GOTU KOLA

Other Common Name: Indian pennywort
Botanical Names: Centella asiatica, Hydrocotyle asiatica
Family: Umbelliferae
Plant Part Used: Aerial parts

Actions
Vulnerary, antiinflammatory, depurative, adaptogenic, nerve tonic

Potential Indications
Based on appropriate evaluation of the patient, practitioners should consider prescribing gotu kola in formulations in the context of:
• Improving the healing response of the skin and subcutaneous tissue (4a,5)
• Diabetic microangiopathy (4a)
• Cellulitis; gastric or duodenal ulcer (4a)
• Leg ulcers (4a,5)
• Leprosy (4,5)
• Scleroderma (4a)
• Venous insufficiency of the lower limbs (4a)
• Varicose and postthrombotic syndromes (4a)
• Keloids and hypertrophic scars (4a)
• Hemorrhoids, in combination with bulking laxatives, if required (4a)
• Mouth ulcers (6)
• Chronic skin and rheumatic conditions (5)
• Improving mental function (2,5)
• Anxiety (4)
• Improving adaptation to stressors (7)
• Producing a rejuvenating tonic effect (4,5)
• Chronic hepatic disorders (4a,6)
• Topical treatment for postthrombotic syndrome and varicose veins (4a)
• Topical treatment for psoriasis, wounds (4,5)
• Topical treatment for burns, leg ulcers, cellulitis (4)
• Topical treatment for leprous ulcers, scar formation after surgery, eczema (5)
• Topical treatment for stretch marks, in combination with α-tocopherol and collagen-elastin hydrolysates (4a)

Contraindications
Known allergy.

Warnings and Precautions
None required.

Interactions
None known.

Use in Pregnancy and Lactation
No adverse effects expected.

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Side Effects

Allergic contact dermatitis has been reported from using gotu kola, but it is a low risk treatment. Both the extract and the triterpene constituents are weak sensitzers.1

Dosage

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<th>Dose per day*</th>
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<td>3-6 ml of 1:2 liquid extract</td>
<td>20-40 ml of 1:2 liquid extract</td>
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Many of the successful clinical trials used a triterpene fraction of gotu kola at higher doses (approximately equivalent to 2.5 to 7.0 g of leaf per day) than the previously outlined liquid doses. Hence these liquid doses may possibly need to be exceeded to achieve similar results. However, on the other hand, an advantage might exist from using the whole extract rather than an isolated fraction.

Traditional Prescribing

Traditional Western herbal medicine uses include:
- Skin and rheumatic conditions, including chronic eczema, chronic rheumatism, leprosy, ulcers2,3
- Topically for poorly healing wounds, leprous ulcers, scar formation after surgery2

Traditional Ayurvedic uses include:
- As a depurative and tonic4
- As a rasayana (rejuvenating) remedy, hence it is used to improve memory and prolong life span5
- Topically for eczema, leprosy, secondary syphilitic ulcers, psoriasis4,5

Gotu kola has been traditionally used in many countries. In Thailand, the whole plant has been used as a depurative, particularly to treat skin diseases and as a diuretic and antidiarrheal remedy.6 In Indonesia, gotu kola has been used for mouth ulcers and oral thrush.7 In Fijian traditional herbal medicine, gotu kola was employed as a tonic for wasting diseases, such as tuberculosis, stomach problems, and rheumatic swelling and pain. Gotu kola was used both internally and topically to relieve pain.8 In TCM, gotu kola is used for traumatic injuries, boils, urinary stones, and to counteract toxicity and reduce swelling.9 In Hong Kong, gotu kola is also used for hepatitis, measles, the common cold, tonsillitis, bronchitis, and to treat poisoning. External uses include treatment of snakebite and bleeding wounds.10 In South Africa, gotu kola has been employed to treat wounds, cancer, leprosy, fever, and syphilis.11

Pharmacologic Research

The aerial parts of gotu kola contain pentacyclic triterpene ester saponins,12 the most abundant of which is asiaticoside. The triterpenoid

*SUPPORTING INFORMATION

*This dose range is extrapolated from the British Herbal Pharmacopoeia 1983. Higher relative doses of the triterpene fraction have been used in most clinical trials.
content of good quality gotu kola dried herb is commonly 2% to 3% when analyzed by high-performance liquid chromatography (HPLC).

- Gotu kola and asiaticoside demonstrated activity against herpes simplex virus-1 (HSV-1) and HSV-2 in vitro.

- The triterpene fraction of gotu kola has demonstrated wound-healing activity in many experimental models (by injection, oral, and topical administration). The mechanism of action includes the stimulation of maturation of scar tissue by the increased production of type I collagen (and hence collagen synthesis) and a decrease in the inflammatory reaction and myofibroblast production. The constituents also stimulated glycosaminoglycan synthesis and acted specifically to shorten the immediate phase of healing. Aqueous extract of gotu kola, particularly as a gel formulation, promoted healing in experimental open wounds. Oral and topical administration of gotu kola extract produced faster epithelialization and a higher rate of wound contraction in vivo compared with controls.

- Asiaticoside demonstrated activity in models of both normal and delayed wound healing after both topical and oral administration. Angiogenesis was promoted in isolated tissue. Topical asiaticoside enhanced the induction of antioxidants at the initial stage of healing.

- Oral administration of gotu kola extract inhibited gastric ulceration in cold- and restraint-induced stress models. Brain GABA levels were increased. Complete mucosal cytoprotection was observed in an experimental model (by oral route).

- The antiulcer activity may be related to a protective effect on stress. Gotu kola extract also prevented the experimental rise in plasma corticosterone levels following immobilization stress. In other studies, oral gotu kola extract demonstrated normalizing effects against a variety of stressors.

- The triterpene fraction of gotu kola reduced experimentally induced acute radiation dermatitis via its antiinflammatory activity (after topical application).

- Oral administration of gotu kola and the partially purified triterpenoid fraction retarded the development of solid and ascites tumors and increased life span in an experimental model.

- An anxiolytic effect was demonstrated in several experimental models for an aqueous extract of gotu kola (by injection and orally). Sedative and antidepressant activity has also been demonstrated. Oral administration of an aqueous extract of gotu kola caused a decrease in the turnover of central monoamines and improved learning and memory in experimental models.

Clinical Studies

Most of the clinical trials listed here used the triterpene fraction of gotu kola (TFGK), with doses ranging from 60 to 180 mg per day (approximately 2.5 to 7.0 g of dried herb equivalent). The majority of these preparations contained 40% asiaticosides, 30% madecassic acid, and 30% asiatic acid.
• Oral administration of TFGK for 60 days demonstrated efficacy in a double-blind, placebo-controlled trial in patients with venous hypertensive microangiopathy. In an uncontrolled trial and in a randomized, single-blind, placebo-controlled trial, TFGK improved symptoms, microcirculation, and capillary permeability in patients with venous hypertension. In another trial, symptoms and ankle edema were improved in patients with venous hypertension after TFGK treatment, with no significant change observed in the placebo group. TFGK treatment (120 mg/day) for 6 months was beneficial for diabetic microangiopathy by improving microcirculation and decreasing capillary permeability. This trial was of prospective, randomized, placebo-controlled design.

• TFGK treatment produced significant improvement in symptoms of heaviness in the lower limbs and edema in a randomized, double-blind, multicenter, placebo-controlled trial involving patients with venous insufficiency of the lower limbs. Two oral doses were trialled (60 mg/day or 120 mg/day) for 8 weeks. Benefit was also demonstrated for TFGK treatment of patients with chronic venous insufficiency in an open study. In a randomized, double-blind, comparative trial, TFGK demonstrated superior efficacy over hydroxyethylrutoside in treating venous insufficiency. In an open trial, TFGK treatment provided an increase in venous return and improvement of symptoms in patients with varicose and postthrombotic syndromes. In a controlled, crossover study involving patients with postphlebitic syndrome and venous insufficiency, oral treatment with TFGK provided better results in microcirculatory measurements than treatment with the flavonoids diosmin or hydroxyethylrutoside.

• Oral treatment with TFGK produced a decrease in the elevated mucopolysaccharide turnover observed in patients with varicose veins.

• Treatment with TFGK caused a significant reduction of circulating endothelial cells in patients with postphlebitic syndrome compared with baseline values. Oral administration of TFGK and bulking laxatives (when required) produced a beneficial effect in patients with first- and second-degree hemorrhoids in an uncontrolled trial.

• Positive results have been recorded in uncontrolled trials for treating gastric and duodenal ulcers (TFGK, oral), gastritis (asiaticoside, oral), and bladder lesions caused by bilharzial infection (TFGK, injection). No benefit was observed for the healing of leg ulcers in patients treated with asiaticoside (by injection) compared with placebo. However, positive results were obtained for oral use of TFGK taken for 3 to 8 weeks in 50 patients with leg ulcers.

• Oral treatment with TFGK for an average of 55 days was successful in treating patients with cellulitis. After 3 months’ oral TFGK treatment, reduced tendency to sclerosis in cellulitic tissue was observed in a double-blind, placebo-controlled study.

• Oral administration of TFGK has been successfully used to treat keloids and hypertrophic scars. In a study involving 227 patients, treatment with TFGK for a period of 2 to 18 months had therapeutic
value in both preventing (together with surgical revision) and reducing keloids. A subset of the patients involved in the curative study confirmed the activity of TFGK in a double-blind, placebo-controlled trial.

- In a preliminary trial, TFGK taken for 3 to 24 months improved histology in 5 of 12 patients with chronic hepatic disorders, including alcoholic cirrhosis and cirrhosis of undetermined origin.

- Gotu kola dried herb (0.5 g/day for 3 months) increased the intelligence quotient, general mental ability, and behavior in mentally disabled children in a randomized, placebo-controlled, clinical trial in India.

- In an uncontrolled trial, gotu kola relieved the symptoms of patients with anxiety and improved mental functioning.

- In a double-blind trial, gotu kola tended to increase the mean level of red blood cells, blood sugar, serum cholesterol, vital capacity, and total protein in normal volunteers. An increase in hemoglobin was statistically significant. This finding was thought to be indicative of a corticosteroid-like activity.

- Gotu kola has been used to treat leprosy patients from very early times and in recent years in both uncontrolled trials and a controlled trial (gotu kola powder or asiaticoside compared with diamino-diphenylsulfone over a period of 1 year).

- Asiaticoside was not successful in treating scleroderma in children. However, TFGK demonstrated symptomatic relief in a small group of patients with systemic scleroderma. The 13 patients received TFGK by intramuscular injection ranging from 1 1/2 months to 1 1/2 years. Two patients received TFGK orally for a portion of their treatment.

- In another small, uncontrolled trial, oral doses of TFGK improved arthralgia and finger joint movement in scleroderma patients.

- A systematic review published in 2000 concluded that, compared with placebo, treatment with a cream containing gotu kola extract, α-tocopherol, and collagen-elastin hydrolysates is associated with fewer women developing stretch marks. This result occurred only for women who had previously encountered stretch marks during pregnancy.

- Topical application of gotu kola or TFGK has been successfully used to treat:
  - Postthrombotic syndrome and varicose veins (double-blind, placebo-controlled trial; TFGK)
  - Chronic venous insufficiency (single-blind, controlled trial of TFGK against oral administration of the drug tribenoside)
  - Psoriasis (uncontrolled trial; water and oil extract of gotu kola)
  - Leg ulcers (uncontrolled trial; placebo-controlled trial, TFGK by injection or topical)
  - Soiled wounds resistant to other treatments (standardized gotu kola extract combined with essential oils; uncontrolled trial)
  - Burns (topical, injection, or both; uncontrolled trials with TFGK or gotu kola extract)
  - Cellulitis (uncontrolled trial; standardized gotu kola extract)
REFERENCES

5. Thakur RS, Puri HS, Husain A: Major medicinal plants of India, Lucknow, India, 1989, Central Institute of Medicinal and Aromatic Plants.