

Nettle

Species (Family)

Urtica dioica L. (Urticaceae)

Synonym(s)

Stinging Nettle, Urtica

Part(s) Used

Herb

Pharmacopoeial and Other Monographs

BHC 1992^(G6)

BHP 1996^(G9)

Complete German Commission E^(G3)

ESCOP 1996 and 1997^(G52)

Martindale 32nd edition^(G43)

Mills and Bone^(G50)

PDR for Herbal Medicines 2nd edition^(G36)

Legal Category (Licensed Products)

GSL^(G37)

Constituents^(G6,G22,G52,G64)

Acids Carbonic, caffeic, caffeoylmalic, chlorogenic, formic, silicic, citric, fumaric, glyceric, malic, oxalic, phosphoric, quinic, succinic, threonic and threono-1,4-lactone.⁽¹⁾

Amines Acetylcholine, betaine, choline, lecithin, histamine, serotonin⁽²⁾ and a glycoprotein.⁽³⁾

Flavonoids Flavonol glycosides (e.g. isorhamnetin, kaempferol, quercetin).⁽⁴⁾

Inorganics Up to 20% minerals, including calcium, potassium and silicon.

Lignans Several lignans, including (–)-secoisolariciresinol.

Other constituents Choline acetyltransferase,⁽⁵⁾ scopoletin,⁽⁴⁾ β-sitosterol and tannin

Other plant parts The rhizome contains lectin (*Urtica dioica* agglutinin) composed of six isolec-

tins,^(6,7) coumarin (scopoletin), triterpenes (β-sitosterol, its glucoside, and six stearyl derivatives),^(8,9) two phenylpropane derivatives, and six lignans.⁽¹⁰⁾

Food Use

Nettle (herbs and leaves) is listed by the Council of Europe as a natural source of food flavouring (category 1) (see Appendix 23).^(G17) Nettle is used in soups and herbal teas. In the USA, nettle is listed by the Food and Drugs Administration (FDA) as a Herb of Undefined Safety.^(G22)

Herbal Use^(G2,G4,G6,G7,G8,G32,G43,G50,G52,G54,G64)

Nettle is stated to possess antihæmorrhagic and hypoglycaemic properties. Traditionally, it has been used for uterine hæmorrhage, cutaneous eruption, infantile and psychogenic eczema, epistaxis, melaena and specifically for nervous eczema. The German Commission E approved internal use of nettle leaf as supportive therapy for rheumatic ailments and as irrigation therapy for inflammatory disease of the lower urinary tract and prevention of kidney gravel; internal and external use for rheumatic ailments.^(G3) The root is approved for difficulty in urination from benign prostatic hyperplasia.^(G3)

Dosage

Dried herb 2–4 g or by infusion three times daily;^(G6,G7) 8–12 g daily;^(G3) fresh juice 10–15 mL three times daily.^(G52)

Liquid extract 3–4 mL (1:1 in 25% alcohol) three times daily.^(G6,G7)

Tincture 2–6 mL (1:5 in 45% alcohol) three times daily.^(G6,G7)

Pharmacological Actions

In vitro and animal studies

The pharmacological properties of nettle have been reviewed.^(G50,G52,G56) Information from these reviews is summarised below.

Anti-inflammatory activity An aqueous ethanol extract and also isolated caffeoylmalic acid partially

inhibited the biosynthesis of arachidonic acid *in vitro*.^(G52) Nettle extract (0.1 mg/mL) and isolated acid (1 mg/mL) inhibited 5-lipoxygenase-derived biosynthesis of leukotriene B₄ by 20.8% and 68.2%, respectively, and inhibited synthesis of cyclooxygenase-derived prostaglandins (IC₅₀ 92 µg/mL and 38 µg/mL, respectively). The same extract significantly reduced tumour-necrosis-factor- α (TNF α) and interleukin 1 β (IL-1 β) concentrations after lipopolysaccharide (LPS)-stimulated secretion of these proinflammatory cytokines in human blood.^(G52) An aqueous ethanol extract (0.25 mg/mL) inhibited platelet-activating factor (PAF)-induced exocytosis of elastase from human neutrophils by 93%, but failed to inhibit biosynthesis of prostaglandins from [¹⁴C]arachidonic acid.^(G52)

In vitro addition of a commercial preparation of nettle leaf (IDS-23) to whole human blood resulted in an inhibition of LPS-stimulated TNF α and IL-1 β secretion, correlating with drug ingestion. The same preparation inhibited phytohaemagglutinin-stimulated production of T helper cell 1 (Th1)-specific interleukin-2 (IL-2) and interferon- γ (IFN γ) in culture in a dose-dependent manner up to 50% and 74%, respectively.⁽¹¹⁾ By contrast, T helper cell 2 (Th2)-specific interleukin-4 (IL-4) production was stimulated. The results suggested that the nettle leaf extract acts by mediating a switch in T helper cell-derived cytokine patterns and may inhibit the inflammatory cascade in autoimmune diseases such as rheumatoid arthritis.⁽¹¹⁾ The transcription factor NF- κ B is elevated in several chronic inflammatory diseases and is responsible for the enhanced expression of some proinflammatory gene products. A nettle leaf extract (IDS 23) potently inhibited NF- κ B activation in a number of cells, including human T cells, macrophages, epithelial cells and mouse L929 fibrosarcoma cells *in vitro*.⁽¹²⁾ It was proposed that part of the anti-inflammatory effects of nettle may be due to its inhibitory effect on NF- κ B activity.

Benign prostatic hyperplasia activity^(G50) Several lignans and their metabolites reduce binding activity of human sex hormone-binding globulin (SHBG) *in vitro*. Lignans from nettle are competitive inhibitors of the interaction between SHBG and 5 α -dihydrotestosterone.^(G50) An aqueous extract of nettle root led to a concentration-dependent (0.6–10 mg/mL) inhibition of SHBG interaction with its receptor on human prostatic membranes. A 20% methanol extract of root inhibited binding capacity of SHBG after preincubation in human serum.^(G50)

Subfractions of an aqueous methanol extract of nettle root inhibited cellular proliferation in benign prostatic hyperplasia (BPH) tissue. A root extract had

a specific and concentration-dependent inhibition of human leukocyte elastase (HLE) activity *in vitro*. (HLE is an important marker in clinically silent genitourinary tract infection and inflammation.) Root extracts inhibited alternative and classic complementary pathways and significantly inhibited prostate growth in mice with induced BPH (by 51%, compared with control; $p < 0.003$).^(G50)

Other activities CNS-depressant activity has been documented for nettle. It has been shown to produce a reduction in spontaneous activity in rats and mice,^(13,14) inhibition of drug-induced convulsions, and a lowering of body temperature in rats.⁽¹³⁾ Nettle has been reported to have no effect on the blood pressure of mice,⁽¹⁴⁾ whereas in cats it has produced a marked hypotensive effect and bradycardia.⁽¹⁵⁾ Atropine was reported to have no effect on these latter actions and a mode of action via α -adrenoceptors was suggested.⁽¹⁵⁾

Nettle is stated to contain both hypoglycaemic and hyperglycaemic principles.⁽¹⁶⁾ The hypoglycaemic component has been termed 'urticin' and nettle has been reported to lower the blood sugar concentration in hyperglycaemic rabbits.⁽¹⁶⁾

An 80% ethanolic and an aqueous extract of nettle administered to mice at a dose of 25 mg/kg orally prior to glucose load, led to hypoglycaemia effects.⁽¹⁷⁾ No diuretic or ion excretion effects were observed in rats after oral administration of an aqueous extract of nettle (1 g/kg).^(14,18) Dried nettle had a potassium ion to sodium ion ratio of 63:1, whereas an aqueous decoction had a corresponding ratio of 448:1.⁽¹⁹⁾ It was suggested that the high potassium ion concentration in aqueous decoctions may contribute to their diuretic activity.

Utero-activity has been documented for nettle in pregnant and non-pregnant mice; betaine and serotonin were stated to be the active constituents.⁽²⁰⁾ A nettle extract was reported to be devoid of antifertility activity following oral administration to mice (250 mg/kg).⁽²¹⁾ Analgesic activity in mice has been documented.⁽¹⁴⁾ Administration of an aqueous extract (1200 mg/kg) to mice showed resistance to stimulation in the hotplate test at 55°C with a 190% increase in reaction time.⁽¹⁴⁾ Conversely, no analgesic activity was noted in the hotplate test on rats given an ethanolic extract, but the same extract did reduce the writhing response to phenylquinone after oral (1 g/kg) and intraperitoneal (500 mg/kg) treatment.⁽¹⁸⁾

The isolectins isolated from the rhizome are reported to cause nonspecific agglutination of erythrocytes, to induce the synthesis of interferon by human lymphocytes,^(6,7) and have carbohydrate-binding properties.^(6,7)

An extract of nettle at a concentration of 1.2 mg/mL has been reported to be active against L-1210 leukaemic cells in mice.⁽²²⁾

Clinical studies

Diuretic effect In an open, uncontrolled study, 32 patients with myocardial or chronic venous insufficiency were treated with 15 mL of nettle juice three times daily for two weeks.^(G52) A significant increase in daily volume of urine was observed throughout the study, the volume by day 2 being 9.2% ($p < 0.0005$) higher than the baseline value in patients with myocardial insufficiency and 23.9% higher than the baseline value ($p < 0.0005$) in those with chronic venous insufficiency. It has been proposed that the diuretic activity of aqueous extracts of nettle may be attributed to the high potassium content.⁽¹⁹⁾ The reputed diuretic effects of nettle require further investigation.

Arthritis and rheumatism An open, uncontrolled multicentre study involving 152 patients with various, mainly degenerative, rheumatic conditions reported that 70% of participants experienced symptom relief by the end of the three-week treatment period.^(G52) In an open, randomised pilot study involving 37 patients with acute arthritis, diclofenac 50 mg plus stewed nettle herb 50 g was compared with diclofenac 200 mg.⁽²³⁾ Assessment was based on the decrease in elevated acute phase C-reactive protein serum concentrations, and clinical signs of acute arthritis. Clinical improvement was observed in both groups to a similar extent. On the basis of the findings, it was suggested that nettle herb administration may enhance the effectiveness of diclofenac in rheumatic conditions. However, this requires further investigation.

Postmarketing surveillance studies involving a total of almost 2000 patients with rheumatoid arthritis treated for three weeks with nettle leaf extract (IDS-23) administered as an adjuvant to non-steroidal anti-inflammatory drugs (NSAIDs), or as monotherapy, have reported that the extract was well-tolerated.^(24,25)

In a randomised, double-blind, crossover study, 27 patients with osteoarthritis pain at the base of the thumb and index finger, received stinging nettle leaf (applied for 30 seconds daily for one week to the painful area) or white dead nettle (*Lamium album*) as placebo, followed by a five-week wash-out period before crossing to the other arm of the study.⁽²⁶⁾ The results indicated that reductions in visual analogue scale scores for pain and in a health assessment questionnaire score for disability were significantly

better for the stinging nettle group, compared with the placebo group ($p = 0.026$ and $p = 0.0027$ for pain and disability, respectively).

Benign prostatic hyperplasia Clinical studies of nettle preparations in the treatment of symptoms of benign prostatic hyperplasia (BPH) have been reviewed.^(G50) Information from this review is summarised below.

Several uncontrolled trials have reported improvements in urological symptoms, compared with baseline values, following administration of nettle root extract (5:1) 600–1200 mg daily for three weeks to 20 months.^(G50) Large observational studies involving patients with BPH who received nettle root extract for two to three months have reported improvements in various symptoms, such as urinary frequency, urinary flow and nocturia.^(G50) These studies provide justification for further, rigorous investigation of the effects of nettle in BPH.

A placebo-controlled trial involving 79 patients with BPH assessed the effects of nettle root extract 600 mg daily for six to eight weeks. Compared with placebo, nettle root extract administration resulted in greater improvements in urinary flow and urine volume and residual volume.^(G50) Another placebo-controlled trial of nettle root extract 600 mg daily for nine weeks in men with BPH ($n = 50$) reported a significant decrease in SHBG concentrations and significant improvement in micturition volume and maximum urinary flow.^(G50)

Rhinitis A randomised, double-blind, placebo-controlled study assessed the effects of a freeze-dried preparation of nettle herb in individuals with allergic rhinitis.⁽²⁷⁾ Participants received nettle herb 600 mg, or placebo, at the onset of symptoms over a one-week period. Assessment was based on daily symptom diaries and global responses recorded at follow-up visits after one week of therapy. Nettle herb was rated more highly than placebo in the global assessment, but was rated less highly on the basis of data from the symptom diaries. It was concluded that there should be further investigation with a larger sample size and involving a longer treatment period.

Side-effects, Toxicity

Consumption of nettle tea has caused gastric irritation, a burning sensation of the skin, oedema and oliguria.^(G22) The leaves are extremely irritant in view of their acetylcholine- and histamine-containing glandular hairs. An LD₅₀ in mice following intraperitoneal administration of nettle has been reported as 3.625 g/kg.⁽¹²⁾ The LD₅₀ for intravenous infusion of

nettle leaf in mice has been documented as 1.92 g/kg, and the LD₅₀ for chronic administration in rats has been stated as 1.31 g/kg.^(G50) An ethanolic extract of nettle (plant part unspecified) showed low toxicity in rats and mice after oral and intraperitoneal administration at doses equivalent to 2 g/kg.⁽¹⁸⁾

Contra-indications, Warnings

In view of the documented pharmacological actions for nettle, excessive use may interact with concurrent therapy for diabetes, high or low blood pressure, and may potentiate drugs with CNS-depressant actions. Gastrointestinal irritation has been documented.

Pregnancy and lactation Nettle is reputed to be an abortifacient and to affect the menstrual cycle.^(G30) Utero-activity has been documented in animal studies. In view of this, the use of nettle during pregnancy should be avoided. Excessive use is best avoided during lactation.

Pharmaceutical Comment

The chemistry of nettle is well documented. Limited pharmacological data are available to support the traditional herbal uses although hypoglycaemic activity *in vivo* has been reported. A number of clinical trials have provided some evidence to support the diuretic and anti-inflammatory effects of nettle, and for the effects of nettle in relief of symptoms of allergic rhinitis. Clinical evidence exists to support the efficacy of root extracts in the treatment of benign prostatic hyperplasia. However, further well-designed clinical trials of nettle involving large numbers of patients are required to establish the benefits. Irritant properties have been documented for nettle and excessive use should be avoided.

References

See also General References G2, G3, G5, G6, G9, G16, G22, G30, G31, G32, G36, G37, G43, G50, G52, G54, G56 and G64.

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