
CENTELLIN® CG

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Centellin® CG is a standardized extract obtained from *Centella asiatica* (fam. Umbelliferae), which is also known as Hydrocotyle, Gotu kola or Indian pennywort. This perennial herb is easy to identify by its small rounded leaves, more or less cordate, borne at the nodes of a long running stem. Umbels with very small flowers characterize this species. The plant contains several biologically important constituents,

including an essential oil, sterols, flavonol glycosides, polyalkynes and saponins. *Centella asiatica* (*Mandukaparni* in Ayurveda) has been used traditionally, since ancient times, to treat dermatitis and heal superficial wounds. It has also been used as a brain tonic¹.

In recent years, scientists attributed the healing properties of this herb to the presence of asiaticosides and their derivatives. *Centella* extracts have been used topically as adjunct therapy in the treatment of surgical wounds and minor burns. They have also been successfully employed in the complementary treatment of ulcers in the legs (in the granulation stage). *Centella* extracts have also been used orally to improve lymphatic and venous circulation and thereby promote wound healing¹.

Chemistry

Centella asiatica contains the biologically active saponins, asiaticoside and madecassoside. These are pentacyclic triterpenoid compounds. Chemically, these compounds are esters in the 28-position of a trisaccharide (α -L-Rha 1→4 β -D-Glc 1→6 β -D-Glc1→) and of acids

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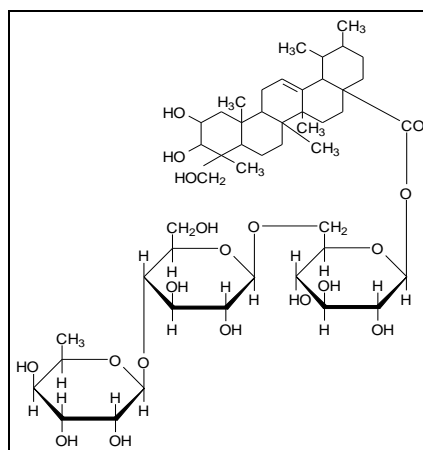
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derived from ursane : asiatic acid ($2\alpha,3\beta,24\alpha$ -trihydroxy-urs-12-en-28-oic acid) and madecassic acid ($2\alpha,3\beta,6\beta,24\alpha$ -tetrahydroxy-urs-12-en-28-oic acid)¹.



Structure of Asiaticoside

The biological activity of the titrated extract from the plant is attributed to the mixture of three terpenoid compounds, asiatic acid (about 30% w/w), madecassic acid (about 30% w/w) and asiaticoside (about 40% w/w)². Asiaticoside has been shown to be converted to asiatic acid *in vivo*³.

Biological effects

The biological effects of *Centella asiatica* have been studied both in preclinical and *in vitro* experiments as well as in controlled clinical trials. Traditionally, the whole plant or the leaves alone, are used medicinally. The powdered drug or standardized extracts have been used in clinical studies.

Preclinical and In vitro studies:

Centella asiatica extract is reported to have been used effectively in the management of keloids, leg ulcers, phlebitis, slow-healing wounds, leprosy lesions, surgical lesions and cellulitis⁴. The effects of the extract from *Centella asiatica* and its individual components *Protocols of studies on cosmeceutical products performed /sponsored by Sabinsa Corporation are based on alternatives to animal testing. Any references to animal tests appearing in product informational materials are related to information from published scientific literature compiled therein.*

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were studied on human foreskin fibroblast monolayer cultures. The extract increased collagen synthesis in a dose-dependent manner and the new collagen formed showed reduced specific activity. Asiatic acid was found to be the only component responsible for collagen synthesis stimulation². Another study reports that the extract at 25 µg/ml concentration did not significantly affect the cell proliferation, total protein synthesis or the biosynthesis of proteoglycans in human skin fibroblast cultures. However, a statistically important increase was observed in the percentage of collagen and in cell layer fibronectin, as revealed by immunofluorescence measurements. The authors concluded that this effect of *Centella asiatica* extract on collagen and fibronectin could be responsible for its wound healing properties⁵.

The effects of *Centella asiatica* extract on dermal wound healing in rats was assessed using both oral and topical modes of administration. The extract was found to exert different actions at various phases of wound repair⁶.

- The extract increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in DNA, protein and collagen content of the granulation tissues.
- Collagen matured and cross-linked more rapidly in treated animals as compared to untreated controls.
- The extract treated wounds were found to form epithelial tissue faster and the wounds contracted more in the treated animals as compared to untreated controls.

The healthful properties of *Centella asiatica* have also been used in the management of burns, scleroderma, gastrointestinal ulcers and chronic liver diseases. Asiaticoside at the level of 1.25 mg/100 g concentration applied subcutaneously for 3 days in rats offered protection against ulcerous lesions caused by cold temperatures¹. In the healing of ulcers and scleroderma, the immune stimulant action of the active constituents, collagen regulation (in *Protocols of studies on cosmeceutical products performed /sponsored by Sabinsa Corporation are based on **alternatives to animal testing**. Any references to animal tests appearing in product informational materials are related to information from published scientific literature compiled therein.*

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such cases, inhibition of collagen biosynthesis) and strong fibrinolytic action have been proposed as the mechanisms of action¹.

In an animal model study, formulations (ointment, cream and gel) of aqueous extract of *Centella asiatica*, when applied topically, thrice daily for 24 days on the open wounds in rats increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in collagen content and tensile strength. Epithelial tissue formation was faster and the rate of wound contraction was higher in treated wounds as compared to control wounds. The gel formulation was found to be the most effective⁷.

An *in vitro* bioassay revealed that the extract of *Centella asiatica* and its individual constituents inhibited the growth of SVK-keratinocytes. Conditions such as psoriasis, are associated with hyperproliferation of keratinocytes. The authors of this study therefore speculate that the potential anti-psoriatic effects of *Centella asiatica* extract merit further investigation⁸.

Clinical studies

Several clinical studies report the efficacy of the extract from *Centella asiatica* in the management of venous insufficiency in the lower limbs^{9,10}. These effects were manifested as reduction of ankle edema, foot swelling and capillary filtration rate as well as improved microcirculation. Patients with venous hypertension showed marked improvement in capillary permeability and increased microcirculation on treatment with tablets containing *Centella asiatica* extract (60 mg three times a day for two weeks)¹¹. Patients with varicose veins treated with a daily oral dose of 60 mg of the extract for three months showed lowered mucopolysaccharide turnover levels, as indicated by serum levels of uronic acids and lysosomal enzymes. Mucopolysaccharide turnover levels are an index of impaired

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metabolism in the connective tissues and show a marked increase in subjects with varicose veins¹².

One study involving 100 women compared the effects of a cream containing *Centella asiatica* extract to those observed with a placebo cream, in the removal of “stretch marks”, (striae gravidarum) which many women develop during pregnancy . Compared to placebo cream application, treatment with a cream containing *Centella asiatica* extract, alpha tocopherol and collagen-elastin hydrolysates was associated with less women developing stretch marks (odds ratio 0.41, 95% confidence interval 0.17 to 0.99)¹³.

Cosmeceutical applications

Centella asiatica extract was shown to enhance the levels of enzymatic and non-enzymatic antioxidants such as superoxide dismutase, catalase, glutathione peroxidase, vitamin E and ascorbic acid in newly formed tissues¹⁴, further validating its role in skin health maintenance. Reported topical applications of *Centella asiatica* extract include OTC skin care products recommended for regeneration of aged skin¹ and innovative scar management products (such as those used after plastic surgery)¹⁵. Products containing *Centella asiatica* extract are also used in the management of dermal itch and other skin irritations¹.

The extract therefore finds a wide range of cosmetic applications including soothing creams, milks, repairing and regeneration creams, anti-aging products, after-shave products, preparations for chapped hands, lip balms, stretch mark removal preparations and related products.

Safety

Asiaticoside was found to be non-toxic up to a dose of 40 to 50 mg/kg body weight (administered intramuscularly) in mice/ rabbits and up to 1 g/kg body weight when orally

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administered. In the doses normally used, no adverse reactions have been reported¹. A recent study reports that oral doses as high as 120 mg daily of the total triterpenic fraction may be safely used in venous hypertension¹⁶. Scientists who studied the topical effects of the herb and its active constituents (asiaticoside, asiatic acid and madecassic acid) on guinea pigs, reported that all the materials studied are very weak sensitizers and that the risk of acquiring contact sensitivity to the plant or its constituents is low⁴.

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