Pharmacological potential and Nanotechnological Advances of Centella asiatica (Thankuni): A Review

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Abstract

Centella asiatica L., commonly referred to as Thankuni, is well recognised in Bangladesh for having substantial medicinal and ethnopharmacological value. Both South africa and Asia are home to this plant. It has high content of asiatic acids, asiaticosides, madecassic acids, and madecassosides as well as also rich in flavonoids, and phytosteroles. The gas chromatography revealed the presence of various pharmacologically active substances like resveratrol, quinine, tannins and naringenols. It is utilized for its benefits related to managing diabetes mellitus; inhibiting inflammatory responses; curing cancers; nerve protection; cardiovascular disease prevention; aiding hepatic functions; having antioxidant properties and aiding wounds repair. Recent studies have explored different nanoformulations, including nanoemulsions, liposomes, hydrogels, nanostructured lipid carriers, and solid lipid nanoparticles, to enhance the bioavailability, targeted distribution, and stability of bioactive components. Using computational techniques, researchers have explored the significance of *C. asiatica* phytochemicals in tackling diabetes, hypertension, along with alzheimer's disease. This review draws these strands together, moving from traditional use through phytochemistry, pharmacology, nanoformulation strategy and *in silico* findings, to outline where the evidence is strong and where it remains preliminary. While preclinical evidence strongly upholds its pharmacological benefits, further clinical studies and advanced nanoformulation research are mandatory to authenticate its efficacy and ease the translation into evidence based therapeutic implementations.

Keywords: *Centella asaitica*, vernacular names, ethnopharmacology, pharmacological properties, nanoparticles, *in silico* and toxicity studies.

1. Introduction

Centella asiatica is a non-woody perennial plant that is classified as part of the Apiaceae (Umbelliferae) family, within the subfamily Hydrocotyle (Brinkhaus et al., 2000). In Bangladesh, it is known by native names such as Thankuni, Thulkuri, Takamanik, Adamoni, Brahmmakuti, Ada gunguni, Adamkipata, Goal pata, and Dhol manik (NatureInfo, 2025). While internationare summarizedarries a distinct set of vernacular names summarized in Table 2 (Nav et al., 2021; Singh et al., 2010; Das, 2011; Kant et al., 2019; Harun et al., 2019). Approximately 50 related species thrive in rice paddies and at higher rocky elevations (James

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& Dubery, 2009; Sabaragamuwa et al., 2018). Working with morphological traits, ISSR molecular fingerprinting and phytochemical profiling, Alqahtani et al. (2017) distinguished three Centella species growing in Australia such as *C. asiatica, C. cordifolia* and *C. erecta*. At a broader scale, the Plants of the World Online database currently recognises 55 accepted species within the genus Centella, among them *C. affinis, C. annua, C. brachycarpa, C. caespitosa, C. erecta, C. eriantha, C. glabrata, C. lanata, C. longifolia, C. pilosa, C. tridentata* and *C. villosa*, distributed across tropical and subtropical regions of Africa, Asia, Australia and the America (Plants of the World Online, 2025). It grows well in warm and humid environments in Bangladesh, India, China, and Malaysia. It is also discovered in Australia, Cambodia, Central America, Madagascar, Thailand, Vietnam, and the Pacific Islands (Bhavna & Jyoti, 2011). This plant features alternately arranged leaves (2-5 cm wide) that are hastate, cordate, palmately lobed, or reniform, with long petioles, sheathing bases, and toothed margins (Figure 1). The flowers are small, dark pink, and borne in simple umbels (3-6 flowers) on short peduncles (<1 cm) from leaf axils. The fruit is tiny, ovoid, with nine ridges, along with a bitter, pungent taste and aromatic smell when crushed (Joshi & Chaturvedi, 2013).

Figure 1. *Centella asiatica* (Thankuni) whole plant and root

It is easy to propagate through stolons, seeds, or roots, and can be harvested within 3-6 months. Recent developments include tissue culture techniques, such as twin-bottle bioreactor systems, which improve mass propagation and biomass production (Wongsa et al., 2023). It is a phytochemically rich medicinal herb whose therapeutic versatility is attributed to a diverse array of bioactive constituents, including triterpenoid saponins, triterpenic acids, flavonoids,

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phenolic acids, essential oils, amino acids, and micronutrients (Belwal et al., 2019; Das et al., 2022). The triterpene acid group is the most prominent, comprising asiatic acid, asiaticoside, madecassic acid, madecassoside (shown in Figure 2) and related acids (terminolic, centic, centellic, centoic, indocentoic, isobrahmic, brahmic, betulic, and madasiatic). Moreover, glycosides include asiaticoside A and B, madecassoside, centelloside, brahmoside, brahminoside, thankuniside, and glycosides D and E. Polyphenolic compounds (quercetin, quercitrin, kaempferol, luteolin, chlorogenic acid) and flavonoids (quercetin and kaempferol derivatives) contribute to its antioxidant activity, alongside a minor alkaloid, hydrocotylin. The plant also contains volatile and fatty acids (glycerides of oleic, palmitic, stearic, lignoceric, linoleic, and linolenic acids), a small essential oil fraction (~0.1%; beta-caryophyllene, trans-beta-farnesene, germacrene D), and a bitter component, vallerine. Nutritionally, it provides phytosterols (campesterol, sitosterol, stigmasterol) (Das et al., 2022). The leaves of centella showed the presence of glutamate, histidine, lysine, isoleucine, aspartate and phenylalanine as the dominant amino acids. Gas-chromatographic analysis further identified proanthocyanin, rutin, naringenin, quinine, spartein, phenol, flavonones, steroids, kaempferol, phytate, resveratrol, tannin and ribalinidine (Belwal et al., 2019). Water and alcohol-based extracts of *C. asiatica* are used to treat a wide array of diseases and conditions, and a large body of laboratory and animal research now backs up the therapeutic effects of two of its key compounds, asiaticoside and madecassoside. Among the many benefits these two phytochemicals offer, their neuroprotective, wound-healing, and skin-protective effects are the most applied. Asiaticoside has been shown to reduce neuronal damage, ease anxiety, and act as a natural antidepressant. Both asiaticoside and madecassoside have also been studied for their potential to treat brain injuries caused by oxygen and blood-flow deprivation, and both are being investigated as possible therapies for neurodegenerative diseases such as Alzheimer's and Parkinson's.

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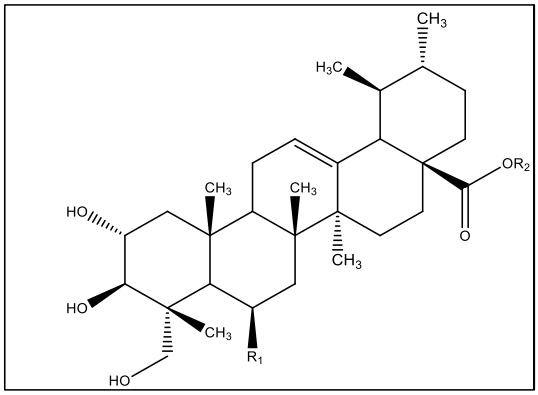

Compound	R_1	R_2
Asiaticoside	H	Glu-Glu-Rha
Madecassoside	OH	Glu-Glu-Rha
Asiatic Acid	H	H
Madecassic Acid	OH	H

Figure 2: Chemical structure of the main active ingredients of triterpenes from *Centella asiatica* using Chemdraw

Beyond their neurological benefits, these compounds also stimulate collagen production, improve skin hydration, and support the healing of scars and burns, which explains their widespread popularity in both medical and cosmetic products. Research further confirms that these triterpene saponins help repair organ damage, reduce inflammation and oxidative stress, and defend against bacterial, fungal, and parasitic infections. On top of that, they show promise as chemotherapeutic agents and appear to play a role in regulating the body's immune responses (Ogunka-Nnoka et al., 2020). In Bangladesh, traditional healers of the Chittagong Hill Tracts use leaf and stem juice for dysentery (Bandopadhyay et al., 2023), while in Tangail district the leaf alone treats fever and pain (Rahman & Rafieian-Kopaei, 2017). In Sylhet Division, whole plant juice is utilized for indigestion and appetite stimulation (Rahmatullah et al., 2010). The Soren clan of the Santal tribe (Rajshahi) prepares an elaborate decoction for male sexual weakness (Rahmatullah et al., 2012). In India, uses include memory enhancement and headache relief (Kerala), dysentery and constipation (Western Himalaya), wound healing via a multi-herb decoction (Tamil Nadu), stomach ailments and cognitive support (Manipur), leucorrhea and eczema (Malasars tribe), mental retardation (Maharashtra, with cow ghee), carbuncles and hemorrhoids (Assam, combined with other herbs), fever/sunstroke (Kanyakumari), rickets in children (Madhya Pradesh), cardiovascular and stomach disorders (Karnataka), leprosy, tuberculosis, asthma (Assam, Lushai tribe), and syphilis, mental disorders, and skin disease (Baiga tribe). In Nepal, whole plant juice serves as a poison antidote and wound treatment (Kathmandu), an extract addresses limb skin tenderness (Jhapa), and leaf

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preparations treat nervous system, respiratory, skin, and digestive complaints (Dolpa). In Cameroon, powdered whole plant is used for varicocele (Jahan et al., 2012).

Table 1. Vernacular names of *Centella asiatica*

Region	Vernacular names
Iran	Ab-boshghabi
Indonesia	Pegagan
Malaysia	Pegaga
India	Mandookaparni
Europe	Indian pennywort or Gotu-kola
USA	Marsh pennywort
China	Fo-ti-tieng (Das, 2011; Kant et al., 2019; Nav et al., 2021; Singh et al., 2010)
Cook Islands	Kapu kapu
Fiji	Totodro
Hawai	Pohe kula
Tahiti	Tohetupou
Sri-Lanka	Thankuni sak
Nepal	Gho tapre
Tonga	Tono (Das, 2011; Kant et al., 2019; Singh et al., 2010)
India	Manimunni and vallerinin
Thailand	Bua-bok (Harun et al., 2019)

2.Methodology

2.1. Literature search strategy

A thorough literature search was conducted across several recognized scientific databases and publishing platforms, including Elsevier, Scopus, Springer, Wiley, Frontiers, ResearchGate, Taylor & Francis, and MDPI, covering the period from 2000 to 2025. The following keywords were used to collect information: *Centella asiatica*, plant appearance, cultivation, taxonomy, vernacular names, ethnopharmacology, phytoconstituents, pharmacological properties anticancer effects, nanoformulations, *in silico* studies, toxicity and safety.

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2.2. Inclusion criteria

The criteria for inclusion in this research consisted of studies that explored the botanical, ethnopharmacological, phytochemical, pharmacological, and anticancer characteristics of *C. asiatica* from various scientific sources. Studies assessing the anticancer effects of *C. asiatica* through *in vitro* and *in vivo* experimental methods were accepted. Research examining nanoformulations and nanotechnology-based delivery systems that incorporate *C. asiatica* was also considered. Relevant studies that focused on mechanisms of action, in silico studies, toxicity, and safety profiles were included.

2.3. Exclusion criteria

The exclusion criteria comprised duplicate publications as well as studies that did not satisfy the predefined inclusion criteria based on their titles and abstracts. Studies that lacked adequate scientific information or pertinent methodological details were also excluded. Furthermore, studies concentrating solely on pharmacological effects that were unrelated to the aims of this review were omitted.

3. Results and discussion

3.1. Pharmacological properties

3.1.1 Anticancer activity

Several strands of evidence point to asiatic acid (AA) as the principal driver of the plant's antitumour activity. In a tongue squamous-cell carcinoma model (Tca8113 line), 15 mg/kg AA lowered both tumour volume and weight; the effect was traced to downregulation of the anti-apoptotic protein Bcl-2, upregulation of pro-apoptotic Bax with cleaved caspase-3, and activation of the IRE1α/JNK arm of the endoplasmic-reticulum stress pathway (Li et al., 2021). A comparable pattern emerged in a murine triple-negative breast cancer model (4T1 cells), where 50 mg/kg AA reduced tumour mass and volume alongside reduced CD31 staining, a marker of angiogenesis consistent with suppressed VEGF expression and VEGFR2 phosphorylation, and therefore reduced vascularisation and metastatic spread (Tian et al., 2021). In a lung-cancer model, AA at 50-100 mg/kg was directly compared with 5-fluorouracil (5-FU): 5-FU produced a stronger antitumour effect, but AA was markedly safer, avoiding the

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systemic toxicity, weight loss and splenic atrophy seen with 5-FU, and worked instead through elevated reactive oxygen species and mitochondrial membrane depolarisation leading to apoptosis (Wu et al., 2017). Combining AA (10 mg/kg) with naringenin (50 mg/kg) produced an additive effect in melanoma and lung carcinoma models, slowing tumour progression while boosting natural killer cell cytotoxicity; mechanistically, AA upregulated Smad7 while naringenin suppressed Smad3, jointly rebalancing the Smad3/Smad7 axis of the TGF-β pathway to favour immune mediated tumour clearance without harming healthy tissue (Lian et al., 2018).

3.1.2 Cardioprotective activity

C. asiatica extract at 200-400 mg/kg has been shown to raise cardiac acetylcholine, thereby improving function (Sun et al., 2020). While isolated asiatic acid (10 μM) protected cardiomyocytes from ischemia or reperfusion by reducing apoptosis, reactive oxygen species (ROS), and restoring mitochondrial function via protein kinase B (Akt)/glycogen synthase kinase 3 beta (GSK-3β) /hypoxia inducible factor 1 (HIF-1) (Bansal et al., 2024).

3.1.3 Hepatoprotective activity

C. asiatica hydroethanolic extract (50 percent) (CA-HE50) significantly lowered ALT (alanine aminotransferase), AST (aspartate aminotransferase), and LDH (lactate dehydrogenase) levels while increasing SOD (superoxide dismutase) activity in an acute liver failure model. The 200 mg/kg CA-HE50 group showed the strongest effect, comparable to silymarin, LEM (lentinus edodes mycelia), DDB (dimethyl-4,4′-dimethoxy-5,6,5′,6′-dimethylenedioxybiphenyl-2,2′-dicarboxylate) (a hepatoprotective drug) and UDCA (ursodeoxycholic acid) indicating strong antioxidant and hepatoprotective properties (Hong et al., 2021).

3.1.4 Wound healing activity

A double-blind, placebo-controlled trial assessed the effects of a topical 0.05% standardized extract of *C. asiatica* (ECa 233) on 30 patients undergoing facial laser resurfacing. The treatment significantly reduced redness and improved overall wound appearance and healing, proving its effectiveness in enhancing post-procedure skin recovery (Damkerngsuntorn et al., 2020). Furthermore, in another study, it was found that an asiaticoside nitric oxide conjugate promotes diabetic wound healing by upregulating miR-21-5p (MicroRNA-21-5p), boosting

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cell migration and proliferation. The study confirmed interactions with target genes SMAD7 (Mothers Against Decapentaplegic Homolog 7), TGF-β1(Transforming Growth Factor Beta 1), and TIMP3 (Tissue Inhibitor of Metalloproteinases 3), indicating that the compound helps healing through the miR-21-5p/TGF-β1 signaling pathway, offering potential for diabetic wound therapy (Liu et al., 2024).

3.1.5 Antiulcer activity

Asiaticoside from *C. asiatica* helped to heal chronic gastric ulcers in rats by boosting new blood vessel formation, encouraging epithelial cell growth, lowering myeloperoxidase activity, and increasing bFGF (Basic Fibroblast Growth Factor) levels at the ulcer site (Wannasarit et al., 2020). Again, it was also proved that fresh *C. asiatica* juice (200-600 mg/kg) effectively protected rats from various types of ulcers, comparable to sucralfate. The juice acts by enhancing gastric mucosal defenses, boosting glycoprotein levels, and reducing epithelial damage, indicating its anti-ulcer effects are cytoprotective rather than due to acid suppression (Bansal et al., 2024).

3.1.6 Antidiabetic activity

C. asiatica ethanol extract formulated as SNEDDS (Self Nanoemulsifying Drug Delivery System) reduced fasting blood glucose by up to 72% in zebrafish (Hayati et al., 2021). Hydroalcoholic leaf extracts confirmed the inhibition of carbohydrate digesting enzymes and enhance glucose utilization, suggesting potential synergy with standard hypoglycemic drugs (Ahmed & Kumar, 2023). The triterpenic fraction of *C. asiatica* (TTFCA) enhanced microcirculation, reduces capillary permeability, and lowers blood glucose and lipid levels in diabetic rats, showing effects comparable to glibenclamide (Bansal et al., 2024).

3.1.7 Neuroprotective activity

A standardized *C. asiatica* extract (ECa 233) was revealed to auppress hyperalgesia, allodynia, and pain related protein expression in a trigeminal neuropathic model, with combined use of ECa 233 and carbamazepine showing added benefits (Wanasuntronwong et al., 2024). In another experiment, *C. asiatica* extract (1000 mg/kg/day) improved cognition, reduced anxiety in aged mice, and showed anticonvulsant and neuroprotective effects in rats without toxicity, supporting its potential in managing pain, cognitive decline, and seizures (Bansal et al., 2024).

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3.1.8. Antiinflammatory activity

The methanol fraction (MCA) reduced inflammatory markers and liver inflammation by blocking IRAK1(Interleukin 1 Receptor Associated Kinase 1)/TAK1(Transforming Growth Factor Beta Activated Kinase 1) signaling in macrophages and an acute hepatitis mouse model (Cho et al., 2020). An ethanolic extract lowered TNF-α levels in an indomethacin induced gastric ulcer model, with the strongest effect at 100 mg/kg body weight (Sriepindonnta et al., 2021). While methanolic extract lowered IL-1β (Interleukin 1 Beta) in salivary neutrophils of children with severe early childhood caries by inhibiting NF-κB (Nuclear Factor Kappa B) and MAPK (Mitogen Activated Protein Kinase) pathways, highlighting its potential for oral inflammation (Luthfi et al., 2023).

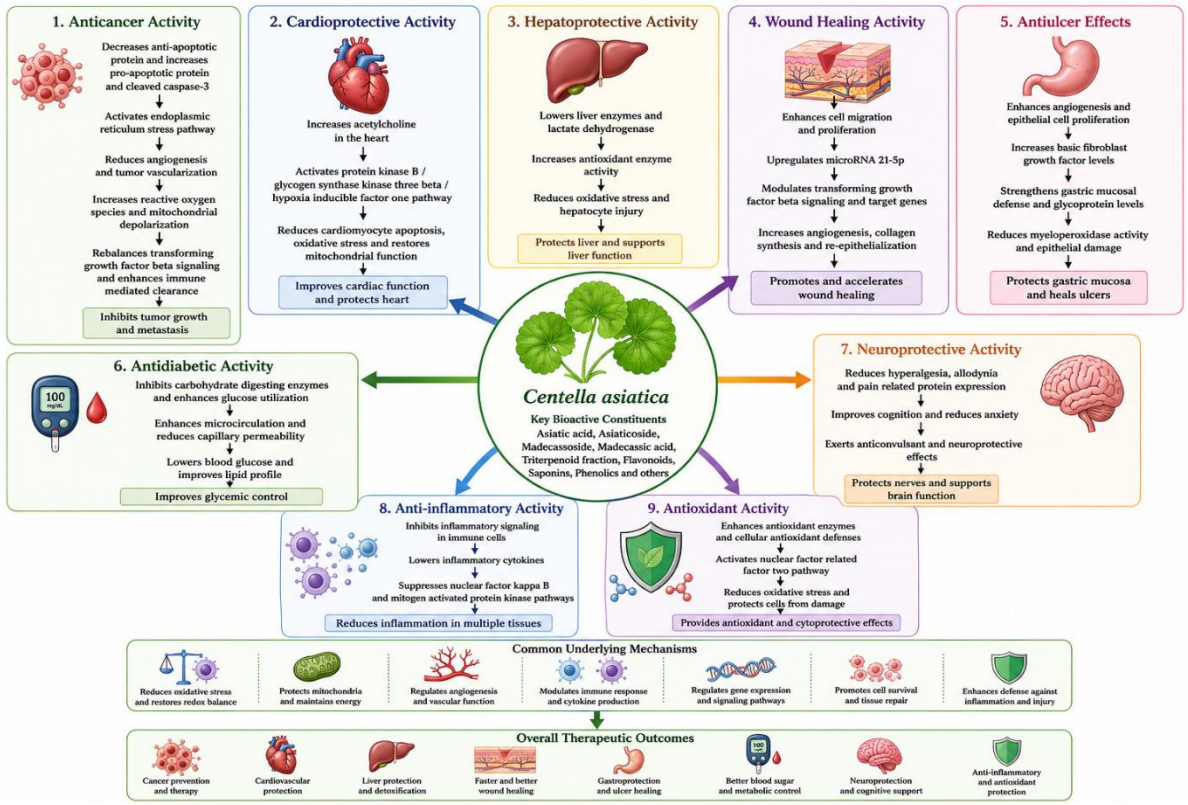

Figure 3. Mechanism of overall pharmacological activity of *Centella asiatica*

3.1.9. Antioxidant activity

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A Phase 1, double blind crossover trial was conducted in four older adults with mild dementia, assessing single oral doses (2 g and 4 g) of standardized *C. asiatica* extract. Key triterpenes (asiatic acid, madecassic acid) appeared in plasma and urine, while their glycosides (asiaticoside, and madecassoside) showed minimal absorption. Caffeoylquinic acids were poorly absorbed, but metabolites were detected. CAP (*C. asiatica* Preparation) also activated NRF2 (Nuclear Factor Related Factor 2) gene expression in blood cells, indicating stimulation of antioxidant defenses. The trial concluded that CAP is safe, bioavailable, and engages antioxidant pathways (Wright et al., 2022).

3.2. Nanobased drug delivery systems

3.2.1. Nanoparticles

Silver nanoparticles synthesised from fresh *C. asiatica* leaf extract were tested at varying concentrations for their effect on peanut plant growth, development and yield, with 5 ppm identified as the optimal concentration for germination, growth and pod production (Vuong et al., 2017). Similarly prepared silver nanoparticles showed strong activity against MCF-7 breast cancer cells, reducing cell viability and triggering apoptosis through increased caspase-3 and caspase-9 gene expression in a dose and time dependent manner (Fard et al., 2018).

3.2.2. Nanoemulsion

A high-pressure homogenisation approach was used to develop NanoSECA, a nanoemulsion intended to improve delivery of *C. asiatica* bioactives to the brain. It showed strong antioxidant and anti-inflammatory activity together with acetylcholinesterase inhibition *in vitro* and achieved high BBB (blood brain barrier) permeability, reducing oxidative stress and pro-inflammatory markers and suggesting potential for central nervous system applications (Jusril et al., 2022). A separate nanoemulsion serum formulated with leaf extract as a natural antioxidant source, prepared via maceration and microwave-assisted extraction, identified squalene, kaempferol and asiaticoside as the key antioxidant compounds, with the microwave assisted extract giving the stronger antioxidant activity; of three candidate SNEDDS formulas tested for stability, only one produced stable, non-irritating, nanosized droplets (Tripathy & Srivastav, 2023).

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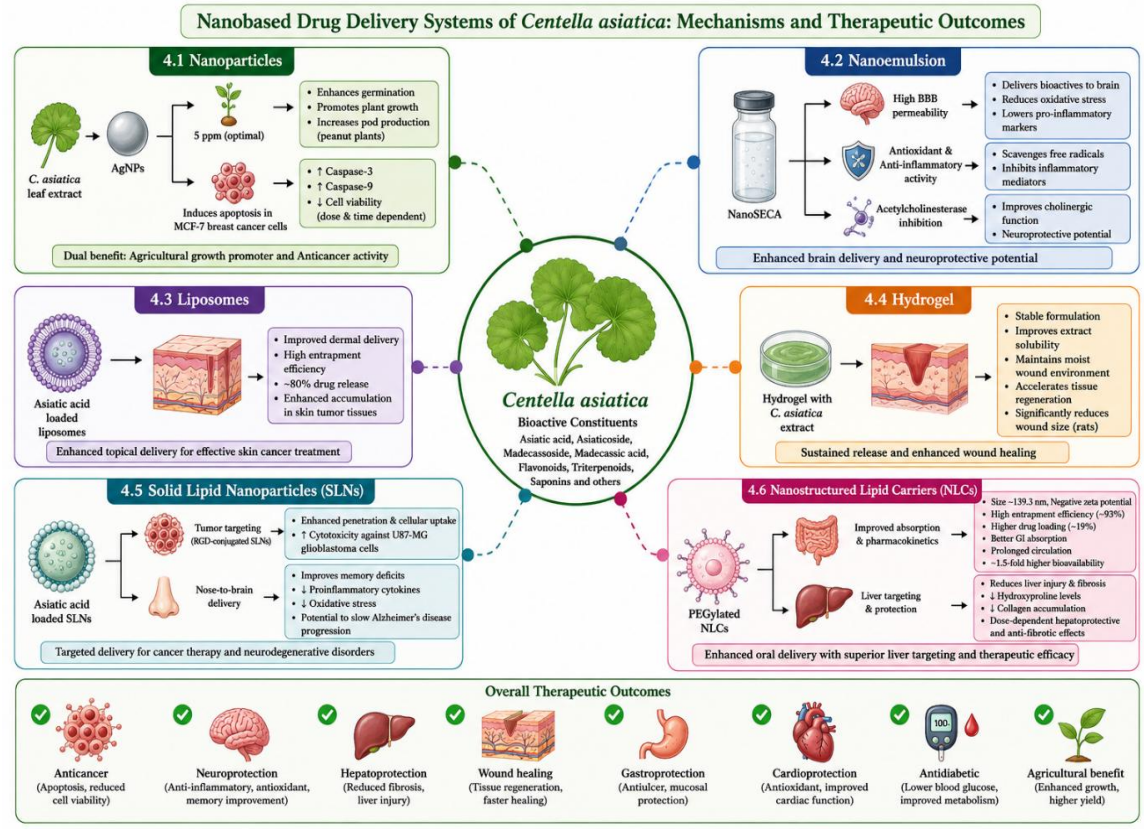

Figure 4. Mechanism of nanobased drug delivery of *Centella asiatica*

3.2.3. Liposomes

Recently, a transliposomal gel loaded with asiatic acid was formulated to improve dermal delivery for the topical treatment of skin cancer. This showed high entrapment efficiency and about 80 percent drug release (Fitri et al., 2024).

3.2.4. Hydrogel

A hydrogel formulation containing titrated *C. asiatica* extract proved stable, improved extract solubility and significantly reduced wound size in rats, indicating strong healing potential (Qadir et al., 2023).

3.2.5. Solid lipid nanoparticles

Asiatic acid loaded solid lipid nanoparticles (SLNs) were designed to enhance its penetration, tumor targeting, and anticancer activity. Using spheroid tumor models, they observed increased

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cytotoxicity against U87-MG (Human Glioblastoma Cell Line) cells and improved cellular uptake with RGD-conjugated SLNs, suggesting these nanoparticles are promising targeted carriers for glioblastoma treatment (Hong et al., 2005). In a separate study, Asiatic acid loaded SLNs were formulated for nose to brain delivery. In mouse models, this approach improved memory deficits, reduced proinflammatory cytokine release, and lowered oxidative stress, indicating potential for slowing the progression of Alzheimer's disease (Islamie et al., 2023).

3.2.6. Nanostructured lipid carriers

A synthesized PEGylated (Polyethylene Glycol-Coated) NLCs, which had an average size of 139.3 ± 1.7 nm, a negative zeta potential, a high entrapment efficiency (93.30 ± 0.90%), and a drug loading (19.03 ± 0.18%), which demonstrated better gastrointestinal absorption, prolonged circulation, and 1.5-fold higher bioavailability compared to non-PEGylated NLCs. Orally administered PEGylated NLCs also significantly alleviated liver fibrosis and associated functional impairments, highlighting their enhanced anti-fibrotic effects. A separate nanostructured lipid carriers (NLCs) loaded with asiatic acid was invented to enhance liver targeting. Their study improved oral absorption and effectively reduced liver injury and fibrosis in a dose-dependent manner, including lowering hydroxyproline levels and collagen accumulation, indicating their potential as carriers for treating liver diseases (Chen et al., 2020).

Table 2. Model, dose, effects and mechasim of *Centella asiatica*

Activity	Model	Dose	Effects	Mechanism	Reference
Anticancer	Tca8113 tongue squamous-cell carcinoma (mice)	15 mg/kg	↓ Tumour volume and weight	↓ Bcl-2; ↑ Bax and cleaved caspase-3; activation of IRE1α/JNK and ER-stress-induced apoptosis	Li et al. (2021)
	4T1 breast cancer (mice)	50 mg/kg	↓ Tumour mass and volume	↓ VEGF and VEGFR2 phosphorylation; ↓ angiogenesis, vascularisation and metastasis	Tian et al. (2021)

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Activity	Model	Dose	Effects	Mechanism	Reference
	Lung cancer model	50–100 mg/kg	↓ Tumour weight; weaker than 5-FU but safer	↑ ROS and mitochondrial membrane depolarisation → apoptosis	Wu et al. (2017)
	Melanoma and lung carcinoma (mice)	AA 10 mg/kg + naringenin 50 mg/kg	↓ Tumour progression; ↑ NK-cell cytotoxicity	Modulation of Smad3/Smad7 signalling; AA ↑ Smad7 and naringenin ↓ Smad3	Lian et al. (2018)
	Human colon cancer cells (in vitro)	Not specified	Inhibited proliferation and apoptosis; anti-metastatic	EMT reversal; ↑ E-cadherin, ↓ N-cadherin/vimentin; inhibition of PI3K/Akt/mTOR/p70 S6K	Hao et al. (2024)
	Osteosarcoma cells	Not specified	Induced apoptosis and autophagy	↑ Bax, ↓ Bcl-2; ↑ LC3-II/I and p62; involvement of PI3K/Akt and ROS/MAPK	Pang et al. (2024)
	Glioblastoma xenograft (mice)	30 mg/kg	60% tumour reduction; safe	Caspase activation, ER stress and ↑ intracellular Ca^{2+}	Kavitha et al. (2024)
	Cardiac model	200–400 mg/kg	Improved cardiac function	↑ Cardiac acetylcholine	Sun et al. (2020)
Cardioprotective	Cardiomyocytes with ischemia/reperfusion injury	10 µM	↓ Apoptosis and ROS; restored mitochondrial function	Akt/GSK-3β/HIF-1 pathway	Bansal et al. (2024)
Hepatoprotective	Acute liver failure model	200 mg/kg	↓ ALT, AST and LDH; ↑ SOD	Antioxidant and hepatoprotective activity	Hong et al. (2021)

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Activity	Model	Dose	Effects	Mechanism	Reference
	30 patients undergoing facial laser resurfacing	0.05% ECa 233	↓ Redness; improved wound appearance and healing	Enhanced post-procedure skin recovery	Damkerngsuntorn et al. (2020)
Wound Healing					
	Diabetic wound model	Not specified	↑ Cell migration and proliferation; promoted wound healing	↑ miR-21-5p; interaction with SMAD7, TGF-β1 and TIMP3	Liu et al. (2024)
	Chronic gastric ulcer rats	Not specified	Promoted ulcer healing	↑ Angiogenesis, epithelial proliferation and bFGF; ↓ MPO activity	Wannasarit et al. (2020)
Antiulcer					
	Rat ulcer models	200–600 mg/kg	Protected against ulcers; comparable to sucralfate	↑ Gastric mucosal defence and glycoproteins; ↓ epithelial damage	Bansal et al. (2024)
	Zebrafish	Not specified	↓ Fasting blood glucose by up to 72%	SNEDDS-enhanced delivery of *C. asiatica* extract	Hayati et al. (2021)
Antidiabetic	Enzyme/glucose-utilisation models	Not specified	Inhibited carbohydrate digestion and enhanced glucose utilisation	Inhibition of carbohydrate-digesting enzymes; ↑ glucose utilisation	Ahmed & Kumar (2023)
	Diabetic rats	Not specified	↓ Blood glucose and lipid levels	↑ Microcirculation; ↓ capillary permeability	Bansal et al. (2024)
Neuroprotective	Trigeminal neuropathic model	Not specified	↓ Hyperalgesia, allodynia and pain	Suppression of pain-related protein expression	Wanasuntronwong et al. (2024)

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Activity	Model	Dose	Effects	Mechanism	Reference
	Aged mice/rats	1000 mg/kg/day	Improved cognition and ↓ anxiety; anticonvulsant effect	Neuroprotective and anticonvulsant activity	Bansal et al. (2024)
	Macrophages and acute hepatitis mice	Not specified	↓ Inflammatory markers and liver inflammation	Inhibition of IRAK1/TAK1 signalling	Cho et al. (2020)
Anti-inflammatory	Indomethacin-induced gastric ulcer model	100 mg/kg	↓ TNF-α	Suppression of inflammatory response	Sriepindonnta et al. (2021)
	Salivary neutrophils of children with severe early childhood caries	Not specified	↓ IL-1β; reduced oral inflammation	Inhibition of NF-κB and MAPK pathways	Luthfi et al. (2023)
Antioxidant	Older adults with mild dementia	2 and 4 g	Safe and bioavailable; antioxidant response	Activation of NRF2 gene expression; triterpenes detected in plasma and urine	Wright et al. (2022)
Nanoparticles	Peanut plants	5 ppm	Improved germination, growth and pod production	*C. asiatica*-mediated Ag nanoparticles enhanced plant growth	Vuong et al. (2017)
	MCF-7 breast cancer cells	Not specified	↓ Cell viability; induced apoptosis	↑ Caspase-3 and Caspase-9 expression	Fard et al. (2018)
Nanoemulsion	In-vitro brain delivery model	Not specified	Strong antioxidant and anti-inflammatory effects; high BBB permeability	Acetylcholinesterase inhibition; ↓ oxidative stress and pro-inflammatory markers	Jusril et al. (2022)

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Activity	Model	Dose	Effects	Mechanism	Reference
	Nanoemulsion/ SNEDDS formulation	Not specified	Stable, non-irritating nanosized droplets	Improved delivery of antioxidant phytochemicals	Tripathy & Srivastav (2023)
Liposomes	Topical skin cancer delivery model	Not specified	High entrapment efficiency; ~80% drug release	Transliposomal delivery enhanced dermal delivery of asiatic acid	Fitri et al. (2024)
Hydrogel	Wound-healing rat model	Not specified	Improved solubility and significantly reduced wound size	Enhanced local delivery of C. asiatica extract	Qadir et al. (2023)
Solid Lipid Nanoparticles	U87-MG glioblastoma cells/spheroids	Not specified	↑ Cytotoxicity and cellular uptake	RGD-conjugated SLNs enhanced cellular uptake and tumour targeting	Hong et al. (2005)
	Mouse model of cognitive impairment	Not specified	Improved memory; ↓ inflammation and oxidative stress	Nose-to-brain delivery of asiatic acid	Islamie et al. (2023)
Nanostructured Lipid Carriers	Liver injury/fibrosis model	Not specified	Improved oral absorption; ↓ liver injury and fibrosis	Enhanced liver targeting; ↓ hydroxyproline and collagen accumulation	Chen et al. (2020)

↓: Decrease/inhibition/downregulation; ↑: Increse/stimulation/upregulation;↓: Decrease/inhibition/downregulation; ↑: Increse/stimulation/upregulation;Bax – Bcl-2-associated X protein; Bcl-2 – B-cell lymphoma 2; LC3-II/I – Microtubule-associated protein 1A/1B-light chain 3-II/I;reactive oxygen species (ROS); vascular endothelial growth factor (VEGF); vascular endothelial growth factor receptor 2 (VEGFR2); endoplasmic reticulum (ER); epithelial–mesenchymal transition (EMT); phosphoinositide 3-kinase (PI3K); protein kinase B (Akt); mechanistic target of rapamycin (mTOR); mitogen-activated protein kinase (MAPK); microtubule-associated protein 1A/1B-light chain 3 (LC3); ; hypoxia-inducible factor 1 (HIF-1); nuclear factor erythroid 2-related factor 2 (NRF2); nuclear factor kappa B (NF-κB); transforming growth factor beta 1 (TGF-β1); tissue inhibitor of metalloproteinases 3 (TIMP3); superoxide dismutase (SOD); myeloperoxidase (MPO); basic fibroblast growth factor (bFGF); tumor necrosis factor alpha (TNF-α); interleukin-1 beta (IL-1β).

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337 **3.3. *In silico* studies**

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3.3.1. BACE1 for alzheimer's disease:

A docking study screened *C. asiatica* compounds (flavonol, germacrene B, sitosterol) for potential inhibition of BACE1 (Beta Site Amyloid Precursor Protein Cleaving Enzyme 1) (β-secretase), which is involved for generating amyloid-β peptides in alzheimer's disease. However, it was noted that none of the tested compounds interacted with the S1 (Secondary Subsite 1 Prime) subsite of BACE1 (important for some types of inhibition), so the authors concluded that further work is needed before any of these compounds could be considered viable leads (Zhang et al., 2021).

3.3.2. Renin inhibition

Combining pharmacophore modelling, molecular docking and *in vitro* fluorometric assays, one study evaluated the triterpene saponins asiaticoside and madecassoside as renin inhibitors. The docking free-energy value for madecassoside approached that of aliskiren, a synthetic renin inhibitor, and this was borne out by *in vitro* assays confirming genuine renin-inhibitory activity (Mawaddani et al., 2020).

3.3.3. SGLT-2 for diabetes

An *in silico* screen of 21 *C. asiatica* phytochemicals against the sodium-glucose co-transporter 2 (SGLT-2), a validated antidiabetic target, identified 11 compounds with binding free energies comparable to existing SGLT-2 inhibitors. Subsequent 100 ns molecular dynamics simulations and MM/PBSA (Molecular Mechanics/Poisson Boltzmann Surface Area) calculations showed that betulinic acid, centellasapogenol and methyl brahmate maintained stable binding, supporting favourable oral bioavailability (Astiani et al., 2023).

3.4. Toxicity and safety

C. asiatica extract (ECa 233) was found to be safe in healthy volunteers at doses up to 500 mg with only mild, temporary symptoms like headache and stomach discomfort (Macalalad & Gonzales, 2022). An HPLC-MS/MS method was developed to detect *C. asiatica* compounds in plasma and urine and applied it in a Phase I trial. Single 2 g and 4 g oral doses of a standardised water extract were safe, with aglycones and metabolites were measurable, while parent glycosides were present only at minimal levels (Songvut et al., 2019).

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4. Conclusion

The main component of *C. asiatica,* asiatic acid, exhibited enhanced anticancer activity when administered in conjunction with other components and in nanotechnology-based formulations. Asiaticosides and related triterpenoids are heart-friendly, reduce liver enzyme levels, help wound healing, and reduce inflammation. This herb is effective against helicobacter pylori infection, prevents ulcers, and helps control glucose and cholesterol levels. Nanoparticles were found to greatly increase the absorption of cognitive resources and antioxidant activity, while micelles were useful in protecting active ingredients for topical skin applications and nutritional supplements. The hydrogel promoted tissue healing, and solid lipid nanoparticles targeted cancer cells in the brain, reducing oxidative stress and cognitive deficits. Nanostructured liposomes have been shown to suppress liver fibrosis and improve absorption in the gastrointestinal tract. Computational assessments indicated promising compounds targeting BACE1, sodium-glucose cotransporter 2 inhibitors, and angiotensin converting enzyme II inhibitors such as renin, which can be useful for the treatment of metabolic disorders, high blood pressure, and dementia. In clinical trials the suggested dosages have not shown significant negative side effects, only mild and temporary symptoms. Despite progress, there are still several limitations. A significant portion of the existing evidence comes from in vitro and animal studies, with relatively few clinical trials available to confirm efficacy and safety in humans. Variations in plant materials, extraction methods, phytochemical compositions, dosages, experimental models, and formulations complicate direct comparisons between studies. Future studies should concentrate on well-structured clinical trials to confirm the therapeutic effectiveness and safety of *C. asiatica* and its primary bioactive components. It is crucial to standardize plant materials, extracts, active ingredients, dosages, and experimental methodologies to enhance reproducibility and enable comparisons across different studies. Further exploration of pharmacokinetics, bioavailability, molecular targets, synergistic effects, and dose response relationships would enhance the understanding of its mechanisms of action. For nanoparticle-based delivery systems, upcoming research should focus on optimizing formulation properties, targeted delivery, stability, tissue distribution, toxicity, and large-scale production. Combining pharmacological research with advanced drug delivery systems may eventually aid in the development of standardized, safe, and clinically applicable *C. asiatica* based therapeutic products.

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Authors' Contribution

Conceptualization, Supervision, Writing-original draft, Writing-review & editing

Conflicts of interest

The authors declare no conflicts of interest in this work.

Ethical approval

Not applicable

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Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

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