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Centella asiatica in Modern Medicine: Phytochemistry, Therapeutic Mechanisms, and Advances in Formulations

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ABSTRACT

Centella asiatica (L.) Urban, a perennial herb widely utilized in traditional medicine across Asia, Africa and the Pacific, has emerged as a pharmacologically significant plant with broad therapeutic potential, particularly in wound healing. This review consolidates current advances in botanical characterization, cultivation practices and phytochemical profiling, with a focus on pentacyclic triterpenoids such as asiaticoside, madecassoside and their corresponding aglycones as the primary bioactive constituents. Mechanistic studies demonstrate that C. asiatica promotes collagen synthesis, angiogenesis and immunomodulation, largely mediated via TGF-β/Smad, VEGF and pro-inflammatory cytokine pathways. Clinical evidence substantiates its efficacy in accelerating wound closure, enhancing tissue regeneration and minimizing scarring, with a favourable safety profile. Furthermore, novel formulation strategies—including nanoemulsions, hydrogels and electrospun scaffolds—have been developed to improve bioavailability and therapeutic outcomes. Despite these advancements, challenges remain in standardization of extracts, optimization of pharmacokinetics and regulatory harmonization. This review highlights the importance of developing standardized phytopharmaceutical formulations, scalable delivery platforms, and robust multicenter clinical trials to firmly validate the therapeutic potential of C. asiatica in wound healing and other medical applications.

This review examines the phytochemical composition, pharmacological effects, and clinical significance of Centella asiatica, focussing particularly on its contribution to wound healing and the most recent formulation strategies.

Keywords: *Centella asiatica, Phytopharmacology, Triterpenoids, asiaticoside, madecassoside, Nano formulations.*

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1. INTRODUCTION

Centella asiatica (L.) Urban, popularly known as Gotu Kola, is a perennial herb from the Apiaceae family that grows naturally across tropical and subtropical regions of Asia, Africa, and the Pacific Islands. With a rich history spanning more than 2,000 years, it has been an important part of traditional healing systems such as Ayurveda, Traditional Chinese Medicine, and Siddha. [1,2] Traditionally, it has been used to manage a wide range of health issues, from skin problems and wounds to neurological and cognitive disorders. Its long-standing use in treating conditions like ulcers, eczema, leprosy, anxiety, and memory loss highlights its reputation as a versatile medicinal plant valued in both folk and tribal practices worldwide.[3,4]

The healing power of *Centella asiatica* comes mainly from its rich mix of phytochemicals, especially pentacyclic triterpenoid saponins like asiaticoside, madecassoside, asiatic acid, and madecassic acid.[5] These compounds have been widely studied for their anti-inflammatory, antioxidant, neuroprotective, wound-healing, and anticancer effects. Of these, its role in wound healing is the most well-documented, with strong preclinical and clinical evidence showing that it boosts collagen production, supports new blood vessel formation, and speeds up skin regeneration. Through these actions, *C. asiatica* helps repair tissue effectively, making it especially useful in treating acute injuries as well as chronic wounds like burns and diabetic ulcers.[6]

Although a lot has been discovered about *Centella asiatica*, there are still hurdles to overcome—such as standardizing its extracts, fully understanding how it works, and improving delivery methods to enhance its absorption and effectiveness in patients.[7] Beyond its well-known benefits in wound healing, new studies are uncovering its potential in treating neurodegenerative diseases, metabolic disorders, and a variety of skin conditions, making it important to bring together and review these growing insights.[8]

This review aims to offer a comprehensive and up-to-date overview of *Centella asiatica*, covering its botanical background, detailed phytochemical profile with structural insights, and wide-ranging therapeutic applications, with particular emphasis on its wound-healing mechanisms.[9] It also examines findings from clinical trials, explores underlying pharmacodynamic pathways, and highlights future prospects involving novel formulation approaches to improve its clinical use. Overall, this synthesis is intended to serve as a valuable reference for researchers, clinicians, and pharmaceutical scientists working to harness the full therapeutic potential of *Centella asiatica*.[10]

2. BIOLOGICAL SOURCE, COLLECTION AND CULTIVATION

2.1 Botanical Identity and Distribution

Centella asiatica (L.) Urban, belonging to the Apiaceae family and the order Apiales, is a perennial herb with creeping stolons that enable vegetative growth and ground spreading. It is characterized by green, kidney-shaped leaves with smooth surfaces and palmately netted veins, held on long petioles. The plant bears tiny, hermaphroditic flowers arranged in small umbels close to the ground, ranging in color from white to pinkish-red. Its fruit, marked by a dense reticulate pattern, serves as a key feature for distinguishing it from related species.

Figure 1. Centella asiatica (L.)

C. asiatica naturally grows in tropical and subtropical wetlands, spanning the Indian subcontinent, Southeast Asia, parts of Africa, Madagascar, Australia, and several Pacific islands. It thrives in moist, shaded places like marshes, riverbanks, and lowland wetlands, preferring loamy to sandy soils. Because of its close link to aquatic habitats, the plant can absorb pollutants from its surroundings, which may affect its phytochemical makeup. [11]

2.2 Collection and Harvesting Practices

Traditionally, *Centella asiatica* is harvested mannually about three months after planting, when the plant reaches full maturity. To allow regrowth, the aerial parts are usually cut just above the rhizome, although in some traditional practices the whole plant is collected. Even with mechanized options available for large-scale farming, manual harvesting is still preferred to ensure better-quality raw material.[12]The leaves contain the highest levels of phytochemicals when picked at peak maturity and processed immediately, but improper drying or storage can lead to the loss of these bioactive compounds, highlighting the importance of careful handling.

The concentration of key triterpenoids, such as asiaticoside and madecassoside, which are crucial for therapeutic activity, are strongly influenced by both the timing of harvest and post-harvest processing.[13.14]

2.3 Cultivation Techniques

Traditional cultivation of *Centella asiatica* relies on vegetative propagation through stolons or seeds in irrigated open fields, often supported by shade management and organic fertilization. More recently, controlled-environment methods such as hydroponics and smart farming have emerged, allowing year-round production while improving both sustainability and phytochemical richness. [15] Hydroponic systems, in particular, offer precise control over nutrients and environmental factors, which enhances the production of triterpenoid saponins.

Growing the plant without soil also reduces the risk of contamination and lowers resource requirements, making it well-suited for producing standardized, pharmaceutical-grade material. These modern approaches hold great potential for increasing both the consistency and quality of *C. asiatica* used in medicine.[16]

3. PHYTOCHEMISTRY OF CENTELLA ASIATICA

3.1 Major Phytoconstituents

Centella asiatica is highly valued for its rich content of pentacyclic triterpenoid saponins, known as centelloids, which serve as the main bioactive compounds driving its wide-ranging pharmacological effects. Among these, the most studied and therapeutically significant are asiaticoside and madecassoside, along with their aglycones, asiatic acid and madecassic acid. These compounds are classified as ursane-type pentacyclic triterpenoids, featuring a five-ring core structure with hydroxyl and carboxyl groups that are key to their biological activity.[17]

Asiaticoside and madecassoside are glycosylated saponins, composed of a triterpene aglycone bound to sugar units—mainly glucose and rhamnose—attached at the C-28 position.[18] This sugar attachment gives the molecules amphiphilic characteristics, influencing their solubility, interactions with cell membranes, and pharmacokinetic behavior. In contrast, their aglycones, asiatic acid and madecassic acid, lack these sugar groups, making them more hydrophobic while still retaining significant biological activity.[19]

In addition to the major centelloids, *Centella asiatica* contains minor triterpenoids like brahmoside, brahmioside, and centellic acid, which add to its phytochemical diversity, though they are present in smaller amounts. These compounds collectively amount to approximately 1-8% of the dried leaf weight, with variations dependent on environmental factors, plant components and extraction methodology.[20]

3.2 Chemical Structures and Properties

Structurally, the core of these triterpenoids is a characteristic pentacyclic skeleton composed of six-membered rings A, B, C, D and a five-membered ring E. Asiaticoside and madecassoside showcase a ursane skeleton modified by hydroxylation at distinct sites and conjugation to sugar chains (trisaccharides) that extend hydrophilicity (Figure2.)

The sugar moieties mainly attach via β-glycosidic linkages, impacting the molecular conformation and receptor binding affinities. The aglycones Asiatic acid and madecassic acid present free carboxylic groups and hydroxyl functionalities, endowing them with the capacity for hydrogen bonding and cellular uptake. [21.22]

Water solubility of these triterpenoids varies; glycosylated asiaticoside and madecassoside are more soluble in aqueous and alcoholic solvents compared to their aglycones, which display lipophilicity and lower aqueous solubility. Stability studies indicate that these compounds are sensitive to heat, acid conditions and prolonged light exposure, which may degrade the sugar moieties, emphasizing the need for appropriate formulation and storage.[23]

Pharmacokinetically, asiaticoside and madecassoside are rapidly absorbed in the gastrointestinal tract, with peak plasma concentrations occurring within 15 to 30 minutes after oral administration. Metabolic cleavage by intestinal and hepatic enzymes produces asiatic acid and madecassic acid, which exert systemic pharmacological actions. These properties present both challenges and opportunities for optimizing Centella-based therapeutics [24,25].

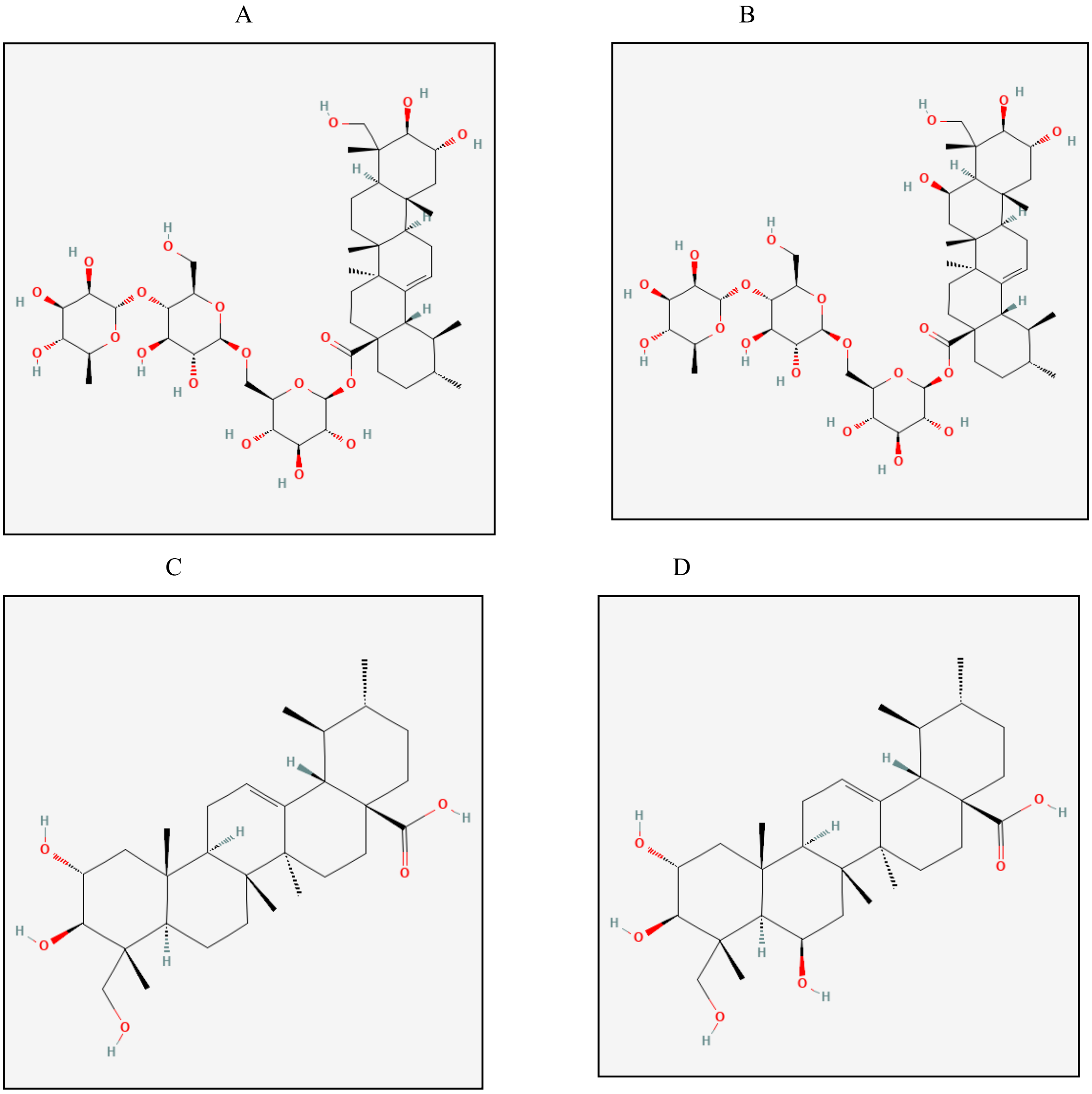

Figure 2. Molecular structures of pentacyclic triterpenoids from *Centella asiatica*: (A) Asiaticoside, (B) Madecassoside, (C) Asiatic acid, (D) Madecassic acid. The figure shows 2D chemical structures with annotations of functional groups and glycosylation sites.

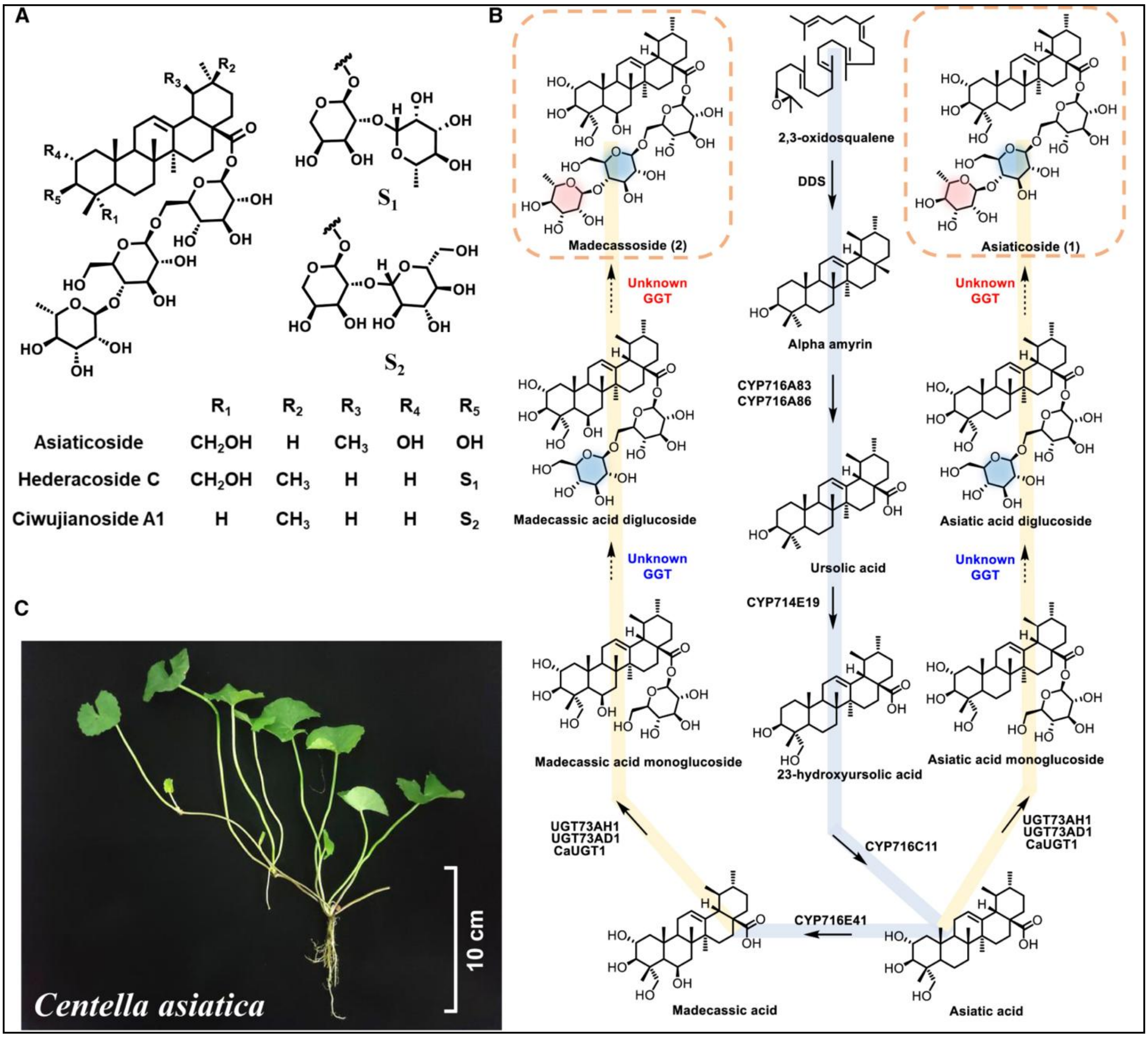

Figure 3. Schematic representation of the biosynthetic pathway for major triterpenoids in *Centella asiatica*, highlighting enzymatic conversions from 2,3-oxidosqualene to asiaticoside and madecassoside.

3.3 Qualitative and Quantitative Analytical Methods

Proper identification and measurement of *Centella asiatica*'s triterpenoids are essential for ensuring quality, standardization, and clinical effectiveness. Analytical approaches mainly rely on chromatographic and spectroscopic techniques. High-performance liquid chromatography (HPLC) with ultraviolet (UV) detection is widely regarded as the standard method for quantifying asiaticoside, madecassoside, asiatic acid, and madecassic acid in both plant extracts and finished products.[26] Using gradient elution with water-acetonitrile mobile phases allows effective separation, while UV detection at around 205 nm takes advantage of the compounds chromophoric properties. [27]

Recent developments, such as ultra-performance liquid chromatography (UPLC) paired with tandem mass spectrometry (MS/MS), offer higher sensitivity, better selectivity, and faster analysis, even in complex biological samples. These advanced methods allow simultaneous measurement of multiple compounds, which is crucial for accurate phytochemical profiling.[28] Complementary techniques, like thin-layer chromatography (TLC), provide quick qualitative checks, especially useful in resource-limited settings or for initial screening, whereas gas chromatography-mass spectrometry (GC-MS) is mainly used for analyzing volatile oils rather than triterpenoids.

For standardization, asiaticoside and madecassoside are commonly used as marker compounds because of their abundance and biological significance. Extracts standardized to defined levels of these compounds help ensure consistent quality and therapeutic effectiveness across different batches, both in research and commercial products.[29]

4. THERAPEUTIC ROLES AND MECHANISTIC INSIGHTS

4.1 Wound Healing

4.1.1 Historical and Ethnomedicinal Use

Centella asiatica has a rich legacy in traditional medicine systems, serving as a primary botanical remedy for wounds, burns, ulcers and dermatological disorders in Ayurveda, Siddha and Chinese medicine. Ethnomedical usage frequently involved topical application of *Centella* paste or decoction to lacerations and ulcerated skin, with empirical reports of accelerated tissue regeneration and reduced scarring supporting its widespread adoption as a "wound herb" in folklore and classical texts. [30,31,32]

4.1.2 Preclinical and Clinical Evidence

Contemporary research has substantiated *Centella asiatica*'s role in wound repair through a diverse portfolio of animal, *in vitro* and human clinical studies. *In vivo* models demonstrate that extracts and isolated triterpenoids notably asiaticoside, madecassoside, asiatic acid, and madecassic acid, facilitate rapid re-epithelialization, contraction and granulation tissue formation.[33] In a key randomized study, patients treated with topical *Centella asiatica* cream experienced faster healing of second-degree burns compared to those using standard silver sulfadiazine, showing quicker re-epithelialization and improved wound contraction.[34] Similar evidence of accelerated healing was found in chronic ulcers and post-surgical wounds, where *Centella*-based formulations reduced inflammatory infiltrate and improved tensile strength of repaired tissue.

Further, animal studies and ex vivo models corroborate *Centella's* efficacy in collagen synthesis, angiogenesis and restoration of extracellular matrix, as histological studies reveal denser collagen fibers, augmented neovascularization and diminished pro-inflammatory cell counts in treated wounds.[35]

4.1.3 Cellular and Molecular Mechanisms

Collagen Synthesis and Matrix Remodeling:
Centella asiatica stimulates production of type I and III collagen, critical for wound tensile strength and scar minimization. Asiaticoside and madecassoside upregulate the TGF-β/Smad signaling axis, activating Smad2/3 phosphorylation and promoting collagen gene transcription in human dermal fibroblasts. Enhanced collagen deposition is a hallmark of *Centella's* wound healing mechanism.[36]

Angiogenesis and Granulation Tissue Formation:
Promoting neovascularization is key to tissue repair. *Centella asiatica* elevates expression of Vascular Endothelial Growth Factor (VEGF) and Fibroblast Growth Factor (FGF), stimulating endothelial cell migration and capillary formation within the wound bed.[37]

Modulation of Inflammatory Cascades:
Centella asiatica reduces levels of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and downregulates cyclooxygenase-2 (COX-2) and prostaglandin E2 (PGE2) synthesis, thereby controlling excessive inflammation and facilitating optimal tissue regeneration. It also impedes infiltration of neutrophils and macrophages at injured sites.[38]

Regulation of Growth Factors:
Centella's triterpenoids bolster FGF and VEGF synthesis, further amplifying cellular proliferation and vascularization necessary for effective wound closure. Additionally, MAPK, Akt, and FAK pathways are activated, governing cell migration, proliferation and matrix remodelling.[39]

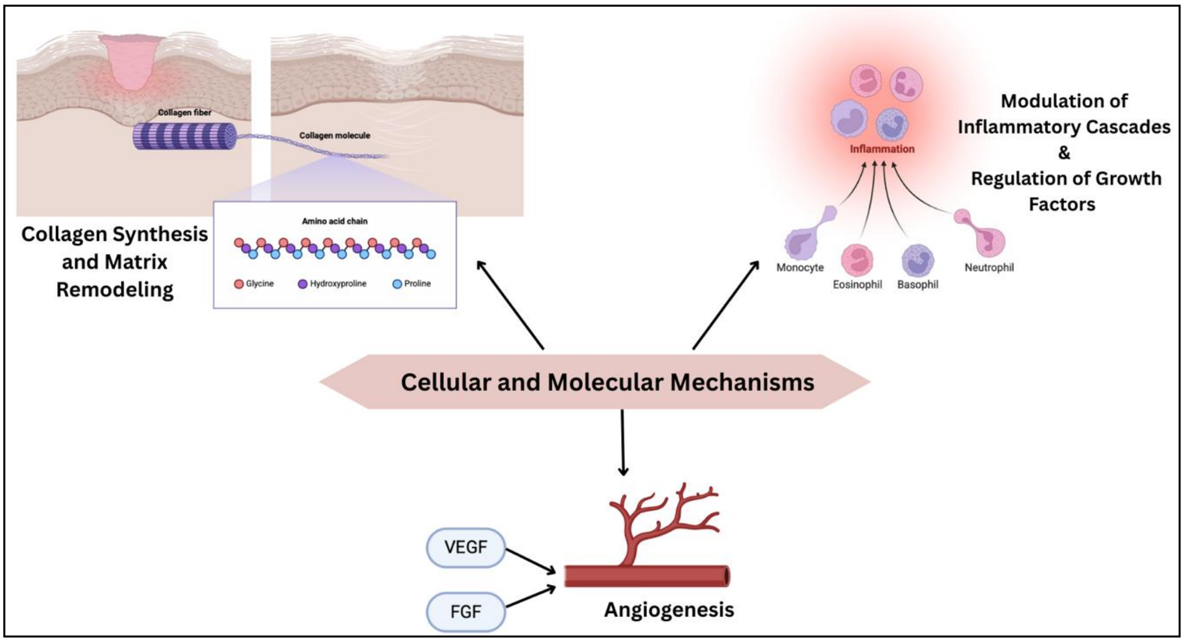

Figure 4. Schematic representation of regulation of growth factors

4.1.4 Advances in Wound Healing Formulations

Recent innovations in *Centella asiatica* delivery systems—hydrogel matrices, nano encapsulated sprays and electrospun fiber membranes—have dramatically improved wound contact, sustained release and bioavailability of active centelloids. Clinical and preclinical data demonstrate superior healing rates, enhanced epithelial thickness and reduced risk of infection with these advanced formulations versus traditional topicals. Formulated hydrogels containing asiaticoside exhibit expedited wound closure, increased granulation and absence of skin irritation, while electrospun membranes support fibroblast proliferation and antibacterial defense. [40,41,43]

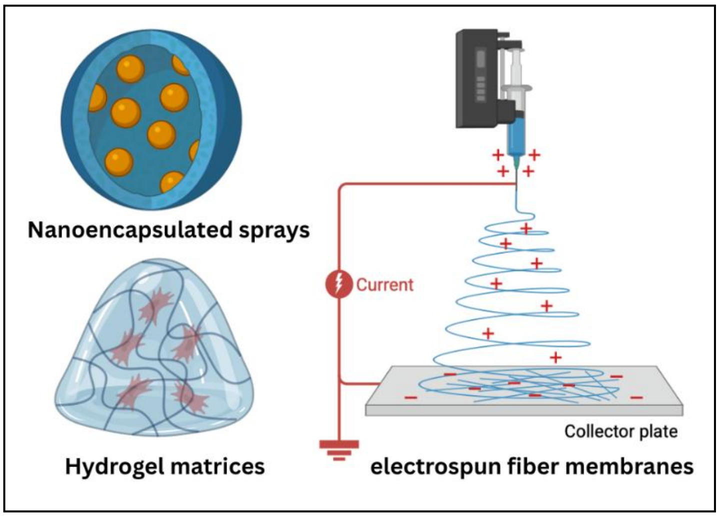

Figure 5. Recent innovations in *Centella asiatica* delivery systems, Nanoencapsulated Sprays, Hydrogel Matrices, and Electrospun Fiber Membranes

4.2 Neuroprotective and Cognitive Benefits

4.2.1 Preclinical Models and Clinical Studies

Numerous animal studies have highlighted the neuroprotective effects of *Centella asiatica* in models of aging, neurodegeneration, and cognitive decline. In these studies, supplementation with the extract enhanced memory, spatial navigation, and synaptic density in rodents experiencing chemical or genetic neuronal damage. Early clinical trials in older adults and individuals with mild cognitive impairment also showed modest benefits, including improved attention and processing speed following oral administration of *Centella* extracts.[44]

4.2.2 Mechanisms: Mitoprotection, Antioxidant Effects, Neurogenesis

Centella asiatica provides neuroprotective effects through several mechanisms. Primarily, it preserves mitochondrial structure and function by maintaining membrane potential and lowering oxidative stress. Second, potent antioxidant activity diminishes reactive oxygen species, supported by upregulation of superoxide dismutase and glutathione peroxidase. Third, it upregulates brain-derived neurotrophic factor (BDNF), driving neurogenesis and synaptogenesis critical for cognitive restoration. Anti-inflammatory effects in the CNS are achieved via suppression of microglial activation and decreased expression of inflammatory mediators (e.g., TNF-α and IL-1β).[45]

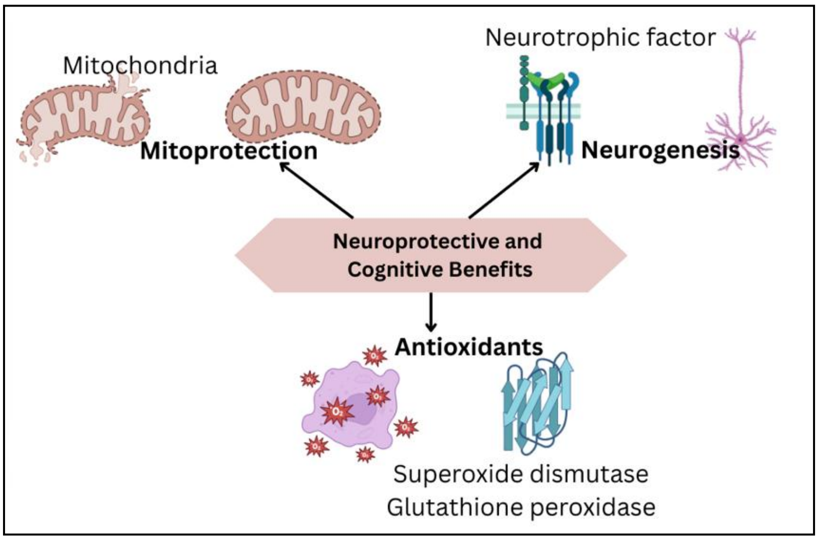

Figure 6. Mechanisms Underlying Neuroprotective and Cognitive Benefits: Mitoprotection, Neurogenesis, and Antioxidant Pathways

4.3 Anti-inflammatory and Antioxidant Activity

4.3.1 Cytokine and Chemokine Suppression

Centella asiatica and its triterpenes robustly attenuate levels of circulating pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and chemokines involved in chronic inflammation, contributing to its broad-spectrum anti-inflammatory profile. Delivery of standardized extracts has been shown to lower serum markers of inflammation in animal and preliminary human studies.[46]

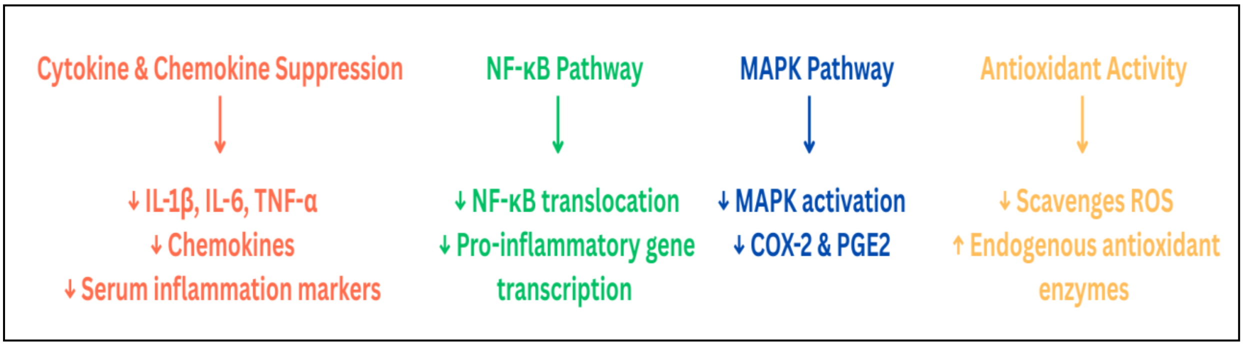

Figure 7. Key Anti-Inflammatory and Antioxidant Mechanisms: Cytokine Suppression, NF-κB and MAPK Pathways, and Antioxidant Activity

4.3.2 Pathway Modulation (NF-κB, MAPK)

Mechanistically, *Centella asiatica* inhibits nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) translocation and reduces activation of mitogen-activated protein kinases (MAPK), thereby limiting downstream pro-inflammatory gene transcription. Modulation of these pathways leads to decreased synthesis of mediators like COX-2 and PGE2 and mitigation of chronic inflammatory processes. Antioxidant function is further heightened by direct scavenging of reactive oxygen species and improvement in endogenous antioxidant enzyme levels.[47]

4.4 Metabolic and Anti-diabetic Roles

4.4.1 Clinical Evidence

Emerging human studies and multiple animal reports indicate that *Centella asiatica* can ameliorate hyperglycemia and insulin resistance, presenting potential as a complementary therapy in diabetes management. Diabetic rats treated with *Centella* extracts displayed lower fasting glucose, improved insulin sensitivity and reduced markers of oxidative stress.[48]

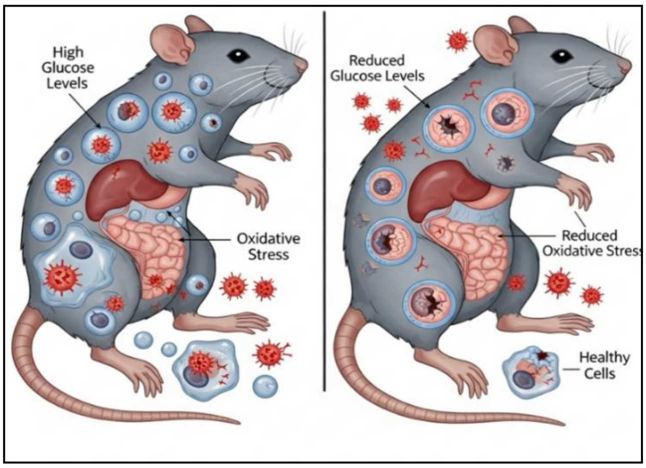

Figure 8. Diagrammatic representation of diabetic rats treated with *Centella* extracts showing lower fasting glucose, improved insulin sensitivity and reduced markers of oxidative stress.

4.4.2 Effects on Glucose and Lipid Metabolism

Centella asiatica enhances peripheral glucose uptake, modulates hepatic gluconeogenesis and normalizes lipid profiles by reducing serum triglycerides and cholesterol, effects attributed to activation of AMP-activated protein kinase and suppression of inflammatory signalling in adipose tissue.[49]

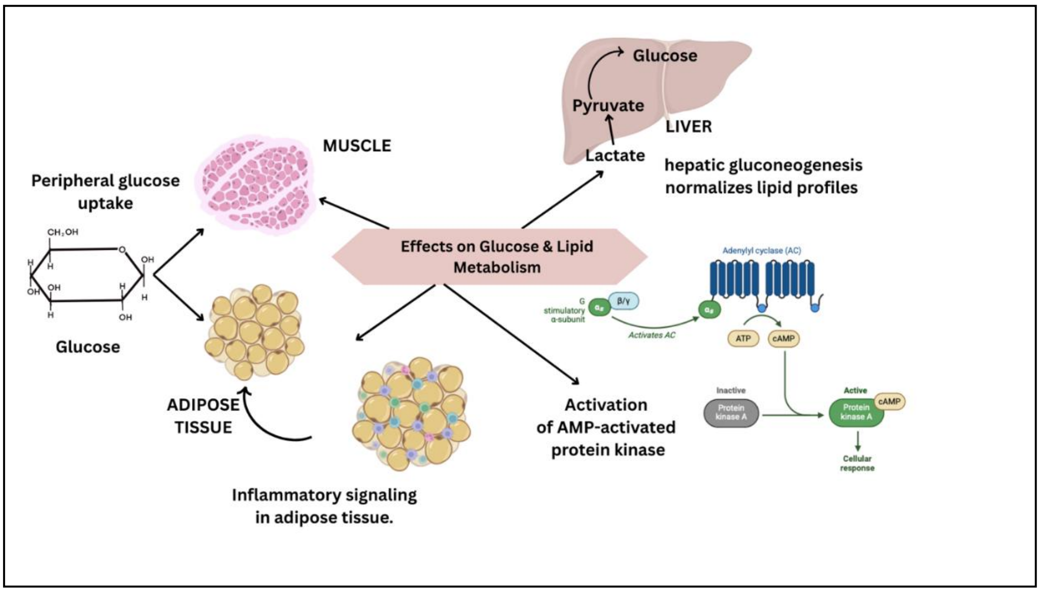

Figure 9. Cellular Regulation of Glucose and Lipid Homeostasis

4.5 Dermatology and Skin Disorders

Centella asiatica is broadly utilized in dermatology for atopic dermatitis, psoriasis and scar management. Topical application reduces pruritus, erythema and plaques while promoting epidermal integrity and elasticity, with triterpenoid saponins playing a principal role in preventing abnormal keratinocyte proliferation and mitigating mast cell recruitment.[50] These mechanisms contribute to decreased scarring, enhanced skin barrier function, and improved patient outcomes. [51]

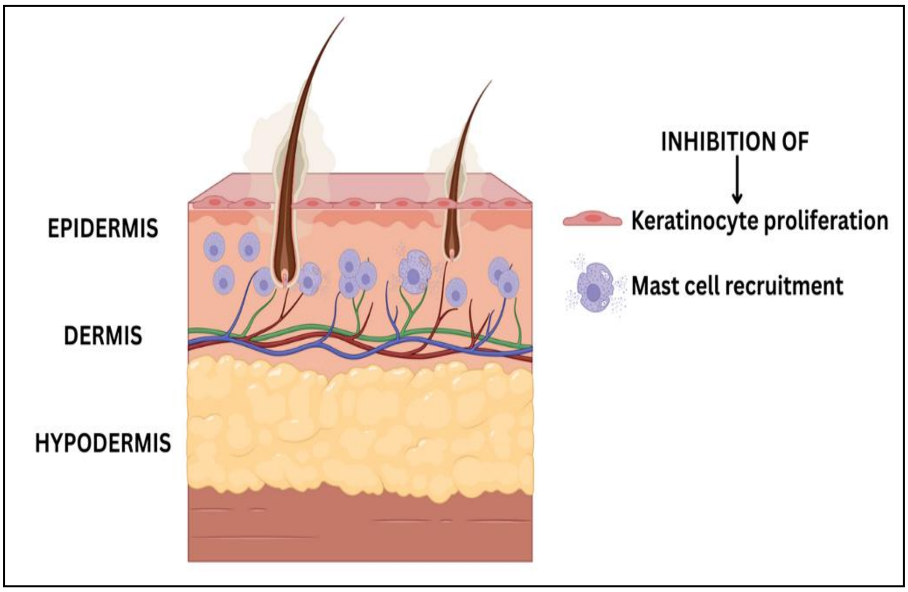

Figure 10. Mechanistic Pathways Inhibiting Keratinocyte Proliferation and Mast Cell Recruitment in Skin Layers

5. CLINICAL TRIALS AND EVIDENCE SYNTHESIS

5.1 Human Studies: Wound Healing

A robust body of clinical research evaluates the efficacy of *Centella asiatica* and its triterpenoid-rich extracts in promoting wound healing—especially in chronic ulcers, burns, and diabetic wounds. A pivotal randomized clinical trial investigated the use of oral *Centella asiatica* extract capsules (containing 50 mg asiaticoside each) among diabetic foot ulcer patients, with three capsules administered per day for up to 21 days. Outcomes demonstrated statistically significant wound contraction, expedited healing times and improvement in granulation tissue compared to placebo controls. Moreover, scar suppression and improved collagen content, measured by increased hydroxyproline concentrations in wound tissue, further substantiated clinical benefit.[52]

Another study compared topical *Centella* creams to silver sulfadiazine in second-degree burn patients, revealing that those receiving *Centella* formulation healed substantially faster—with an average healing time of 14.67 ± 1.78 days, versus 21.53 ± 1.65 days in controls ($p<0.001$). Re-epithelialization and wound closure were similarly improved, alongside reductions in local pain, erythema and infection rates. Adverse events were infrequent and mild, mainly consisting of transient localized irritation. No systemic toxicity or severe drug reactions were reported, confirming a favourable safety profile.[53]

Further multicenter clinical investigations have employed titrated extracts and specific dressings containing *Centella asiatica* (Cytol Centella), demonstrating augmented angiogenesis, matrix remodelling, and a significant decrease in inflammatory cell infiltration. Histopathological analysis of burn wounds revealed increased vascularization and maturation of collagen fibres, supporting regenerative outcomes. Studies in chronic anal fissure and after laser resurfacing procedures also showed faster bleeding cessation, reduced pain scores, and improved cosmetic wound appearance in Centella-treated groups as compared to standard management.[54]

Emerging topical delivery platforms such as hydrogels, Nano encapsulated sprays, or electro spun membranes loaded with asiaticoside or madecassoside provide controlled release and optimized tissue penetration, leading to even greater efficacy in clinical wound closure and tissue quality. The consistency across trials suggests reproducible benefits of standardized *Centella* extracts, both orally and topically, for wound and burn management—although wider studies with standardized extract composition and dosing are recommended.[55]

5.2 Other Clinical Indications

Centella asiatica's therapeutic spectrum extends to cognitive function, metabolic and skin disorders. Early-phase trials have evaluated oral *Centella* supplementation in elderly patients with mild cognitive impairment, observing improved attention, psychomotor speed and memory performance relative to placebo—though effect sizes are moderate and long-term data remain limited. Safety endpoints were satisfactory, with no major adverse reactions noted.[56]

In diabetes management, pilot studies in animal and human models report improved glycaemic indices, increased insulin sensitivity, and improved lipid profiles following administration of *Centella asiatica* extracts. Patients showed decreased fasting glucose and serum triglycerides, accompanied by improved antioxidant capacity and reduced markers of oxidative stress.[57] These trials highlight *Centella asiatica's* potential as an adjunct for metabolic disorders; however, multicenter human trials are sparse and standardization challenges persist.

In dermatologic practice, randomized studies of *Centella*-based creams and ointments on patients with atopic dermatitis, psoriasis and hypertrophic scars document reductions in pruritus, erythema, plaque thickness and post-inflammatory hyperpigmentation.[58] Topical Centella formulations demonstrated anti-pruritic and anti-inflammatory effects that outperformed conventional emollients, with significant improvements in patient-reported outcomes and skin barrier restoration.[59]

5.3 Meta-analyses and Systematic Reviews

Comprehensive systematic reviews have aggregated the available evidence regarding *Centella asiatica's* wound healing and broader therapeutic activities. Arribas-López et al. (2022) synthesized four randomized human clinical trials and found consistent improvements in wound contraction, re-epithelialization rates and granulation tissue, particularly for chronic wound and burn settings. The meta-analysis emphasized marked reductions in pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), enhanced collagen synthesis via TGF-β/Smad pathways and significant gains in cosmetic and functional wound quality.[60]

Other meta-analyses have examined the impact of *Centella asiatica* in cognitive enhancement, dermatologic and metabolic endpoints, reporting overall moderate-to-high efficacy compared to placebo or standard care—while reiterating the need for harmonized, standard extract compositions and consistent dosing criteria.[61]

Safety data across studies are favourable, with adverse events confined to mild, transient skin reactions or gastrointestinal discomfort; severe events have not been observed. Systematic assessment of reporting bias and study heterogeneity suggest moderate confidence in the beneficial wound healing effect, but recommend further well-powered trials for applications outside wound repair.[62]

6. NOVEL FORMULATIONS AND FUTURE PROSPECTS

6.1 Modern Pharmaceutical Technologies

Cutting-edge formulation technologies have dramatically enhanced the therapeutic application and bioavailability of *Centella asiatica* derivatives, driving its emergence in wound healing, dermatology and systemic therapy. Among the most promising are Nano emulsions, which utilize submicron droplets to encapsulate triterpenoids like asiaticoside and madecassoside, vastly improving skin penetration and stability. These Nano emulsions demonstrate superior release kinetics and targeted delivery to inflamed and damaged tissues, making them highly suitable for topical and transdermal wound care.[63]

Hydrogels composed of natural polymers integrated with *Centella* extracts offer biocompatibility, moisture retention and sustained release of active molecules. In wound care, Centella-loaded hydrogels accelerate epithelialization and granulation while preventing infection and irritation. Their viscoelastic properties facilitate coverage of complex wound surfaces and their ease of application supports patient comfort and compliance.[64]

The development of functional bandages and electro spun nanofibers incorporates *Centella* derivatives into a scaffold, promoting cellular proliferation, angiogenesis and tissue integration. Electrospinning enables control of fibre composition and architecture, maximizing the surface area and interaction between active phytoconstituents and the healing tissue. Recent products demonstrate reduction in scar formation and improved cosmesis for hypertrophic and post-procedural wounds.[65]

Emerging interest also surrounds microencapsulation, which stabilizes *Centella* actives against environmental degradation and facilitates incorporation into oral supplements, beverages or multifunctional ointments. These developments reflect the growing demand for plant-based products and help ensure both regulatory compliance and consumer safety.[66]

6.2 Challenges in Standardization and Bioavailability

Despite these technological improvements, challenges remain. Ensuring consistent extract standardization is still a major issue, as differences in cultivation, harvesting, and processing lead to considerable variation in active triterpenoid levels between batches. While analytical methods like high-performance liquid chromatography (HPLC) and PCR-based molecular authentication now allow for more accurate quantification and verification of *Centella* products, globally accepted standardized practices have yet to be fully implemented.[67]

The bioavailability of centelloids, especially the hydrophobic aglycones, remains a significant challenge. Nanoencapsulation and polymeric delivery systems have produced meaningful improvements in absorption and tissue distribution, but pharmacokinetic variability across patient populations and product formats necessitates ongoing research. Furthermore, stability and compatibility of *Centella asiatica* derivatives with various excipients require detailed evaluation to optimize formulation longevity and efficacy.[68]

6.3 Roadmap for Clinical Translation

For transition of novel formulations from laboratory to clinic, robust and scalable standardization protocols are essential, supported by regulatory alignment and transparent labelling.[69] Future clinical trials should prioritize direct comparisons of standardized nanoemulsions, hydrogels and advanced wound dressings in target populations, employing validated biomarker endpoints (e.g., collagen synthesis, angiogenesis) and stringent adverse event monitoring.[70]

Partnerships between agricultural producers, processing units and pharmaceutical manufacturers are imperative to secure traceable sourcing and sustainable production frameworks. International certification (such as organic, GMP, and sustainability labels) will strengthen global market positioning. [71]Regulatory agencies should facilitate harmonized standards, enabling the approval of multifunctional *Centella asiatica* products for indications like scar minimization, chronic wound care, and preventive dermatology.[72]

Expanding research into combination therapies (i.e., *Centella* with other phytochemicals or conventional drugs), molecular synergies and adaptive delivery vehicles will further enhance clinical utility. Ultimately, advancing *Centella asiatica* formulations demands interdisciplinary collaboration—from plant genomics and extraction science to pharmacology and clinical medicine—to fully realize its therapeutic promise.[73]

7. DISCUSSION

The extensive body of preclinical and clinical evidence substantiates *Centella asiatica* as a multifaceted phytotherapeutic agent with robust activities in wound healing, neuroprotection, anti-inflammatory modulation, metabolic regulation, and dermatological applications. Nevertheless, several gaps and controversies challenge its full translational realization.[74,75,76]

A major challenge lies in the chemical complexity and variability inherent in botanical extracts. Unlike single-molecule drugs, *C. asiatica* preparations comprise multiple bioactive triterpenoids, flavonoids and phenolics with variable concentrations depending on cultivation, harvesting and extraction processes.[78] This variability makes it difficult to standardize dosages and achieve consistent results in clinical trials, often resulting in unpredictable efficacy. The lack of widely accepted standardization methods and validated biomarkers also hampers regulatory approval and incorporation into clinical guidelines.[79]

Another challenge lies in the bioavailability and pharmacokinetics of *Centella asiatica* compounds. The hydrophobic characteristics of major triterpenoids, particularly asiatic acid and madecassic acid, limit their systemic absorption and tissue distribution.[80] Although recent developments in nanoformulations and controlled-release hydrogels offer potential solutions, these approaches require thorough validation to ensure that preclinical benefits translate into effective clinical outcomes.[81]

When compared to other medicinal plants like *Panax ginseng* and *Ginkgo biloba*, *Centella asiatica* shares similar challenges, mainly its chemical complexity and variability between batches.[82] Yet, its ability to promote wound healing and support cognitive function often exceeds that of these herbs, likely due to the action of specific triterpenoids and a generally safe profile. These unique qualities position *C. asiatica* as a standout example in pharmacognosy and a strong candidate for integrative therapeutic approaches.[83]

Centella asiatica holds significant potential for use alongside conventional treatments. When combined with standard wound care, neuroprotective drugs, or anti-inflammatory medications, it may boost therapeutic outcomes while reducing side effects. [84,85] Especially in chronic wounds and neurodegenerative conditions, integrating *C. asiatica* formulations with existing therapies could speed up healing, lessen inflammation, and enhance patients' quality of life.[86,87,88]

For *Centella asiatica* to achieve successful clinical translation, it is essential to ensure rigorous quality control, develop optimized delivery systems, and conduct large, well-designed randomized controlled trials targeting meaningful clinical outcomes.[89,90]Collaboration across disciplines—including phytochemistry, clinical medicine, and regulatory affairs—is crucial to navigate regulatory requirements and accelerate the integration of this botanical into mainstream healthcare.[91,92,93]

8. CONCLUSION

Centella asiatica is a chemically diverse medicinal plant with proven benefits in wound healing, neuroprotection, inflammation control, metabolic regulation, and skin health. Its key bioactive triterpenoids, especially asiaticoside and madecassoside, drive many of these effects via well-understood molecular mechanisms. Clinical studies have confirmed its effectiveness and safety, particularly in promoting wound repair and supporting cognitive function.

Nevertheless, challenges such as chemical variability, limited bioavailability, and the absence of standardized dosage forms hinder widespread clinical use. Continued progress in pharmaceutical formulation and well-designed clinical research is crucial to unlock the full therapeutic potential of *Centella asiatica*.

Future research should focus on creating and validating standardized extracts, developing optimized nano- and hydrogel-based delivery systems, and conducting large multicenter clinical trials with clearly defined outcomes. Integration with conventional therapeutics offers a promising avenue for enhanced patient outcomes..

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