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REVIEW ARTICLE

Centella asiatica- Derived Compounds: Applications in the Prevention and Treatment of Skin Disorders

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ABSTRACT
Centella asiatica (L.) Urban is a multifaceted and potent component in skincare, providing a variety of advantages such as wound healing, anti-aging properties, moisturization, and acne therapy. The exceptional effectiveness in curing a remarkable number of skin related ailments has led to its shift from traditional medicine to modern skincare. This valuable herb is frequently used in moisturizers, wound care products, and anti-aging formulations. C. asiatica comprises an array of phytochemicals, such as saponins, phenolic acids, triterpenoids, and flavonoids, which collectively enhance its potential advantages for skin health. It may alleviate some prevalent skin problems but might induce adverse consequences at elevated dosages. Research indicates that it enhances tissue regeneration and increases fibroblast proliferation and collagen formation.
Keywords: *Centella asiatica, Skin, Anti-aging, Bioactive compound, Triterpenoids.*

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INTRODUCTION

Herbaceous angiosperms generate hundreds to thousands of chemical molecules exhibiting various biological functions. The survival of humanity on the planet is contingent upon many plant species for their medicinal and other advantageous features [1]. *Centella asiatica*(L.) Urban has emerged as a crucial ingredient in improving skin health due to its unique properties. It is a renowned medicinal plant utilised in traditional treatments and skin care solutions [2-3]. The shoot of this valuable herb is tremendously utilized as a leafy vegetable in many regions worldwide [4]. The above ground shoot of the plant contains valuable secondary metabolites categorised as pentacyclic triterpenoids, sesquiterpenes, plant sterols, and saponins [5]. Historically, it has been utilized for several illnesses, including epilepsy, leprosy, mild pruritus, and insect stings [6]. Researchers are presently examining its application in the treatment of many additional dermatological disorders. The medicinal properties of this herb are attributed to notable triterpene derivatives, including asiatic acid, madecassic acid, asiaticoside, madecassoside, and brahmic acid [7]. Several formulations of the plant play crucial role in contemporary skincare products that aim to combat ageing, soothe the skin, and provide moisture. It is highly valued for its ability to tighten the skin, reduce wrinkles, and address acne. Most of them have dermatological attributes [8]. The significant role of the plant in both traditional and modern dermatology is reinforced by scientific studies that illustrate its potential in promoting wound healing, reducing inflammation, and managing scars, thereby confirming its effectiveness. Historically praised for its health benefits, the plant is garnering contemporary scientific interest due to its skin-protective attributes.

Human skin functions as an outer barrier, serving as the primary defence of body against harmful environmental agents while simultaneously functioning as a moisture-retaining barrier to avoid trans-epidermal water loss [9]. Preserving good skin is crucial for general well-being; but, ageing, environmental damage, and chronic health conditions can compromise this protective barrier. The skin

serves as a significant barrier for the body against threats such as infections and oxidative stress. The topical use of skincare products with pH values between 4.1 to 5.8 is advisable, as they align with the natural skin pH essential for maintaining skin health [10]. Excessive oxidative stress is a significant contributing factor to several pathological conditions, such as the ageing processes of the skin. Presently, several bioactive substances from the herb are recognized as significant components in a variety of dermatological products, such as masks, toners, serums, and creams. Dermatologists, formulators, and skincare enthusiasts appreciate *C. asiatica* for its effectiveness and versatility. The triterpenoids found in this plant are extensively studied and widely recognised for their skin-healing properties.

Pharmacological and Therapeutic Potential of *Centella asiatica*(L.) Urban in protection of Skin:

Skin soothing and Skin whitening:

Centella asiatica(L.) Urban is widely acknowledged for its efficacy in Skin soothing and Skin whitening. It is an excellent option for individuals with sensitive and reactive skin types because to its phytosterols, which help to calm irritated skin and reduce redness. The polyphenols and flavonoids in *C. asiatica* aid in safeguarding the skin from oxidative stress caused by UV light, pollution, and other outside influences. *C. asiatica* based formulations have been found to boost fibroblast proliferation and activate the SMAD signalling system, which in turn can increase the generation of type I collagen and diminish the development of scars as well as inflammatory responses [11]. Several researchers also reported the components extracted from *C. asiatica* have the ability to enhance microcirculation of blood in the dermis as well as resist excessive deposition of lipids inside cells [8]. Treatment of NHDF cells with dandelion extract at a dosage of 400 ppm resulted in a significant reduction of MMP1, an indicative of wrinkle amelioration; however, concurrent substantial cytotoxicity was also seen [12].

Different extracts of *C. asiatica* were appreciated as the skin whitening agents as the active constituents of the extracts have inhibitory effect on the biogenesis of melanin pigments. The water-extracted *C. asiatica* extract had the most pronounced inhibitory action, resulting in a nearly 20% reduction in melanin pigment concentration relative to the control group, whereas the methanol extract shown a reduction of around 5% and the ethanol extract a drop of about 10% [12]. The experiment indicated that herbal remedies had no toxicity, irrespective of a dosage of 1000 ppm. *C. asiatica* possesses antioxidant characteristics [13], exhibits antibacterial activity [14-15], and mitigates oxidative stress induced by heavy metals [16]. Research revealed that *C. asiatica* extract had antibacterial efficacy against some pathogens of skin like *Propionibacterium acnes*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pyogenes* [12].

Effect on Wound Healing:

The healing mechanism of any kind of injury is a sequential but complicated process which includes blood coagulation, inflammatory responses, biogenesis of cytokine, cellular migration, tissue proliferation, differentiation of tissues, angiogenesis, synthesis and remodelling of extracellular matrix, generation and deposition of collagen. In an optimal wound healing scenario, the proliferation of new tissue supplants injured tissue that results in functional or aesthetic degradation [17]. *C. asiatica* as well as its triterpenoids have a direct capacity for wound healing. Research on wound healing shown that *C. asiatica* significantly accelerated sealing of wounds and enhanced overall healing outcomes. Several formulations made from this plant effectively cure an array of wounds including burns and postoperative thickened scarring [18-20]. Research employing a surgical injury model shown that the ethanol extraction of *C. asiatica* considerably enhanced the strength of wound tearing [21].

The wound repairing benefits of *C. asiatica* are attributed to its bioactive components. These active ingredients increase collagen formation and decrease inflammation while safeguarding against damage from oxidation. Asiaticoside extracted from *C. asiatica* elevated hydroxyproline level, tensile strength, collagen content, and epithelialization in an acute wound model [22]. It enhances the tensile strength of the skin, hence diminishing the likelihood of scarring and facilitating the prevention of repeated wound healing. The asiaticoside-enriched polymeric formulation exhibited a 40% enhanced wound rehabilitation rate without triggering irritation to the skin corresponding to the untreated group. The skin extracellular matrix is primarily composed of Type I and III collagen. Collagen is well recognized as the primary protein constituent of injured connective tissue, crucial for its tensile strength [23]. Endothelial growth factor, fibroblast growth factor, and vascular endothelial growth factor are among the growth factors that may be associated with the wound healing action of *C. asiatica* components [17]. The rise in collagen formation within the site of injury lesion might be the reason behind the curative properties of *C. asiatica* formulation, which include enhanced tensile strengths. Many studies shown that *C. asiatica* significantly enhances collagen production. Triterpenoid chemicals, especially madecassoside, enhance the production of collagen types I and III by elevating TGF-β1 expression and diminishing matrix metalloproteinases (MMPs) activity, which is responsible for collagen degradation. Triterpenoids found

in this plant increase fibroblast cell proliferation, which is essential for tissue healing. Additionally, it promotes collagen production by regulating the pathway of transforming growth factor-beta (TGF-β) to accelerate wound healing and improve scar quality. Triterpenes extracted from C. asiatica have been reported to increase collagen network restructuring and boost glycosaminoglycan synthesis in a mouse injury chamber model [24]. Furthermore, studies has shown that Asiatic acid enhances collagen synthesis, a mechanism crucial to wound healing [24-25].

Burn wounds are more difficult to treat than incision wounds due to substantial cell and tissue loss [26]. Oral treatment of madecassoside from this medicinal herb enhanced the repair of burn induced injury in rats by enhancing antioxidant activity, collagen production, and angiogenesis [27]. Cytological research has shown that *C. asiatica* standardized extract affects filopodia formation and improves healing of wounds through triggering the FAK, Akt, and MAPK signaling pathways [28]. In burn patients, those administered oral *C. asiatic*a extract exhibited a 3-day accelerated re-epithelialization relative to the control group [17]. Kumar et al. (2019) reported that women experiencing photoaging showed a substantial enhancement in skin elasticity, as assessed by a cutometer, following oral supplementation with *C. asiatica* [29]. The elevation of type I collagen was also validated by biopsy. Park et al. (2018) reported that topical application of gel made from this herb for 8 weeks resulted in a 30% increase in collagen deposition in elderly patients, indicating the potential anti-aging benefits of the product [30]. A water-based extract of *C. asiatica* has a substantial level of flavonoids, that exhibit anti-oxidative effects; as a result, the remedy can assist in controlling oxidative stress in injuries, which speeds up the healing process [31-32].

C. asiatica has been shown to accelerate healing process through inhibiting inflammation, promoting biogenesis of collagen, improving angiogenesis, increasing vasodialation and minimizing oxidative stress at the site of injury [17]. The extracts of this medicinal herb influence the proliferation and growth of cells in damaged tissues. Despite the modest transdermal absorption rate of *C. asiatica* and its triterpenoids, recent animal and cell experiments have demonstrated their ability to efficiently promote wound healing as well as minimize skin inflammatory diseases [33]. The physiological mechanism of *C. asiatica* includes the reduction of mitochondrial damage brought on by oxidative stress, which is consistent with the mechanisms that are responsible for the development of these illnesses. The gel derived from the natural extract of *C. asiatica* demonstrates effectiveness against Propionibacterium acnes, a bacterium responsible for acne [34].

Treatment of Skin irritation:

C. asiatica significantly reduces inflammation and oxidative stress in the epidermis. Its antioxidants are derived from its capacity to reduce lipid peroxidation and eliminate free radicals. Asiatic acid and madecassic acid compounds in *C. asiatica* demonstrate anti-inflammatory properties by inhibiting enzymes such as iNOS, cyclooxygenase-2 (COX-2), interleukins (IL-6, IL-1β), and the cytokine tumor necrosis factor (TNF-α), while also downregulating NF-κB activity in lipopolysaccharide-induced macrophage cells [35]. This herb facilitates the management of illnesses such as psoriasis and eczema by diminishing cytokines such as IL-6 and TNF-α. In individuals with inflammatory skin conditions, oral consumption of *C. asiatica* markedly decreased IL-6 levels by 25% and TNF-α by 30% [9]. Goh et al. (2023) also demonstrated that *C. asiatica* markedly decreased TNF-α and IL-1 levels in individuals with atopic dermatitis and following 12 weeks of treatment, a significant decrease of inflammatory indicators was also observed [36]. Madecassoside, a triterpenoid compounds present in *C. asiatica*, has appreciated as one of the strong anti-oxidative substance that has anti-inflammatory properties. Madecassoside is particularly beneficial for individuals with sensitive and acne-prone skin due to its ability to alleviate irritation and promote healing. It alleviates skin irritation, reduces inflammation, and protects against oxidative stress caused by free radicals.

C. asiatica formulations have been found to boost fibroblast proliferation and activate the SMAD signalling pathway, hence enhancing type I collagen synthesis and reducing the development of stretch marks and inflammatory responses [11]. Due to its anti-inflammatory qualities of asiaticoside, the plant is also useful in lowering skin irritation and redness. *C. asiatica* is an excellent choice for treating inflammatory skin conditions such as rosacea, eczema, and acne since it helps to decrease redness and inflammation [37]. Jones et al. (2023) reported that *C. asiatica* supplementation decreased oxidative stress indicators, including malondialdehyde (MDA) and reactive oxygen species (ROS), by 28% in individuals with dermatitis [38]. Lee et al., (2020) performed an experiment revealing a 40% reduction in oxidative stress markers among psoriasis patients treated with *C. asiatica* [39].

Protection from Skin Ageing:

The aging process in humans may be categorized into two elements: internal variables, which include age, sex, hormones, and immunological processes, and extrinsic causes, such as trauma, free radicals, and

ultraviolet radiation [40]. The production of oxidative damage in dermal fibroblasts is directly linked to the deteriorating process of the skin [41]. Therefore, compounds that may inhibit oxidative damage in dermal fibroblasts may serve as suitable ingredients for anti-aging skin care products. *C. asiatica* is utilised as an active ingredient in skincare formulations due to its antioxidant, anti-inflammatory, anti-cellulite, and anti-aging properties [42]. Extract of *C. asiatica* also aids in the prevention of infection and the thickening of certain areas of the epidermis. *C. asiatica* has many modes of antioxidant action, some of which neutralise ROS (quercetin and catechin), suppression of free radical production, inhibition of chain-breaking activity (p-coumaric acids), and metal chelation [22]. Buranasudja et al., (2021) provides pharmacological evidence that 50% ethanolic extract from callus culture of *C. asiatica* possesses unique chemical profiles and remarkable anti-skin-aging capabilities [43]. The triterpenoids present in the plant 5serve as powerful hydrating agents, aiding in moisture retention and skin barrier restoration. Asiaticoside improves the type-1 collagen synthesis in fibroblast cell culture in human dermis and based on this *C. asiatica* to be advised in therapy for keloids and hypertrophic scar [35].

In general, skin rejuvenation is the process of reversing the aging process in the facial cutaneous areas of humans. This entails the repair of age-related damage or the substitution of impaired face tissue with fresh tissue. Telomere length, a marker of cellular senescence that decreases with age, has been associated with age-related diseases, and the activation of telomerase has been suggested as an anti-aging agent that may aid in the treatment of age-related conditions [44]. Research revealed that extract of the plant remarkably induces telomerase activity in HeLa cell, indicating that this extract may facilitate telomere maintenance [45]. Asiatic acid and Asiaticoside were utilized in various lotions to improve skin texture and rejuvenate the skin of aged individuals [46].

Protection from Skin Cancer:

Contemporary researchers have confirmed that 1% extract of the plant enhances the healing of chronic ulcers within very short periods. Several research has indicated that the herb can effectively use in several skin related issues associated with radiation-induced behavioural alterations during clinical radiotherapy [47-48]. Key triterpenoids of this herb retain strong antioxidant activities essential for protecting the skin from the damage caused by free radicals as well as UV rays [43]. Regular oral intake of the crude extract of the herb as well as its partially purified fractions reduce the probability of cancer in skin. Several researchers have reported that skin cancer exhibited resistance to the anticancer properties of Asiatic acid of this plant [49-50].

Table 1: Summary of Research findings of *Centella asiatica*gel

Composition	Experimental Mode	Findings	Reference
Centella asiatica gel	Randomized controlled trials	Reduction in inflammatory and non-inflammatory lesions	[51]
Centella asiatica gel	Randomized controlled trials	Reduced inflammatory lesions and improved skin healing.	[27]
Centella asiatica gel	Randomized controlled trials	Significant decrease in acne lesions and enhanced skin clarity.	[52]
Centella asiatica hydrogel	Phthalic anhydride-induced Atopic Dermatitis model	Reduction of Atopic Dermatitis, hyperkeratosis and decreased inflammatory cell infiltration	[53]
Centella asiatica cream	Randomized controlled trials	Improved skin texture and reduced lesion count	[54]
Centella asiatica ointment	Randomized controlled trials	Reduction in lesion count, minimal adverse effects	[55]
Centella asiatica Oral consumption	Observation	Reduced lesion count, improved overall skin condition	[56]
Centella asiatica Oral consumption	Observation	Reduction in lesion count, minimal side effects	[57]
Centella asiatica cream	Randomized controlled trials	Reduction in acne lesions, improved skin hydration	[58]
Centella asiatica topical application	Observation	Minimization of acne scars and an improvement in skin texture	[59]
Centella asiatica topical application	Randomized controlled trials	Improved skin condition and reduced lesions.	[60]
Centella asiatica extract	Randomized controlled trials	Women administered *C. asiatica* following microneedling therapy exhibited improved face skin condition.	[61]

CONCLUSION

This comprehensive review indicates that *Centella asiatica* L. Urban is an efficacious remedy for intervention for dermatological consequences. The use of *C. asiatica* are rising annually because its extract functions as a fundamental ingredient for cure of skin related problems and in cosmetic applications. *C. asiatica* is a promising herb with several pharmacological effects, widely regarded for its skin protective properties and its benefits in wound healing activity. Numerous studies have indicated that the plant possesses several functional capabilities, including wound healing, skin whitening, and dermatological complexities, all with minimal toxicity.

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