups compared to the control group. Additionally, a mild degree of alterations in renal tissue and considerable hepatic damage were found via histopathological examination. It was determined that giving rats *C. asiatica* at a dose of 1,000 mg/kg bw for 30 days may seriously harm their liver tissue (Oruganti et al., 2010).

Deshpande et al. (2015) assessed the acute oral toxicity, sub-chronic toxicity, and mutagenic potential of a standardized extract of *C. asiatica* leaves. The extract of *C. asiatica* leaves had a lethal dose of 2000 mg/kg and a level of no-observed-adverse-effect level (NOAEL) of 1000 mg/kg, respectively. When comparing the treatment groups to the control group, there were no appreciable variations in the gross microscopic appearance of the organs, hematological parameters, clinical chemistry values, or organ weights. Using the reverse mutation experiment, it was determined to be nonmutagenic (Deshpande et al., 2015). Following the *in vivo* acute and sub-acute injection of ethanolic extracts from *E. alsinoides* and *C. asiatica*, Yadav et al. (2019) extensively examined the general behavior, clinical symptoms of of toxicity, body weight, food and water consumption to evaluate the toxicological consequences. In acute and sub-acute toxicity studies, it is discovered that extracts from *E. alsinoides* and *C. asiatica*, at varying concentrations, do not result in fatality. Furthermore, histology of the kidney, liver, heart, and brain revealed no changes to the morphology of the tissues (Yadav et al., 2019).

https://doi.org/10.24191/IJPNaCS.v9i1.09

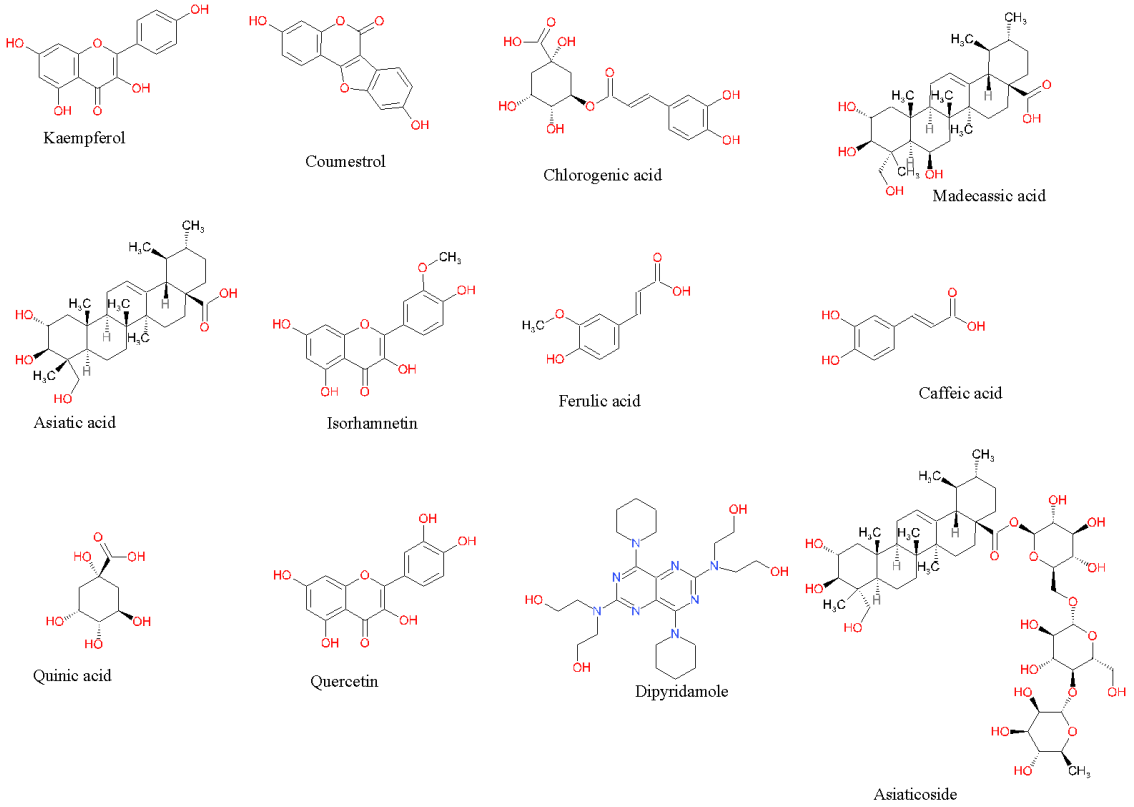

Fig 2. Some of the important chemical constituents found in *C. asiatica*.

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Table 2. The different biological activities reported in *C. asiatica*

Pharmacological properties	Extract/constituents	Application field	Mode of action	References
Antioxidant & anti-inflammatory	Methanol extract	Anti-arthritis	Reduces the expression of cytokines, joint inflammation, and antioxidant imbalance.	Sharma et al. (2014)
	Methanol extract	Hepatoprotective agent	Mechanism of lipid peroxidation	Dwijayanti et al. (2015)
	Methanol extract	Drug toxicity	Reduce the expression of cytokines that promote inflammation and boost those that reduce it.	Viswanathan et al. (2019)
	-	Psoriasis	Reduce the expression of inflammatory factors' mRNA (IFN-γ, CCL20, IL-6, and TNFα) while increasing the expression of factors that protect barriers (AQP3 and FLG).	Lin et al. (2023)
	-	Wound healing	Reduce wound oxidative stress, encourage angiogenesis, stimulate collagen formation, inhibit inflammation, and cause vasodilation.	Balevi & Balevi (2023)
	Ethanolic callus extract	Anti-aging agent	Increase expression of antioxidant enzymes within cells and decrease activation of matrix metalloprotease 9	Buranasudja et al. (2021)
Neuroprotective	Ethanol extract	Alzheimer's disease	Reduces the neurotoxicity caused by Aβ in differentiated PC12 and IMR32 cells by strengthening their antioxidative defense mechanism.	Chen et al. (2016)
	Asiaticoside	Multiple sclerosis	Limit the synthesis of nitric oxide and TNFα in primary microglia and astrocyte cultures triggered by lipopolysaccharide (LPS).	Madhu & Prabha (2018)
	ECa233	Parkinson disease	Protect mitochondrial complex I, reduce lipid peroxidation, and increase the expression of antioxidant enzymes.	Teerapattarakan et al. (2018); Doulah et al. (2020)
	-	Alzheimer's disease	Reduce the concentration of acetylcholinesterase and avoid the oxidative stress and cognitive disruption caused by colchicine.	Doulah et al. (2020)
	Asiaticoside	Vascular Dementia	Activate the mTOR (mechanistic target of rapamycin) pathway and inhibit autophagy.	Guo et al. (2021)
Antimicrobial	Ethanolic extract	Antibacterial	Inhibition of energy metabolism, cytoplasmic membrane function, and nucleic acid synthesis	Pitinidhipat & Yasurin (2012)
	Methanol extract	Anti-fungal	Effects of antifungals that demelanize *A. niger* and immunomodulatory actions in RAW264.7 macrophage cells.	Mahmud et al. (2020)
	Ethanol extract	Anti-acne	Diminishes bacterial cell walls and decreases membrane permeability by forming complexes with bacterial cell proteins.	Awaluddin et al. (2022)
	Silver nanoparticles from *C. asiatica* extracts	Anti-HIV agent	Diminished levels of HIV-1 p24, IL-6, TNF-α, IL-1β, and NF-κB gene expression HIV-1.	Maduray et al. (2022)
Antidiabetic	-	Diabetes	Restore the damaged pancreatic β-cells and encourage the production of insulin.	Rahman et al. (2011)
	Asiatic acid	Diabetes	β-cell regeneration and altered hepatic enzymes in charge of glucose metabolism.	Ramachandran & Saravanan (2013)

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	-	Diabetes	Inhibit α-amylase, intestinal disaccharidase, and glucose-fiber binding.	Kabir et al. (2014)
	Ethanol extract	Diabetes	Restore alterations in the levels of the enzymes involved in the metabolism of carbohydrates, inhibit lipid peroxidation, boost antioxidant levels, and raise the enzymes involved in the metabolism of fat.	Muhlishoh et al. (2019)
	Ethanol extract	Diabetes	Modifying aryl hydrocarbon receptor signaling in mice exposed to bisphenol A to lessen the disruption of pancreatic endocrine function.	Banerjee et al. (2023)
Cardioprotective	Ethanolic extract	Thrombosis	Inhibit platelet aggregation	Lestari et al. (2016)
	Asiatic acid	Atherosclerosis	Anti-hyperpermeability agent that prevented TNF-α-induced structural rearrangement of vascular endothelial cells and stabilized F-actin, β-catenin and cadherin.	Fong et al. (2019)
	Ethanol extract	Hypertension	By downregulating the expression of $p47^{phox}$, scavenge reactive oxygen species and prevent the overproduction of O_2 in aortic tissue and plasma MDA.	Bunaim et al. (2021)
	-	Cardiac hypertrophy	Modifying several pathways, primarily those related to processes that are anti-inflammatory, antioxidant, and anti-apoptotic.	Ding et al. (2022)
	Asiaticoside	Myocardial ischemia	Apoptotic protein expression was downregulated, and PI3K, AKT, and GSK3β phosphorylation were increased.	Zeng et al. (2022)

Toxicological data compiled on *C. asiatica* were also reviewed by Prasesti and Kurniati (2022). Most studies demonstrated a high degree of safety for *C. asiatica*. Even at a dose of 7,000 mg/kg, *C. asiatica* juice did not exhibit any harmful effects in whole-plant studies. Oral doses of 250 mg and 500 mg of *C. asiatica* extract were well tolerated in single and repeated clinical tests. With few adverse effects recorded and a high level of safety, *C. asiatica* is a promising candidate for therapeutic development (Prasesti & Kurniati, 2022). A safe therapeutic window of *C. asiatica* is defined as the amount of the substance that results in beneficial effects but does not lead to significant toxicity. In general, the recommended human dosage is 60–120 mg/day of purified standardized extract or 600–1,800 mg/day of powdered dried herb (National Center for Biotechnology Information [NCBI], 2024). According to clinical studies, the tolerability of the standardized extract at dosages of 250 mg and 500 mg per day in single and multiple doses was satisfactory; patients experienced only mild side effects such as headache, nausea, dizziness, bloating, and slight gastrointestinal symptoms (Songvut et al., 2021). At the same time, isolated cases of hepatotoxicity after prolonged use of *C. asiatica* were reported. Consequently, short-term use in low to moderate doses is recommended (NCBI, 2024). In animals, the dosage of *C. asiatica* ranges from 100 to 300 mg/kg/day when investigating its antioxidant, anti-inflammatory, neuroprotective, and nephroprotective properties (Kotagiri & Chaitanya, 2017).

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6. HERBAL DRUGS AND FORMULATIONS

As previously mentioned, *C. asiatica* has been shown to exhibit neuroprotective effects. However, the delivery of the active phytocompounds to the brain poses significant challenges due to poor permeability across the blood–brain barrier (BBB). Using nanotechnology, researchers may be able to enhance the lipophilicity of *C. asiatica* extract and improve absorption into the central nervous system as well as other sites of pharmacological action. In some studies, nanoformulations have also been utilized to improve the bioavailability and pharmacological effects of *C. asiatica* extract.

Fard et al. (2018) synthesized green silver nanoparticles (AgNPs) from *C. asiatica* leaf extract and they examined the effects of these nanoparticles on MCF-7 breast cancer cell line cytotoxicity and apoptosis induction. In MCF-7 cancer cells, biosynthesised AgNPs demonstrated concentration- and time-dependent cytotoxicity, anti-cancer, apoptosis induction, and enhanced expression of genes encoding for caspases 3 and 9 (Fard et al., 2018). The extract of *C. asiatica* has a modest skin absorption rate while being highly soluble in water. To overcome this, Lala et al. (2019) created a water-in-oil nanoemulsion loaded with *C. asiatica* extract. They optimized and assessed the nanoemulsion's potential as a delivery system for the treatment of photoaging. When compared to an aqueous solution of *C. asiatica* extract, the nanoemulsion formulations showed a considerable increase in permeability parameters. When applied topically to the hindlimbs of rats, a cream containing the *C. asiatica* nanoemulsion significantly decreased the formation of wrinkles on their UV-exposed skin (Lala et al., 2019).

Nowadays, polymer–drug conjugates are being developed to effectively penetrate the central nervous system for the treatment of neurological disorders. A polymer hybrid nasal nanocomposite was created by Haroon et al. (2021b) to improve *C. asiatica* distribution to the central nervous system. EDAC hydrochloride was used to complex thiolated chitosan with *C. asiatica* to form the composite. At 8 hours, the nanocomposite exhibited good permeation across the nasal mucosa and no signs of nasal ciliotoxicity. The nanocomposite was found to be less cytotoxic than the free drug, according to the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay (Haroon et al., 2021b). Asiaticoside, which is present in *C. asiatica*, has been shown to dissolve amyloid protein *in vitro* but has no impact *in vivo*. Brain-targeted polymers were used by Haroon et al. (2021a) to create a nasal formulation of *C. asiatica* that circumvents the BBB and increases brain penetration. At 8 hours, the nanoparticles showed no signs of nasal ciliotoxicity and a satisfactory penetration rate. The MTT assay showed that, in comparison to the free drug, the nanocomposite exhibited improved permeability and decreased toxicity (Haroon et al., 2021a). The possibility of creating a *C. asiatica* nanoemulsion (NanoSECA) with a D-optimal mixture design for improved brain bioavailability was investigated by Jusril et al. (2022). The *in vitro* acetylcholinesterase (AChE) inhibitory, antioxidant, anti-inflammatory, and parallel artificial membrane permeability assay (PAMPA) properties of NanoSECA were noteworthy. Improvements in cell viability were observed on SH-SY5Y and RAW 264.7 cell lines in a dose-dependent manner. Additionally, NanoSECA demonstrated strong experimental permeability across the BBB. The phytopharmaceutical products containing *C. asiatica* are listed in Table 3.

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Table 3. The phytopharmaceutical products containing *C. asiatica*.

Name of products	Dosage form	Main ingredients as labeled	Claims
Solgar Standardized Gotu Kola Aerial Extract Vegetable Capsules	Capsules	Standardized Gotu Kola extract (aerial) (triterpene glycosides 6 mg)	• Helps improve metabolism, combat venous insufficiency and cellulite. • Improves connective tissue structure. • Decreases cellulite formation and appearance • Strengthens blood vessel wall cells • Can be used as an adjunct to venous insufficiency, leg ulcers and cellulitis
Gotu Kola 425mg 100 Capsules Nature's Sunshine	Capsules	*C. asiatica* herb powder	• Support the nervous system • Help the body adapt to stress • Improve memory and cognition • Brain tonic
Asiatic spark 90 tablets of 500mg Naturmil	Tablets	*C. asiatica* leaf	• Improves the appearance of the skin by normalizing the production of collagen fibers • Prevents the accumulation of fat and fluid retention. • Eliminates fibrosis and fight localized fat
Pegaga By PurelyB	Fine powder	Pegaga (Gotu Kola)	• Helps to ease skin conditions like eczema & acne • Strengthen immunity & energy • Improve gut health & digestion • Calm & reduce stress, anxiety • Anti-Inflammation & ease allergies
Oomph Pegaga Extract (*C. asiatica* extract) 230g	Liquid	Pegaga extract	• Natural botanical energizer • Supports healthy immune function • Promotes healthy circulation
Kiehl's Centella Sensitive Cica-Cream	Cream	Madecassoside	• Repairs and protects skin's barrier while intensively moisturizing skin. • Visibly reduces skin redness and dry fine lines after 3 days of use. • Clinically-demonstrated to help repair the moisture barrier of compromised skin.
COSRX Centella Blemish Cream	Cream	*C. asiatica* leaf water	• Reduces redness and irritation. • Prevents acne marks and post acne hyperpigmentation (PIE). • Helps skin barrier to recover and replenish.
Purito Centella Unscented Toner	Toner	*C. asiatica* extract	• Reduces redness and irritation. • Prevents acne marks and post acne hyperpigmentation (PIE). • Helps skin barrier to recover and replenish.
Allies Liquid Panacea Centella Kombucha Firming Recovery Booster	Serum	*C. asiatica* leaf extract	• Firms and soothe skin • Provide antioxidant protection

Disclaimer Table 3: Claims are based on manufacturer labelling and may not be clinically validated.

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7. CONCLUSION

In summary, because of this plant's remarkable therapeutic potential, further thorough investigation is warranted given its effectiveness and adaptability. As more herbal remedies containing *C. asiatica* enter the market, there is an increased risk of complications arising from incorrect usage, a lack of medical supervision, or potential interactions with other medications.

8. LIMITATIONS AND FUTURE MEDICAL APPLICATIONS

Although *C. asiatica* demonstrates significant therapeutic potential, several limitations restrict its wider medical application. First, there is variability in its phytochemical composition due to differences in plant varieties, growing locations, harvesting periods, and extraction methodologies. Additionally, the majority of studies conducted to date have relied on *in vitro* or animal models; hence, clinical trials in humans have not been fully explored. Consequently, further research is required to establish standard dosages, evaluate long-term effects, conduct rigorous toxicity assessments, and identify potential drug-herb interactions.

Conversely, *C. asiatica* holds immense potential for future clinical applications owing to its strong antioxidant, anti-inflammatory, wound-healing, and neuroprotective activities, which could help alleviate symptoms associated with chronic illnesses such as Alzheimer's disease, Parkinson's disease, diabetes, and dermatological disorders. Furthermore, *C. asiatica* can serve as an ingredient in the development pharmaceutical formulations such as nanoparticles, creams, capsules, and dietary supplements.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

AUTHORS' CONTRIBUTIONS

Liyana Suraya: Literature review, and writing of the original draft; **Kamran Ashraf**: Conceptualization, supervision, writing and critical revision of the manuscript.

DECLARATION OF GENERATIVE AI IN THE WRITING PROCESS

During the preparation of this work, the authors used ChatGPT (OpenAI) and Grammarly to improve language, grammar, and readability. All content was reviewed and edited by the authors, who take full responsibility for the final manuscript.

ETHICS STATEMENT

Ethical approval was not required for this study as it did not involve human subjects, animal experimentation, or collection of personal/confidential data.

REFERENCES

Abu Bakar, I. N., Mohd Fauzi, N. A., Ismail, N., Rahmat, A., & Bakar, M. F. A. (2022). Characterization of asiaticoside concentration and antioxidant activity of *Centella asiatica*. *Biocatalysis and Agricultural Biotechnology*, 44, Article 102471. https://doi.org/10.1016/j.bcab.2022.102474

Alqahtani, A., Tongkao-on, W., Li, K. M., Razmovski-Naumovski, V., Chan, K., & Li, G. Q. (2015). Seasonal variation of triterpenes and phenolics in *Centella asiatica*. Phytochemical Analysis, 26(6), 436-443. https://doi.org/10.1002/pca.2578

Awaluddin, N., Awaluddin, S. W., Awaluddin, A., & Suryani, A. I. (2022). Formulation and test of antibacterial activity of antiacne patch preparations of *Centella asiatica* leaf ethanol extract against the growth of *Propionibacterium acnes*. *Proceedings of the 2nd International Conference on Law, Social Science, Economics, and Education (ICLSSEE 2022), Semarang, Indonesia*. EAI. https://doi.org/10.4108/eai.16-4-2022.2319706

Bakar, F. I. A., Bakar, M. F. A., Abdullah, N., Endrini, S., & Rahmat, A. (2018). A review of Malaysian medicinal plants with potential anti-inflammatory activity. *Advances in Pharmacological Sciences*, 2018, Article 8603602. https://doi.org/10.1155/2018/8603602

Balevi, M., & Balevi, A. (2023). Effect of *Centella asiatica* cream on scar development after surgery. *Journal of Hand Therapy*, 36(2), 245-251. https://doi.org/10.1016/j.jht.2022.11.001

Bandopadhyay, S., Banerjee, S., Ghosh, A., Mondal, S., & Bandyopadhyay, D. (2023). Therapeutic properties of asiaticoside and madecassoside from *Centella asiatica. Journal of Cellular and Molecular Medicine*, 27(5), 593-608. https://doi.org/10.1111/jcmm.17635

Banerjee, O., Ghosh, A., Roy, S., Chatterjee, S., & Das, S. (2023). Protective efficacy of *Centella asiatica* against BPA-induced pancreatic toxicity. *Toxicology*, 500, Article 153631.

Bunaim, M. K., Kamisah, Y., Mustazil, M. N. M., Zuhair, J. S. F., Juliana, A. H., & Muhammad, N. (2021). Centella asiatica prevents hypertension and protects the heart. *Frontiers in Pharmacology*, 12, Article 772924. https://doi.org/10.3389/fphar.2021.742562https://doi.org/10.1016/j.tox.2023.153693

Buranasudja, V., Rani, D., Malla, A., Kobtrakul, K., & Vimolmangkang, S. (2021). Antioxidant and anti-skin-aging potential of *Centella asiatica* callus extract. Scientific Reports, 11, Article 15254. https://doi.org/10.1038/s41598-021-92958-7

Chen, C. L., Tsai, W. H., Chen, C. J., & Pan, T. M. (2016). *Centella asiatica* extract protects against amyloid β-induced neurotoxicity. Journal of Traditional and Complementary Medicine, 6(4), 362-369. https://doi.org/10.1016/j.jtcme.2015.07.002

Chinedu, E. (2013). The importance of toxicity testing. *Journal of Pharmaceutical Biosciences*, 4, 146-148.

Deshpande, P. O., Mohan, V., & Thakurdesai, P. (2015). Preclinical safety assessment of standardized *Centella asiatica* extract. *Toxicology International*, 22(1), 10-20. https://doi.org/10.4103/0971-6580.172251

Ding, B., Wang, Y., Liu, X., Zhang, H., Chen, L., & Zhao, Y. (2022). *Centella asiatica* attenuates cardiac hypertrophy through multi-level mechanisms. *Journal of Ethnopharmacology*, 291, Article 115145. https://doi.org/10.1016/j.jep.2022.115106

Doulah, A., Mahmoodi, G., & Borujeni, M. P. (2020). Pre-treatment effect of *Centella asiatica* on long-term potentiation in Alzheimer's rat model. *Neuroscience Letters*, 729, Article 135026.

https://doi.org/10.1016/j.neulet.2020.135026

Dwijayanti, A., Frethernety, A., Hardiany, N. S., & Purwaningsih, E. H. (2015). Hepatoprotective effects of Acalypha indica and *Centella asiatica* against hypoxia. *Procedia Chemistry*, 14, 11-14. https://doi.org/10.1016/j.proche.2015.03.003

Minarti, Megawati, & Fajriah, S. (2021). Total phenolic, total flavonoid content, and α-glucosidase inhibitory activity of *Centella asiatica* (L.) Urb. *Proceedings of the 2nd International Conference on Contemporary Science and Clinical Pharmacy 2021 (ICCSCP 2021)*, 222–226. https://doi.org/10.2991/ahsr.k.211105.033

Fard, S. E., Tafvizi, F., & Torbati, M. B. (2018). Silver nanoparticles biosynthesised using *Centella asiatica* leaf extract induce apoptosis in MCF-7 cells. *IET Nanobiotechnology*, 12(7), 994-1002. https://doi.org/10.1049/iet-nbt.2018.5069

Fong, L. Y., Ng, C. T., Yong, Y. K., Hakim, M. N., & Ahmad, Z. (2019). Asiatic acid stabilizes cytoskeletal proteins and protects vascular endothelial cells. *Vascular Pharmacology*, 117, 15-26. https://doi.org/10.1016/j.vph.2018.08.005

Gohil, K. J., Patel, J. A., & Gajjar, A. K. (2010). Pharmacological review on *Centella asiatica*: A potential herbal cure-all. *Indian Journal of Pharmaceutical Sciences*, 72(5), 546-556. https://doi.org/10.4103/0250-474X.78519

Gray, N. E., Magana, A. A., Lak, P., Wright, K. M., Quinn, J., Stevens, J. F., & Soumyanath, A. (2018). *Centella asiatica*: Phytochemistry and mechanisms of neuroprotection and cognitive enhancement. *Phytochemistry Reviews*, 17(1), 161-194. https://doi.org/10.1007/s11101-017-9528-y

Guo, M., Xu, J., Wang, S., & Dong, B. (2021). Asiaticoside improves memory through regulation of the mTOR pathway. *Molecular Medicine Reports*, 24(3), Article 1-8. https://doi.org/10.3892/mmr.2021.12284

Hamzah, N. M. (2013). Growth and yield performance of Pegaga (*Centella asiatica*) to different types of organic fertilizer and levels of planting media. In Konferensi Akademik (KONAKA) (pp. 163-168).

Haroon, H. B. B., Mukherjee, D., & Jayaraman, A. (2021a). Brain-targeted intranasal formulation of *Centella asiatica* for Alzheimer's disease. *Alzheimer's & Dementia*, 17(S9), Article e057168. https://doi.org/10.1002/alz.053363

Haroon, H. B. B., Mukherjee, D., Anbu, J., & Teja, B. V. (2021b). Thiolated chitosan-*Centella asiatica* nanocomposite as a brain targeting strategy. *AAPS PharmSciTech*, 22(8), Article 251. https://doi.org/10.1208/s12249-021-02131-6

Hashim, P. (2011). *Centella asiatica* in food and beverage applications and its antioxidant potential. *Journal of Medicinal Plants Research*, 5(18), 4368-4372.

Hou, Q., Li, M., Lu, Y. H., Liu, D. H., & Li, C. C. (2016). Burn wound healing properties of asiaticoside and madecassoside. *Experimental and Therapeutic Medicine*, 12(3), 1269-1274. https://doi.org/10.3892/etm.2016.3459

Huang, X., Wang, Y., Zhang, Z., Ma, X., Liu, Y., & Wang, H. (2016). Asiatic acid attenuates myocardial ischemia/reperfusion injury via Akt/GSK-3β/HIF-1α signaling. *Molecules*, 21(9), Article 1243. https://doi.org/10.3390/molecules21091248

Idris, F. N., Nadzir, M. M., & Abd Shukor, R. S. (2020). Optimization of solvent-free microwave extraction of Centella asiatica using response surface methodology. Journal of Environmental Chemical Engineering, 8(3), Article 10 3766. https://doi.org/10.1016/j.jece.2020.103766

Islam, S., Alam, R., & Kim, S. (2022). Improved coverage of plant metabolites using FT-ICR MS for *Centella asiatica* metabolomics. *Food Chemistry*, 373, Article 131527. https://doi.org/10.1016/j.foodchem.2021.131541

Jusril, N. A., Bakar, S. I. A., Khalil, K. A., Saad, W. M. M., Wen, N. K., & Adenan, M. I. (2022). Development and optimization of nanoemulsion of *Centella asiatica* to improve blood-brain barrier permeability. *Evidence-Based Complementary and Alternative Medicine*, 2022, Article 1-10. https://doi.org/10.1155/2022/3483511

Kabir, A. U., Samad, B. M., D'Costa, N. M., Akhter, F., Ahmed, A., & Hannan, J. M. A. (2014). Anti-hyperglycemic

activity of *Centella asiatica* mediated by carbohydrase enzyme inhibition. *BMC Complementary and Alternative Medicine*, 14, Article 31. https://doi.org/10.1186/1472-6882-14-31

Kandasamy, A., Subramaniam, S., Ramanathan, S., Murugaiyah, V., & Ismail, S. (2023). Phytochemical analysis and antioxidant activity of *Centella asiatica* extracts. *Plants*, 12(20), Article 3547. https://doi.org/10.3390/plants12203547

Khobragade, P. (2017). Cost effective cultivation of *Centella asiatica* Linn. *Journal of Research in Traditional Medicine*, 2(5), 135-137. https://doi.org/10.21276/jrtm.2017/345

Kim, S. L., & Lean, K. S. (2013). Herbal medicines: Malaysian women's knowledge and practice. *Evidence-Based Complementary and Alternative Medicine,* 2013, Article 438139. https://doi.org/10.1155/2013/438139

Kotagiri, D., & Chaitanya, V. (2017). Antimicrobial and antioxidant activities of root, stem and leaf extracts. Advances in Biotechnology & Microbiology, 3(1), 1-5. https://doi.org/10.19080/AIBM.2017.03.555618

Kumari, P., Singh, R., Jha, A., Prasad, K., & Singh, S. (2022). Optimization of ultrasound-assisted extraction of asiaticoside from *Centella asiatica*. *Industrial Crops and Products*, 176, Article 114325. https://doi.org/10.1016/j.indcrop.2021.114320

Lala, R. R., Patel, P., & Kundnani, K. M. (2019). Nanoemulsion formulation for improved permeability of *Centella asiatica* extract. *International Journal of Pharmaceutical Sciences and Research*, 10(1), 1-7.

Leite, K. C. S., Oliveira, G. L. S., Silva, M. R. M., Bezerra, C. F., Silva, N. H., & Souza, I. A. (2018). Antioxidant activity evaluation of dried herbal extracts of *Centella asiatica*. *Revista Brasileira de Farmacognosia*, 28(3), 325-332. https://doi.org/10.1016/j.bjp.2018.04.004

Lestari, A. B. S., Fudholi, A., Nugroho, A., & Setyowati, E. (2016). In vitro antiplatelet aggregation activity of *Centella asiatica* extract. *Indonesian Journal of Pharmacy*, 8, 280-283.

Liew, K. Y., Hafiz, M. F., Chong, Y. J., Harith, H. H., Israf, D. A., & Tham, C. L. (2020). A review of Malaysian herbal plants and their active constituents with potential therapeutic applications in sepsis. *Evidence-Based Complementary and Alternative Medicine*, 2020, Article 8257817. https://doi.org/10.1155/2020/8257817

Lin, P., Shi, H. Y., Lu, Y. Y., & Lin, J. (2023). *Centella asiatica* alleviates psoriasis through JAK/STAT3-mediated inflammation. *Journal of Ethnopharmacology*, 317, Article 116847. https://doi.org/10.1016/j.jep.2023.116746

Ling, Y., Gong, Q., Xiong, X., Sun, L., Zhao, W., Zhu, W., & Lu, Y. (2017). Protective effect of madecassoside on H_2O_2-induced oxidative stress and autophagy activation in human melanocytes. *Oncotarget, 8*(31), 51066–51075. https://doi.org/10.18632/oncotarget.17654

Madhu, K., & Prabha, T. (2018). Asiaticoside counteracts activation of microglia and astrocytes. *Biomedicine & Pharmacotherapy*, 107, 303-305. https://doi.org/10.1016/j.biopha.2018.08.010

Maduray, K., Moodley, R., Ramdhani, S., & Parboosing, R. (2022). Anti-HIV activity of silver nanoparticles synthesized from *Centella asiatica*. *Journal of Herbal Medicine*, 35, Article 100584. https://doi.org/10.1016/j.hermed.2022.100592

Mahmud, N., Wan-Mohtar, W. A. A. Q. I., Ramasamy, S., & Manickam, S. (2020). Synergistic-antagonistic interaction of traditional herbs against bacteria. *Malaysian Journal of Microbiology*, 16(5), 382-395.

Masi, F., Chianese, G., Peterlongo, F., Riva, A., & Taglialatela-Scafati, O. (2022). Phytochemical profile of *Centella asiatica* and identification of a new oleanane-type saponin. *Fitoterapia*, 158, Article 105154. https://doi.org/10.1016/j.fitote.2022.105163

Mohammad Azmin, S. N. H., & Mat Nor, M. S. (2020). Chemical fingerprint of *Centella asiatica*'s bioactive compounds in relation to extraction methods. *Advances in Biomarker Sciences and Technology*, 2, 35-44. https://doi.org/10.1016/j.abst.2020.10.001

Mohapatra, P., Ray, A., Jena, S., Nayak, S., & Mohanty, S. (2021). Influence of extraction methods on antioxidant activity of *Centella asiatica*. *Biocatalysis and Agricultural Biotechnology*, 33, Article 101971.

https://doi.org/10.1016/j.bcab.2021.101971

Mohd Fuad, F., & Mohd Nadzir, M. (2023). Ultrasound-assisted extraction of *Centella asiatica* using natural deep eutectic solvents. *Industrial Crops and Products*, 192, Article 116052. https://doi.org/10.1016/j.indcrop.2022.116069

Monton, C., Settharaksa, S., Luprasong, C., & Songsak, T. (2019). Optimization of dynamic maceration of *Centella asiatica* leaves by response surface methodology. *Revista Brasileira de Farmacognosia*, 29(2), 254-261. https://doi.org/10.1016/j.bjp.2019.01.001

Muhlishoh, A., Wasita, B., & Nuhriawangsa, A. M. P. (2019). Antidiabetic effect of whole plant extract of *Centella asiatica*. *Indonesian Journal of Nutrition and Dietetics*, 6(1), 14-22. https://doi.org/10.21927/ijnd.2018.6(1).14-22

National Center for Biotechnology Information. (2024). *Centella asiatica* - LiverTox. NCBI Bookshelf. *National Library of Medicine*. https://www.ncbi.nlm.nih.gov/books/NBK603561/

Ondeko, D. A., Juma, B. F., Baraza, L. D., & Nyongesa, P. K. (2020). LC-ESI/MS and GC-MS analysis of methanol extract of *Centella asiatica*. *Asian Journal of Chemical Sciences*, 8(1), 32-51. https://doi.org/10.9734/ajocs/2020/v8i319046

Oruganti, M., Roy, B. K., Singh, K. K., Prasad, R., & Kumar, S. (2010). Safety assessment of *Centella asiatica* extract in albino rats. *Pharmacognosy Journal*, 2(16), 5-13. https://doi.org/10.1016/S0975-3575(10)80043-4

Park, K. S. (2021). Pharmacological effects of *Centella asiatica* on skin diseases. *Evidence-Based Complementary and Alternative Medicine*, 2021, Article 6673248. https://doi.org/10.1155/2021/5462633

Pingale, S. S. (2008). Acute toxicity study for *Centella asiatica* whole plant powder. *Pharmacologyonline Newsletter, 3*, 80–84

Pitinidhipat, N., & Yasurin, P. (2012). Antibacterial activity of *Chrysanthemum indicum*, *Centella asiatica* and *Andrographis paniculata* against *Bacillus cereus* and *Listeria monocytogenes* under osmotic stress. *AU Journal of Technology, 15*(4), 239–245.

Polash, S. A., Saha, T., Hossain, M. S., & Sarker, S. R. (2017). Phytochemical contents, antioxidant and antibacterial activity of the ethanolic extracts of *Centella asiatica* (L.) Urb. leaf and stem. *Jahangirnagar University Journal of Biological Sciences, 6*(1), 51–57. https://doi.org/10.3329/jujbs.v6i1.33731

Prasesti, G. K., & Kurniati, N. F. (2022). Toxicity studies of *Centella asiatica* for drug development. *Biointerface Research in Applied Chemistry*, 12(6), 8081-8093. https://doi.org/10.33263/BRIAC126.80818093

Quyen, N. T. C., Quyen, N. T. N., Quy, N. N., & Quan, M. P. (2020). Evaluation of total polyphenol and flavonoid content of *Centella asiatica*. *IOP Conference Series: Materials Science and Engineering*, 991, Article 012104. https://doi.org/10.1088/1757-899X/991/1/012020

Rafi, M., Nurrulhidayah, A. F., Wulansari, D., Darusman, L. K., & Rafiqa, S. (2018). Simultaneous quantification of four triterpenes of *Centella asiatica* using HPLC. *Industrial Crops and Products*, 122, 93-97. https://doi.org/10.1016/j.indcrop.2018.05.062

Rahman, S., Jamal, M. A. H., Parvin, A., Mahfuz-Al-Mamun, M., & Islam, M. R. (2011). Antidiabetic activity of *Centella asiatica* in alloxan-induced diabetic rats. *Journal of Biological Sciences*, 19, 23-27. https://doi.org/10.3329/jbs.v19i0.12996

Ramachandran, V., & Saravanan, R. (2013). Effect of asiatic acid on carbohydrate metabolism enzymes in streptozotocin-induced diabetic rats. *Phytomedicine*, 20(3-4), 230-236. https://doi.org/10.1016/j.phymed.2012.09.023

Sabaragamuwa, R., Perera, C. O., & Fedrizzi, B. (2022). Ultrasound-assisted extraction and UHPLC-MS/MS quantification of bioactive compounds in *Centella asiatica*. *Food Chemistry*, 371, Article 131145. https://doi.org/10.1016/j.foodchem.2021.131187

Samuel, K., Medikeri, A., Pasha, T., Ansari, M. F., & Saudagar, A. (2022). *Centella asiatica*: A traditional herbal medicine. *World Journal of Advanced Research and Reviews*, 15(1), 512-524. https://doi.org/10.30574/wjarr.2022.15.1.0726

Seong, E., Heo, H., Jeong, H. S., Lee, H., & Lee, J. (2023). Enhancement of bioactive compounds of *Centella asiatica* through ultrasound treatment. *Ultrasonics Sonochemistry*, 94, Article 106315.https://doi.org/10.1016/j.ultsonch.2023.106353

Setyaningsih, W. A. W., Arfian, N., Fitriawan, A. S., Yuniartha, R., & Sari, D. C. R. (2021). Ethanolic extract of *Centella asiatica* inhibits glomerular injury in diabetic rats. *Evidence-Based Complementary and Alternative Medicine*, 2021, Article 8855276. https://doi.org/10.1155/2021/6671130

Sharma, S., Gupta, R., & Thakur, S. C. (2014). Attenuation of collagen-induced arthritis by *Centella asiatica* methanol fraction. *Biomedical and Environmental Sciences*, 27(12), 926-938.

Sieberi, B. M., Omwenga, G. I., Wambua, R. K., Samoei, J. C., & Ngugi, M. P. (2020). Screening of dichloromethane:methanolic extract of *Centella asiatic*a for antibacterial activities. *The Scientific World Journal*, 2020, Article 6378712. https://doi.org/10.1155/2020/6378712

Songvut, P., Chariyavilaskul, P., Khemawoot, P., Tansawat, R., Tantisira, M. H., & Rodsiri, R. (2021). Pharmacokinetics and metabolomics investigation of an orally modified formula of standardized *Centella asiatica* extract in healthy volunteers. *Scientific Reports*, 11, Article 6850. https://doi.org/10.1038/s41598-021-86267-2

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, Article 568032. https://doi.org/10.3389/fphar.2020.568032

Teerapattarakan, N., Benya-aphikul, H., Tansawat, R., Wanakhachornkrai, O., Tantisira, M. H., & Rodsiri, R. (2018). Neuroprotective effect of standardized *Centella asiatica* extract ECa233. *Phytomedicine*, 44, 65-73. https://doi.org/10.1016/j.phymed.2018.04.028

Thong-on, W., Pathomwichaiwat, T., Boonsith, S., Koo-amornpattana, W., & Prathanturarug, S. (2021). Green extraction optimization of *Centella asiatica* using response surface methodology. *Scientific Reports*, 11, Article 13826. https://doi.org/10.1038/s41598-021-01602-x

Viswanathan, G., Dan, V. M., Radhakrishnan, N., Nair, A. S., Nair, A. P. R., & Baby, S. (2019). Protection of mouse brain from paracetamol-induced oxidative stress by *Centella asiatica. Journal of Ethnopharmacology*, 236, 474-483. https://doi.org/10.1016/j.jep.2019.03.017

World Health Organization. (2003). *WHO policy perspectives on medicines: Effective medicines regulation—Ensuring safety, efficacy and quality* (WHO Policy Perspectives on Medicines, No. 7). World Health Organization. https://www.rhsupplies.org/uploads/tx_rhscpublications/WHO_Effective%20medicines%20regulation_2003.pdf

Yadav, M. K., Sharma, A., Kumar, A., Singh, P., & Verma, R. (2019). In vivo toxicity study of ethanolic extracts of *Centella asiatica* in mice. *Open Access Macedonian Journal of Medical Sciences*, 7(7), 1071-1076. https://doi.org/10.3889/oamjms.2019.209

Yi, C., Zhang, Y., Li, X., Zhao, H., Wang, J., & Liu, P. (2022). Asiatic acid alleviates myocardial ischemia injury by regulating oxidative stress and inflammation. *Oxidative Medicine and Cellular Longevity*, 2022, Article 1-12. https://doi.org/10.1155/2022/3267450

Yingngam, B., Chiangsom, A., & Brantner, A. (2020). Modeling and optimization of microwave-assisted extraction of *Centella asiatica* using response surface methodology. *Industrial Crops and Products*, 147, Article 112231. https://doi.org/10.1016/j.indcrop.2020.112231

Yuan, Y., Zhang, X., Wang, J., Liu, H., Chen, L., & Zhao, Y. (2023). Determination of four active compounds in *Centella asiatica* by HPLC-MS/MS. *Journal of Chromatography A*, 1708, Article 463395.

Zainal Abidin, H., & Kamaruddin, H. (2005). Pegaga (*Centella asiatica*). In Y. Musa, M. Muhammad Ghawas, & P. Mansor (Eds.), *Penanaman Tumbuhan Ubatan & Beraroma* (pp. 70–76). Serdang, Selangor, Malaysia: Malaysian

Agricultural Research and Development Institute (MARDI).

Zakaria, F., Ibrahim, W. N. W., Ismail, I. S., Ahmad, H., Manshoor, N., Ismail, N., Zainal, Z., & Shaari, K. (2019). LCMS/MS metabolite profiling and analysis of acute toxicity effect of the ethanolic extract of *Centella asiatica* on zebrafish model. *Pertanika Journal of Science and Technology, 27*(2), 985–1003.

Zeng, X., Yu, J., Liu, P., Liu, Y., Zeng, T., & Li, B. (2022). Asiaticoside alleviates cardiomyocyte apoptosis via PI3K-AKT-GSK3β signaling pathway. *Annals of Transitional Medicine*, 10(2), Article 69.https://doi.org/10.21037/atm-21-6667

Zheng, J., Zhou, Q., Cao, X., Meng, Y., Jiang, G., & Xu, P. (2022). Two new flavonol derivatives isolated from C*entella asiatica. Phytochemistry Letters*, 47, 34-37. https://doi.org/10.1016/j.phytol.2021.10.012