Centella Asiatica

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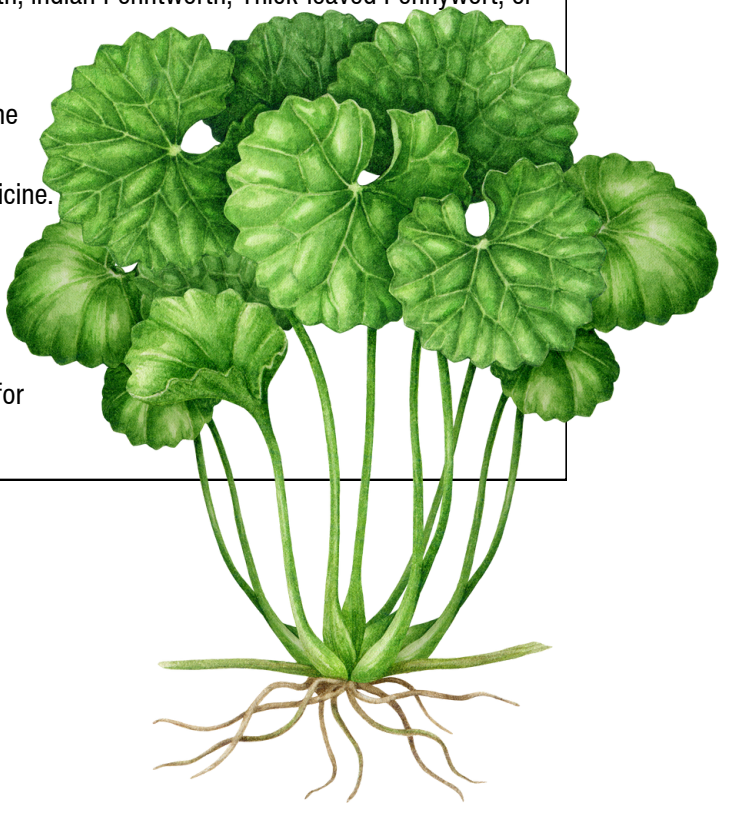
Centella asiatica (L.) Urban is a perennial plant that grows in swampy areas of tropical and subtropical regions of India, Southeast Asia, and Malaysia, as well as some temperate regions of China, Korea, Japan, and Taiwan.
This medicinal herb belongs to the Apiacae family and is also known as Brahmi in Unani medicine, Mandookaparni in Ayurvedia, Gotu kola in the Western world, Asiatic Pennyworth, Indian Penntworth, Thick-leaved Pennywort, or Tiger Grass.
C. asiatica was initially described and published under the name Hydrocotyle asiatica by Carl Linneus until it was reclassified in the valid botanical systematics of C. asiatica (Linn.) Urban.
C. asiatica sits at the intersection of traditional and modern medicine. It has been used in India since ancient times, particularly as an adaptogen to enhance cognitive function, where it is known as Brahmi, or “brain food”.
In Ayurveda, it is described as Mandookaparni.
The leaves, roots, and stems of the C. asiatica plant are utilized for medicinal purposes.



COSMETIC EFFICACY*

- ☑ ANTIOXIDANT
- ☑ ANTI-PHOTOAGEING
- ☑ CELLULITE
- ☑ STRETCH MARKS (PREGNANCY TEST)
- ☑ WOUND HEALING
- ☑ PREVENTS DEHYDRATION
- ☑ IMPROVES SKIN BARRIER
- ☑ HELPS AGAINST PSORIASIS
- ☑ CALMING
- ☑ SOOTHING
- ☑ PURIFYING

*claim derived and synthesized, see bibliography

NUTRACEUTICAL EFFICACY

- ☑ reduces the appearance of cellulite
- ☑ supports microcirculation
- ☑ promotes memory and cognitive function

MAXIMUM RECOMMENDED CONCENTRATION

- up to 5% glycolic extract in emulsions to counteract wrinkles, cracks, and redness

ARDA NATURA PROPOSAL

- 002880 E.G. CENTELLA ASIATICA 1:2 PE - Propylene Glycol, Aqua, Centella asiatica Extract
- 007273 E.GLICERICO CENTELLA AS. U.C. PE - Glycerin, Aqua, Centella asiatica Extract
- 006545 E.G. BUTIL. CENTELLA PE - Butylene Glycol, Aqua, Centella asiatica Extract
- 005821 E.GLICERICO CENTELLA AS. U.A. - Glycerin, Aqua, Centella asiatica Extract
- 002966 E.L. CENTELLA 1:2 - Helianthus annuus Seed Oil, Centella asiatica Extract

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C. asiatica sits at the intersection of traditional and modern medicine. It has been used in India since ancient times, particularly as an adaptogen to enhance cognitive function, where it is known as Brahmi, or “brain food”. In Ayurveda, it is described as Mandookaparni.

The leaves, roots, and stems of the C. asiatica plant are utilized for medicinal purposes.

C. asiatica contains numerous compounds responsible for its medicinal properties (Figure 1). [2]

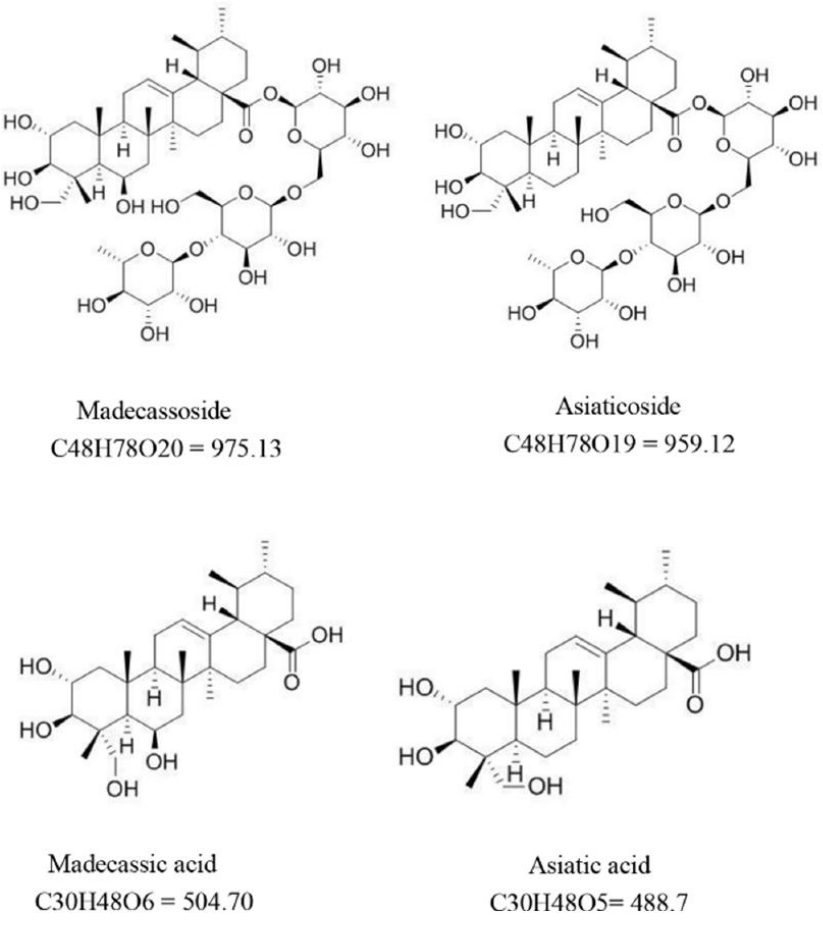

Figure 1. Chemical structure of main active compounds

The most important compounds in C. asiatica include triterpene acids known as sapogenins, such as asiatic, madecassic, terminolic, centic, centellic, brahmic, isobrahmic, betulinic, and madasiatic acids, along with triterpene glycosides like asiaticoside A, asiaticoside B, madecassoside, entelloside, brahmoside, brahminoside, and indocentelloside. [6]

These triterpene saponins (up to 8%) are secondary plant metabolites that consist of a hydrophobic triterpenoid structure (aglycone) attached to a hydrophilic sugar chain (glycone), which is responsible for the saponins' biological activity. The primary chemical components contributing to its pharmacological activity are **asiaticoside** (0.5‑3.7%), asiatic acid (0.04‑0.58%), **madecassoside** (0.29‑6.09%), and madecassic acid [6, 7].
The plant is also known to contain other compounds, including fatty oils like glycerides of palmitic, stearic, lignoceric, oleic, and linoleic acids, as well as tannins, phytosterols, vitamins, minerals, and
Sugars [3,6].

ACTIVITY STUDIES

Studies on rats have shown that asiaticoside (0.2%) applied topically **increases the levels of enzymatic and non-enzymatic antioxidants in the newly created tissues** [8]

Asiaticoside caused an **increase** in hydroxyproline and also in **tensile strength**, a **rise in collagen content** and **better epithelization of punch/puncture wounds** in guinea pigs or on delayed-type wounds of guinea pigs with experimentally induced diabetes [9].

Centella asiatica herb water extracts also show the **anti-psoriatic activity** [10] [11]

In cosmetology C. asiatica has been used as an effective **anti-photoaging agent**, mainly due to enhancement of type I collagen, which amount in skin decreases with age.
The action was confirmed in a randomized, double blind clinical trial conducted among 20 female participants (45-60 years old) with photoaged skin to examine the impact of topically applied 0.1% madecassoside in conjunction with 5% vitamin C on their skin. Six-month treatment resulted in a significant improvement in firmness, elasticity and skin hydration, which was confirmed by appropriate biometrological tests. It is considered that the beneficial effect
of C. asiatica on improving the condition of skin was due to madecassoside, a known inducer of collagen expression by activating the SMAD signaling pathway. In the previous study, the same investigators confirmed the beneficial effect of 5% vitamin C on photoaged skin, which resulted from stimulation of collagen synthesis in fibroblasts and control of matrix metalloproteinase enzymes responsible for degradation of collagen, while in photoaged skin, the level of vitamin C in tissues was significantly reduced. Thus, it follows that the mixture of vitamin C and madecassoside is an attractive combination of two active compounds characterized by different mechanisms of activity, which exert an additive or synergistic effect "causing the remodeling of the superficial dermis" [12]

Centella asiatica is a common ingredient of cosmetics used in **cellulite** and **striae**.
A randomized, double-blind, placebo-controlled trial of the cream Trofolastin®, containing an extract of C. asiatica, α-tocopherol, hydrolyzed collagen and elastin, was carried out on 100 **pregnant women**. Half of the

women, who qualified for the study, received a placebo, the other half were applied a tested cosmetic preparation. The cream was applied daily on breasts, abdomen, buttocks and hips, starting from the third month of pregnancy. The test lasting 30 months was carried through by 80 of the women (39 in the placebo group and 41 in the group using the cream). The results indicated that in the placebo group, striae occurred in 56% of the women (22 patients), whereas in the group that used the cream with the extract of C. asiatica, the problem affected 14 women only. The study also assessed the severity of striae on a scale of 0-3. Among the patients using the cream the average numerical value of the parameter adopted
was 1.42, and 2.13 among those receiving the placebo. The tested cream provided significant protection for the women who had had striae during puberty (89% of the women) [13]

Finally, an interesting study shows how the combination of HA and CAE not only inhibits LPS-induced high expression of MMP-1 inHaCaT cells but also significantly increases the expression of **skin barrier-related proteins AQP3 and FLG**. This combination reduces IL-17 secretion, enhances the inhibitory effect of CAE on IFN-γ and IL-6, **prevents skin dehydration** and inflammation, and **improves skin barrier function**, ultimately alleviating psoriasis-like inflammatory damage. [14]

TABLE 1: Pharmaceutical effect of C. asiatica on **acne, *in vitro***.

Material tested	Cell line/assay system	Maximum concentration	Effect	Reference
C. asiatica methanol extract	Disk diffusion assay	15 mg/ml	Low antibacterial activity against *P. acnes*	[15]
Herbal mixture containing *C. asiatica* extract	Disk diffusion assay	ND	MIC for *P.* acnes = 31.25)g/ml	[16]
Purified madecassoside	*P. acnes*-stimulated THP-1 human monocytic cell line	500 µM	TLR2 expression and nuclear translocation of NF-kB ↓	[17]

ND: not determined; MIC: minimum inhibitory concentration

TABLE 2: Pharmaceutical effect of C. asiatica on **burns**.

In vivo				
Material tested	*Animal model*	*Dose, duration*	*Effect*	*Reference*
Each of asiaticoside and Madecassoside	*Male SD rats*	*0.5 µl on the area of burning wounds, 14 d*	*Collagen synthesis and cell proliferation ↑; burn wounds ↓*	*[18]*
Cytol Centella (titrated extract of C. asiatica)	*Male Wistar rats*	*0.13 mg/mm² on the area of burning wounds, 33 d*	*Burn wound contraction ↑; collagen synthesis ↑*	*[19]*
Clinical trial				
Material tested	*Study design/volunteer (n)*	*Dose, duration*	*Effect*	*Reference*

Centiderm ointment containing C. asiatica ethanol extract	*RCT, DB/patients with second-degree burn wounds on their limbs (n = 60)*	*Appropriate amounts on the area of burning wounds, 25 d*	*Objective and subjective signs ↑; mean of reepithelialization and healing completion ↑*	*[20]*
Polyester coated with herbal extracts (5% C. asiatica extract and 2.5% Aloe vera extract)	*RCT, DB/patients with second-degree burn wounds (n = 35)*	*Covering the area of burning wounds with the dressings with change every 3 days, 21 d*	*Burn wound healing ↑; sizes of burn wounds with higher % epithelialization ↓; pain scores ↓*	*[21]*

RCT: randomized controlled trial; DB: double blind; objective: pliability, vascularity, pigmentation, height, and visual acuity score; subjective: dryness, itching, and irritation.

TABLE 3: Pharmaceutical effect of C. asiatica on **atopic dermatitis**, ***in vivo***.

Material tested	*Animal model*	*Dose, duration*	*Effect*	*Reference*
Titrated extract of *C. asiatica* (TECA)	Phthalic anhydride-induced AD model	40 or 80 μg/cm^2, 3 times a week for 4 wk	Development of AD ↓; hyperkeratosis and inflammatory cell infiltration ↓	[22]
C. asiatica phytosome	Phthalic anhydride-induced AD model	20μ)l/cm^2, 3 times a week for 4 wk	Inflammatory cell infiltration ↓; expression of iNOS and COX-2 ↓; activity of NF-kB and release of TNF-α, IL-1β, and IgE ↓	[23]
TECA and astaxanthin combination ointment	Phthalic anhydride-induced AD model	20 μg/cm^2, 3 times a week for 4 wk	Phthalic anhydride-induced skin morphological changes and ear thickness ↓	[24]
C. asiatica ethanol Extract	2,4-Dinitrochlorobenzeneinduced AD model	80 μg/cm^2 (topical) or 200 mg/kg/d (oral), 14 d	Mast cell infiltration ↓; expression of various cytokines ↓	[25]

TABLE 4: Pharmaceutical effect of C. asiatica on **skin wounds**

in vitro				
Material tested	Cell line/assay system	Maximum concentration	Effect	Reference
Standardized extract of *C. asiatica* (ECa 233)	Human keratinocyte cell line (HaCaT)	100 µg/ml	Cell migration ↑ wound healing activity ↑	[26]
In vivo				
Material tested	*Animal model*	*Dose, duration*	*Effect*	*Reference*
C. asiatica hydrogel	New Zealand white albino rabbits for an incision model	Appropriate amounts on the area of incisional wounds, 12 d	Wound healing ↑; formation of a thick epithelial layer, keratin, granulation tissues, fibroblasts, and collagen ↑	[27]
Gelatin membranes containing *C. asiatica* methanol extract	Male SD rats for an incision model	Covering the wound surfaces, 14 d	Wound healing ↑; collagen deposition and angiogenesis ↑	[28]
Topical spray containing *C. asiatica* methanol Extract	Male Wistar rats for excision wound model	2.5 ml, once daily for 14 d	Wound healing ↑	[29]
Asiaticoside nitric oxide Gel	Male SD rats for an incision model	0.2 ml, twice daily for 14 d	Healing rate of diabetic cutaneous ulcer wounds ↑; growth of bacteria in the wound surface ↓	[30]
Clinical trial				
Material tested	*Study design/volunteer (n)*	*Dose, duration*	*Effect*	*Reference*
Standardized extract of *C. asiatica* (ECa 233 gel)	RCT, DB/patients with bilateral atrophic facial acne scars (*n* = 30)	Appropriate amount on half-side of the face, twice daily for 3mo	Post-laser-resurfacing wound healing ↑	[31]
Standardized dose of asiaticoside vs placebo	Diabetic wound patients (n= 170)	3x100 µg asiaticoside for 3 weeks	↑ Wound contraction, ↑ Wound granulation	[32]

Standardized dose of topical Centiderm vs control group with Silver Sulfadizine	Burn wound patients (75)	Topical 3% Centiderm for 3.5 weeks	↓ VSS score, ↓ VAS score, ↑Re-epithelialization, ↓Healing time, Infection, ↓Pigmentation	[33]
Oral and topical assumption of standardized dose of *C. asiatica* vs untreated control group	Chronic anal fissure patients (n = 98)	2 _ 60 mg oral + 3 g topical C. asiatica for 8 weeks	↓ Bleeding time, ↓ Pain (VAS scores)	[34]

TABLE 5: Pharmaceutical effect of C. asiatica on **skin diseases, *in vitro***

Material tested	Cell line/assay system	Maximum concentration	Effect	Reference
Madecassoside	*Human epidermal melanocytes*	*100 µg/ml*	*Damage of mitochondria ↓; oxidative stress ↓*	[35]
TECA	*Human dermal papilla cells*	*25 µg/ml*	*Potential of hair inductive capacity ↑*	[36]

Intended cosmetic effects and recommended maximum concentration in cosmetic products

Smoothing, soothing, purifying.
Up to 0.5% selected triterpenes.
Up to 5% glycolic extract in emulsions for wrinkled, chapped, reddish skins.
Aftersun products. Lotions, gels and creams for body massage.
Toothpastes and mouth washes for atonic gums. [37]

Conclusions

Centella asiatica (Gotu kola) is effective in treatment of wounds, also in infective wounds, burns, and hypertrophic scar. The active compounds include pentacyclic triterpenes, mainly asiaticoside, madecassoside, asiatic and madecassic acids.
The mechanism of action involves promoting fibroblast proliferation and increasing the synthesis of collagen as well as acidic mucopolysaccharides, increasing intracellular fibronectin content and mitotic activity in the germ layer, significantly improving the tensile strength of newly formed skin as well as by inhibiting the inflammatory phase of hypertrophic scars and keloids.

Some studies suggest that the use of *C. asiatica* or its components may be useful in the treatment of psoriasis and scleroderma. *Centella asiatica* is a common ingredient of cosmetics applied on photoaging skin also in cellulite and striae. [38]

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THE HEART OF NATURE

ARDA NATURA

PLEASE NOTE: All the medicinal plants used to obtain the extracts are stored in a warehouse with controlled temperature and humidity to guarantee always the better quality.

002880	**E.G. CENTELLA ASIATICA 1:2 PE**	**Propylene Glycol, Aqua, Centella asiatica Extract**
007273	E.GLICERICO CENTELLA AS. U.C. PE	Glycerin, Aqua, Centella asiatica Extract
006545	**E.G. BUTIL. CENTELLA PE**	**Butylene Glycol, Aqua, Centella asiatica Extract**
005821	E.GLICERICO CENTELLA AS. U.A.	Glycerin, Aqua, Centella asiatica Extract

Extraction strategy: $T_{extraction} > T_{room}$

Solvent mixture in constant movement

002966	**E.L. CENTELLA 1:2**	**Helianthus annuus Seed Oil, Centella asiatica Extract**

Extraction strategy:

Maceration at room temperature in steel baskets

Daily stir

The Angel's Share

There's a volume part for each extract which is simply lost during the process or by evaporation, or because of the solvent is absorbed by the vegetable drug or finally because of final filtration process. According to which is the solvent, the vegetable species and the filter this part goes around 10 to 20%.

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