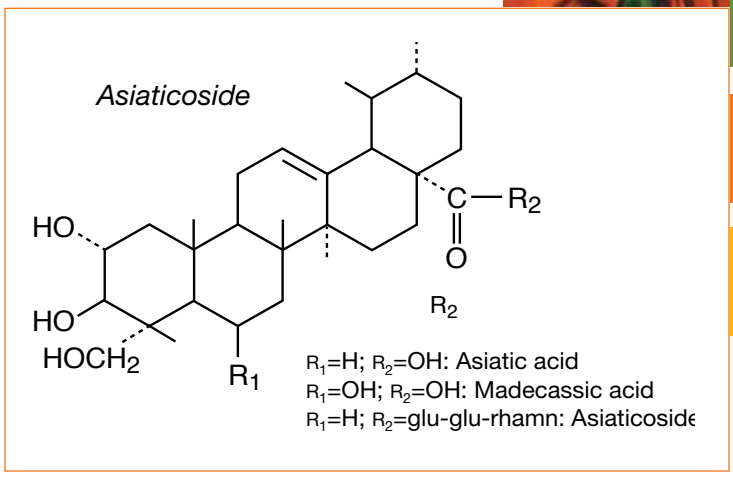
Monograph

Centella asiatica



Description

Centella asiatica (also known as gotu kola and *Hydrocotyle asiatica*) is a perennial, herbaceous creeper with kidney-shaped leaves, found in India, Sri Lanka, Madagascar, South Africa, Australia, China, and Japan. Centella prefers to grow in shady, moist, or marshy areas.[1,2]

Active Constituents

Centella contains several active constituents, of which the most important are the triterpenoid saponins, including asiaticoside, centelloside, madecassoside, and asiatic acid. In addition, Centella contains other components, including volatile oils, flavonoids, tannins, phytosterols, amino acids, and sugars.[3]

Mechanisms of Action

Centella has several pharmacological actions, based primarily on *in vivo* experiments. After oral and topical administration in rats, increased cellular hyperplasia and collagen production were noted at the site of injury, measured by increased granulation tissue levels of DNA, protein, total collagen, and hexosamine. More rapid maturation and cross-linking of collagen were seen in animals treated with the herbal extract, as evidenced by elevated stability of acid-soluble collagen and increases in aldehyde content and tensile strength. Compared to control wounds, rats treated with gotu kola had a higher degree of epithelialization and a significantly more rapid rate of wound contraction.[4,5]

In addition to improving wound healing, Centella may also have an effect on connective tissue of varicosities. After receiving 30 mg total triterpenoid fraction of *Centella asiatica* (TTFCA) twice daily for three months, individuals with varicose veins had significantly reduced serum enzymes involved in mucopolysaccharide metabolism (beta-glucuronidase, beta-N-acetylglucosaminidase, and arylsulfatase) compared to baseline values ($p<0.01$).[6]

The capacity to regenerate axons is an important component of healing following nerve damage. Rats given Centella extract in their drinking water recovered more quickly after nerve damage than controls, with increased axonal regeneration and more rapid functional recovery.[7]

The fresh juice extract of gotu kola at 200 and 600 mg/kg twice per day has proven to be protective against aspirin- and ethanol-induced gastric ulcers,[8,9] with similar effects as the medication sucralfate.[8] Centella significantly induced gastric mucin secretion and mucosal cell glycoprotein production, markers of increased gastric mucosal defense factors.[8]

Pharmacokinetics

A pharmacokinetic study suggests the active ingredients in TTFCA are well absorbed in human volunteers.[10] After single oral administration of 30 and 60 mg of the extract, maximum plasma levels of asiatic acid were reached at 4.5 and 4.2 hours, respectively. Plasma half-lives were 2.2 hours in the 30-mg dose and 3.4 hours in the 60-mg dose, with no detectable levels of the saponin present 24 hours after single dosing. Seven-day treatment with the herb at the same dosing schedule resulted in higher peak plasma concentrations, longer half-lives, and greater area-under-the-curve values.[10]

Clinical Indications

Venous Insufficiency

In a double-blind study, 94 patients (86 men, 8 women; ages 20-80) with venous insufficiency of the lower extremities for an average of 14 years, were randomized to one of three treatment groups: a triterpenoid extract of *Centella asiatica* (TECA) at a daily dose of 60 or 120 mg or placebo for three months. Individuals who took gotu kola at either dose demonstrated significant clinical improvements in limb heaviness ($p=0.033$), edema ($p=0.026$), and global evaluation of efficacy ($p=0.05$). Venous distension, measured by plethysmography, was significantly better in the active group at 40 mmHg ($p=0.08$), 50 mmHg ($p=0.055$) and 60 mmHg ($p=0.09$), compared to deteriorating placebo values.[11]

Venous Hypertensive Angiopathy

Forty patients (21 males, 19 females; mean age 48 years) with severe venous hypertension, ankle swelling, and lipodermatosclerosis, were randomized to receive TTFCA 60 mg twice daily or placebo for eight weeks; patients in the study did not wear compression stockings. After trial conclusion, patients taking the herbal extract experienced a significant decrease in skin flux and rate of ankle swelling compared to baseline values ($p<0.05$). In addition, patients in the active group reported rapid clinical improvement, reflected by a reduction in the analogue scale line score (e.g., symptoms of edema, pain, restless limbs, swelling, and change in skin condition/color) from 9.5 at baseline to 4.5 after eight weeks.[12] In another study using Laser doppler evaluation, subjects taking 60 mg TTFCA twice daily for six weeks demonstrated a 29-percent decrease in resting flux ($p<0.05$), 52-percent increase in venoarteriolar response ($p<0.05$), and 66-mL reduction in leg volume. Similarly, those utilizing the herbal extract demonstrated 7.2-percent increase in pO_2 and 9.6-percent reduction in pCO_2 ($p<0.05$).[13]

Airline Flight Microangiopathy

Physical consequences of long-distance flights range from simple swelling of the lower limbs to the formation of dangerous blood clots. Centella's effectiveness was evaluated in 66 flight passengers (33 men, 33 women; mean age 38) traveling in economy class for 3-12 hours. Subjects were randomized to receive 60 mg TTFCA three times per day or a placebo two days before, the day of, and two days after the flight. Results showed significant improvements in microcirculatory function (transcutaneous pO_2 and pCO_2, laser doppler flowmetry, venoarteriolar response, rate of ankle swelling, and edema) in those utilizing TTFCA ($p<0.05$), with edema and rate of ankle swelling approached normal values in those given TTFCA ($p<0.025$).[14]

Echolucency in Carotid and Femoral Plaques

Carotid artery plaques that are echolucent on ultrasound have greater amounts of certain physiological components (e.g., lipids, blood elements) and limited amounts of collagen, making plaque inherently weaker and increasing the risk of embolization. This unstable plaque is associated with a higher clinical risk of stroke and asymptomatic cerebral lesions.[15]

Asymptomatic patients (49 men, 38 women; mean age 56) with high-risk, echolucent carotid artery plaques were randomized to receive 60 mg TTFCA or placebo three times daily for one year; patients also took platelet anti-aggregating medication throughout the trial. After 12 months, sonographic evaluation indicated a significant decrease in plaque echolucency in the TTFCA group. Incidence of positive MRI images indicating cerebral ischemic lesions was seven percent in the TTFCA group and 17 percent in the control group ($p<0.05$).[15]

In a second study testing a similar dose of gotu kola, patients with femoral plaques demonstrated a decrease in plaque echolucency after 12 months of therapy, compared to no change in the control group. Degree of stenosis and walking distance did not change in the two groups.[16]

Diabetic Microangiopathy

Diabetes is characterized by increased skin blood flow and decreased venous return, resulting in blood pooling. Forty-eight patients with diabetic microangiopathy were randomized to one of three treatment groups for six months: 60 mg TTFCA twice daily, placebo, or no treatment. Using laser doppler flowmetry measurements, the researchers concluded those taking TTFCA had significant reductions in skin blood flow at rest after three ($p<0.05$) and six ($p<0.01$) months

compared to baseline values. In addition, VAR scores (decrease of skin blood flow on standing) increased significantly from 6.4 percent to 23.9 percent at three months and 25.9 percent at six months ($p<0.05$). During the investigation period, pO_2 increased ($p<0.05$) while pCO_2 values decreased ($p<0.01$) significantly in the Centella group. Fasting blood sugar and hemoglobin A1C values did not change.[17]

Keloid and Scar Management

Centella has long been recommended for the treatment of keloids and/or hypertrophic scars. In one open clinical trial, 227 patients were divided into two groups and treated with oral Centella alone or surgical scar revision plus Centella at doses of 60-150 mg daily for up to 18 months. In the Centella-only group, 116 of 139 patients (82%) experienced relief of symptoms and disappearance of inflammation. In the 88 subjects in the combined surgery and Centella group, 72 percent demonstrated improvement.[18] In addition to its oral use, Centella has been used as a topical cream in a comprehensive scar management program. Observationally, it was found to improve scar maturity from an average of six months without treatment to three months with treatment.[19]

Anxiety

Centella is used in Ayurvedic medicine for the treatment of anxiety. A 2000 study supports this ancient claim. After assessing baseline measurements of acoustic startle response (ASR), mood self-rating scale, heart rate, and blood pressure, 40 healthy subjects (21 males, 19 females; ages 18-45 years) were randomized to receive 12 g non-standardized Centella dissolved in 300 mL grape juice or placebo. Evaluations were recorded at 30, 60, 90, and 120 minutes after beginning therapy. Centella significantly decreased ASR amplitude compared to placebo at 30 ($p<0.02$) and 60 ($p<0.001$) minutes; heart rate, blood pressure, and mood did not change.[20]

Other Indications

Centella may also have potential application for scleroderma,[21] alcohol-induced liver cirrhosis,[22] leg ulcers,[23] and as adjunctive treatment in leprosy.[24] Animal studies indicate it may have potential for prevention of aspirin- or ethanol-induced gastric ulcers.[8,9]

Side Effects and Toxicity

Alcoholic extracts of gotu kola have shown no toxicity at doses of 350 mg/kg when given i.p. to rats.[1] Reported adverse effects include GI upset and nausea. Topical use of the extract has led to reports of rash.[25] Three cases of jaundice with elevated liver enzymes were reported in Argentina following dosing of Centella. Patients had taken Centella (standardization and dose unknown) for 20-60 days, and recovered on discontinuation of the herb.[26]

Dosage

In adults, the recommended daily dose of TTFCA (or TECA) extracts standardized for asiaticoside, asiatic acid, and madecassic acid is 60-120 mg. The recommended daily dosages of crude herb and 1:5 tincture are 0.5-6 g and 10-20 mL, respectively.[27]

Warnings and Contraindications

Gotu kola should be avoided during pregnancy, due to its emmenagogue action.[28]

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