

# Hydrangea

## Species (Family)

*Hydrangea arborescens* L. (Saxifragaceae)

## Synonym(s)

Mountain Hydrangea, Seven Barks, Smooth Hydrangea, Wild Hydrangea

## Part(s) Used

Rhizome, Root

## Pharmacopoeial and Other Monographs

BHP 1996<sup>(G9)</sup>

PDR for Herbal Medicines 2nd edition<sup>(G36)</sup>

## Legal Category (Licensed Products)

GSL<sup>(G37)</sup>

## Constituents<sup>(G22,G40,G41,G48,G64)</sup>

Limited information is available on the chemistry of hydrangea. It is stated to contain carbohydrates (e.g. gum, starch, sugars), flavonoids (e.g. kaempferol, quercetin, rutin), resin, saponins, hydrangin and hydrangenol, a stilbenoid,<sup>(1)</sup> and to be free from tannins.

## Food Use

Hydrangea is not used in foods. In the USA, hydrangea is listed as a 'Herb of Undefined Safety'.<sup>(G22)</sup>

## Herbal Use

Hydrangea is stated to possess diuretic and antilithic properties. Traditionally, it has been used for cystitis, urethritis, urinary calculi, prostatitis, enlarged prostate gland, and specifically for urinary calculi with gravel and cystitis.<sup>(G7,G64)</sup>

## Dosage

*Dried rhizome/root* 2–4 g or by decoction three times daily.<sup>(G7)</sup>

*Liquid extract* 2–4 mL (1:1 in 25% alcohol) three times daily.<sup>(G7)</sup>

*Tincture* 2–10 mL (1:5 in 45% alcohol) three times daily.<sup>(G7)</sup>

## Pharmacological Actions

### *In vitro* and animal studies

None documented for hydrangea. Synthesised hydrangenol derivatives have been reported to possess anti-allergic properties, exhibiting a strong inhibitory action towards hyaluronidase activity and histamine release.<sup>(2)</sup>

## Side-effects, Toxicity

Hydrangea has been reported to cause contact dermatitis,<sup>(G51)</sup> and it is stated that hydrangin may cause gastroenteritis.<sup>(G22)</sup> Symptoms of overdose are described as vertigo and a feeling of tightness in the chest.<sup>(G22)</sup> An extract has been reported to be non-toxic in animals.<sup>(G64)</sup>

## Contra-indications, Warnings

None documented.

*Pregnancy and lactation* The safety of hydrangea has not been established. In view of the lack of phytochemical, pharmacological and toxicity data, the use of hydrangea during pregnancy and lactation should be avoided.

## Pharmaceutical Comment

Limited information is available on the chemistry of hydrangea, although related species have been investigated more thoroughly.<sup>(G41)</sup> No scientific evidence was located to justify the herbal uses. In view of the lack of toxicity data, excessive use of hydrangea should be avoided.

## References

See also General References G7, G9, G22, G32, G36, G37, G40, G41, G48, G51 and G64.

- 1 Harborne JB, Baxter H. *Phytochemical Dictionary*. London: Taylor and Francis, 1993.
- 2 Kakegawa H *et al.* Inhibitory effects of hydrangeol derivatives on the activation of hyaluronidase and their anti-allergic activities. *Planta Med* 1988; 54: 385–389.

# Hydrocotyle

## Species (Family)

*Centella asiatica* (L.) Urban (Umbelliferae)

## Synonym(s)

Centella, Gotu Kola, *Hydrocotyle asiatica*, Indian Pennywort, Indian Water Navelwort

## Part(s) Used

Herb

## Pharmacopoeial and Other Monographs

BHP 1983<sup>(G7)</sup>  
Martindale 32nd edition<sup>(G43)</sup>  
PDR for Herbal Medicines 2nd edition<sup>(G36)</sup>  
WHO volume 1 1999<sup>(G63)</sup>

## Legal Category (Licensed Products)

GSL (for external use only)<sup>(G37)</sup>

## Constituents<sup>(G22,G44,G60,G64)</sup>

**Amino acids** Alanine and serine (major components), aminobutyrate, aspartate, glutamate, histidine, lysine and threonine.<sup>(1)</sup> The root contains greater quantities than the herb.<sup>(1)</sup>

**Flavonoids** Quercetin, kaempferol and various glycosides.<sup>(2-4)</sup>

**Terpenoids** Triterpenes, asiaticoside, centelloside, madecassoside, brahmoside and brahminoside (saponin glycosides). Aglycones are referred to as hydrocotylegenin A-E;<sup>(5)</sup> compounds A-D are reported to be esters of the triterpene alcohol R<sub>1</sub>-barrigenol.<sup>(5,6)</sup> Asiaticentoic acid, centellic acid, centoic acid and madecassic acid.

**Volatile oils** Various terpenoids including  $\beta$ -caryophyllene, *trans*- $\beta$ -farnesene and germacrene D (sesquiterpenes) as major components,  $\alpha$ -pinene and  $\beta$ -pinene. The major terpenoid is stated to be unidentified.

**Other constituents** Hydrocotylin (an alkaloid), valerine (a bitter principle), fatty acids (e.g. linoleic

acid, linolenic acid, lignocene, oleic acid, palmitic acid, stearic acid), phytosterols (e.g. campesterol, sitosterol, stigmasterol),<sup>(7)</sup> resin and tannin.

The underground plant parts of hydrocotyle have been reported to contain small quantities of at least 14 different polyacetylenes.<sup>(8-10)</sup>

## Food Use

Hydrocotyle is not used in foods.

## Herbal Use

Hydrocotyle is stated to possess mild diuretic, anti-rheumatic, dermatological, peripheral vasodilator and vulnerary properties. Traditionally it has been used for rheumatic conditions, cutaneous affections, and by topical application, for indolent wounds, leprosy ulcers, and cicatrization after surgery.<sup>(G7,G64)</sup>

## Dosage

*Dried leaf* 0.6 g or by infusion three times daily.<sup>(G7)</sup>

## Pharmacological Actions

### *In vitro* and animal studies

The triterpenoids are regarded as the active principles in hydrocotyle.<sup>(7)</sup> Asiaticoside is reported to possess wound-healing ability, by having a stimulating effect on the epidermis and promoting keratinisation.<sup>(11)</sup> Asiaticoside is thought to act by an inhibitory action on the synthesis of collagen and mucopolysaccharides in connective tissue.<sup>(11)</sup>

Both asiaticoside and madecassoside are documented to be anti-inflammatory, and the total saponin fraction is reported to be active in the carrageenan rat paw oedema test.<sup>(12)</sup>

*In vivo* studies in rats have shown that asiaticoside exhibits a protective action against stress-induced gastric ulcers, following subcutaneous administration,<sup>(13)</sup> and accelerates the healing of chemical-induced duodenal ulcers, after oral administration.<sup>(14)</sup> It was thought that asiaticoside acted by increasing the ability of the rats to cope with a stressful situation, rather than via a local effect on the mucosa.<sup>(13)</sup>

*In vivo* studies in mice and rats using brahmoside and brahminoside, by intraperitoneal injection, have

shown a CNS-depressant effect.<sup>(15)</sup> The compounds were found to decrease motor activity, increase hexobarbitone sleeping time, slightly decrease body temperature, and were thought to act via a cholinergic mechanism.<sup>(15)</sup> A hypertensive effect in rats was also observed, but only following large doses.<sup>(15)</sup> *In vitro* studies with brahmoside and brahminoside indicated a relaxant effect on the rabbit duodenum and rat uterus, and an initial increase, followed by a decrease, in the amplitude and rate of contraction of the isolated rabbit heart.<sup>(15)</sup> Higher doses were found to cause cardiac arrest, although subsequent intravenous administration in dogs caused no marked change in an ECG.<sup>(15)</sup>

*In vitro* antifertility activity against human and rat sperm has been described for the total saponin fraction.<sup>(16)</sup> Asiaticoside and brahminoside are thought to be the active components, although no spermicidal or spermostatic action could be demonstrated for the pure saponins.<sup>(16)</sup> A crude hydrocotyle extract has been reported to significantly reduce the fertility of female mice when administered orally.<sup>(10)</sup> No mechanism of action was investigated.

Teratogenicity studies in the rabbit have reported negative findings for a hydrocotyle extract containing asiatic acid, madecassic acid, madasiatic acid and asiaticoside.<sup>(17)</sup>

Fresh plant juice is reported to be devoid of antibacterial activity,<sup>(18)</sup> although asiaticoside has been reported to be active versus *Mycobacterium tuberculosis*, *Bacillus leprae* and *Entamoeba histolytica*, and oxyasiaticoside was documented to be active against tubercle bacillus.<sup>(16,18)</sup> The fresh plant juice is also stated not to exhibit antitumour or antiviral activities, but to possess a moderate cytotoxic action in human ascites tumour cells.<sup>(18)</sup>

### Clinical studies

Several studies describing the use of hydrocotyle to treat wounds and various skin disorders have been documented. A cream containing a hydrocotyle extract was found to be successful in the treatment of psoriasis in seven patients to whom it was applied.<sup>(19)</sup> An aerosol preparation, containing a hydrocotyle extract, was reported to improve the healing in 19 of 25 wounds that had proved refractory to other forms of treatment.<sup>(11)</sup> A hydrocotyle extract containing asiaticoside (40%), asiatic acid (29–30%), madecassic acid (29–30%) and madasiatic acid (1%) was stated to be successful as both a preventive and curative treatment, when given to 227 patients with keloids or hypertrophic scars.<sup>(17)</sup> The effective dose in adults was reported to be between 60 and 90 mg. It was proposed that the triterpene constituents in the hydrocotyle extract act in a similar

manner to cortisone, with respect to wound healing, and interfere with the metabolism of abnormal collagen.<sup>(17)</sup>

The triterpene constituents are reported to be metabolised primarily in the faeces in a period of 24–76 hours, with a small percentage metabolised via the kidneys.<sup>(17)</sup> An extract containing asiatic acid, madecassic acid, madasiatic acid and asiaticoside reached peak plasma concentrations in 2–4 hours, irrespective of whether it is administered in tablet, oily injection or ointment formulations.<sup>(17)</sup>

Hydrocotyle has been used in the treatment of patients with chronic lesions such as cutaneous ulcers, surgical wounds, fistulas and gynaecological wounds.<sup>(G44,G45)</sup> Hydrocotyle has also been reported to improve the blood circulation in the lower limbs. Stimulation of collagen synthesis in the vein wall resulted in an increase in vein tonicity and a reduction in the capacity of the vein to distend.<sup>(10)</sup>

The juice of the leaves or the whole plant is documented to be effective for relieving the itching associated with prickly heat.<sup>(G51)</sup>

Asiaticoside has also been documented to improve the general ability and behavioural pattern of 30 mentally retarded children, when given over a period of 12 weeks. It also increased the mean concentrations of blood sugar, serum cholesterol and total protein, and lowered blood urea and serum acid phosphatase concentrations, in 43 adults.<sup>(16)</sup> Vital capacity was also increased.

### Side-effects, Toxicity

A burning sensation was reported by 4 of 20 patients during the period of application of an aerosol preparation containing hydrocotyle.<sup>(11)</sup> However, it is not clear whether other components in the formulation contributed to this reaction. Ingestion of hydrocotyle is stated to have produced pruritus over the whole body.<sup>(G51)</sup>

### Contra-indications, Warnings

It is stated that hydrocotyle may produce photosensitisation.<sup>(G7)</sup> Excessive doses may interfere with existing hypoglycaemic therapy and increase serum cholesterol concentrations; hyperglycaemic and hypercholesterolaemic activities have been reported for asiaticoside in humans. Brahmoside and brahminoside have been reported to exert a CNS-depressant action in animal studies.<sup>(15)</sup>

**Pregnancy and lactation** Hydrocotyle is reputed to be an abortifacient and to affect the menstrual cycle.<sup>(G30)</sup> Relaxation of the isolated rat uterus has been documented for brahmoside and brahmino-

side.<sup>(15)</sup> Triterpene constituents have been reported to lack any teratological effects in rabbits.<sup>(17)</sup> In view of the lack of toxicity data, the use of hydrocotyle during pregnancy should be avoided. Excessive use should be avoided during lactation.

### Pharmaceutical Comment

The chemistry of hydrocotyle is well studied and its pharmacological activity seems to be associated with the triterpenoid constituents. Documented clinical and animal data support the herbal use of hydrocotyle as a dermatological agent, and warrants further research into the potential role of hydrocotyle in wound management. In view of the lack of toxicity data, excessive ingestion of hydrocotyle should be avoided.

### References

See also General References G7, G22, G30, G31, G36, G37, G43, G51, G60, G63 and G64.

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- 2 Rzadkowska-Bodalska H. Flavonoid compounds in herb pennywort (*Hydrocotyle vulgaris*). *Herba Pol* 1974; 20: 243–246.
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- 4 Hiller K *et al.* Isolierung von Quercetin-3-O-(6-O- $\alpha$ -L-arabinopyranosyl)- $\beta$ -D-galaktopyranosid, einem neuen Flavonoid aus *Hydrocotyle vulgaris* L. *Pharmazie* 1979; 34: 192–193.
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- 13 Ravokatra A, Ratsimamanga AR. Action of a pentacyclic triterpenoid, asiaticoside, obtained from *Hydrocotyle madagascariensis* or *Centella asiatica* against gastric ulcers of the Wistar rat exposed to cold (2°). *C R Acad Sci (Paris)* 1974; 278: 1743–1746.
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