NETTLE LEAF

Urtica dioica L.

Family

Urticaceae.

Parts Used

Leaf.

Description

Nettle is found in temperate climates across both Europe, Asia and America. This well known plant is often considered a weed as it tends to grow prolifically in unwelcome places - dictating the presence of a soil rich in nitrogen. Like many weeds, nettle is in fact a very useful plant that has both nutritive and medicinal properties.

Nettle has heart shaped, finely toothed leaves and the whole plant is downy and covered with hairs that give the notorious sting when touched. The base of each hair contains small cells containing the venom which is released on slight pressure. The flowers are green and form long branched clusters, similar to catkins, at the axils of the leaves. Most plants contain either male or female flowers, which are open-pollinated by wind. The plant reproduces both by seed and underground rhizomes.

Urtica dioica is the more common species, with *Urtica urens*, having smaller leaves and short unbranched clusters of both male and female flowers on each plant. The plant is rich in chlorophyll and can be used as a natural dye or food colouring.

Traditional Use

In many European cultures, nettle regularly crossed the bridge between being a food and a medicine.

The young spring greens offered a mineral rich and pleasant tasting vegetable (similar to spinach) that was sort after by peasants and more noble classes alike. After long, harsh winters with a lack of greens, nettle was prized along with other greens such as dandelion as a 'spring cure'. Many traditional recipes can be found for nettle salads, soups, pudding and beers. Nettle has also been used historically as a fibre (similar to flax or hemp) that was called upon particularly when shortages of cotton and other fibres occurred. Biodynamic farming also employs nettle as an important ingredient in composts. Nettles also support over 40 species of insects including colourful butterflies. The presence of the stings has allowed the relationship with numerous insect species to develop as the stinging hairs of the nettle were thought to have developed as a defence against grazing animals. A group in the UK working for wellbeing of people and wildlife has initiated a "Be Nice to Nettle Week" to raise awareness of this important plant's role.[1]

In Western herbal medicine, nettle has traditionally been used as a tonic herb and recommended for complaints associated with rheumatoid arthritis, osteoarthritis and urinary tract infections. Being rich in minerals such as iron,nettle was used for lethargy and depleted states and recovery after childbirth. Nettle juice and lotion was thought to be a good tonic for the hair and scalp. 'Urtication' or flogging with nettles was a traditional remedy for chronic rheumatism and general muscle weakness.[2]
This has lead to modern research into the herbs action in respect to this. Its astringent action was employed in cases of bleeding, with Culpeper reporting it good for nose bleeds and bleeding of the mouth.[3]

Constituents

Historically, nettle was found to contain an array of constituents – formic acid, histamine, mucilage, minerals (including iron and calcium), vitamins, ammonia, carbonic acid, chlorophyll and water.[4,5]

Specific constituents have been isolated more recently including beta-sitosterol, trans-ferulic acid, dotriacotane, erucic acid, ursolic acid, scopoletin, rutin, quercetin, polysaccharides and p-hydroxylbenzalcohol.[6]

The venom in stinging nettles was initially attributed to formic acid - the same chemical contained in ant venom. Although formic acid is present, research has shown that the main chemicals involved are histamine, leukotriene, acetylcholine and 5-hydroxytryptamine (serotonin).[7,8]

Actions

Anti-inflammatory, anti-allergic, antioxidant, astringent, diuretic, hepatoprotective, irritant (topical), nutritive tonic

Pharmacological Activity

Anti-inflammatory Activity

Nettle has been shown to possess anti-allergic and anti-inflammatory actions *in vitro*. A nettle extract was shown to inhibit several key inflammatory events *in vitro* that cause the symptoms of seasonal allergies. These include activity against or inhibition of Histamine-1 receptor, mast cell tryptase, COX-1 & COX-2, and haematopoietic prostaglandin D(2) synthase - thus inhibiting prostaglandin production involved in pro-inflammatory pathways.[9] Another study suggested that part of the antiinflammatory effect of Urtica extract may be due to its inhibitory effect on NF-kappaB activation.[10]

An early study looked at the benefits of nettle leaf on allergic rhinitis. The double-blind randomized study compared the effects of *Urtica dioica* with placebo in 69 patients. Assessment was based on daily symptom diaries, and global response recorded at the follow-up visit after one week of therapy. *Urtica dioica* was rated higher than placebo in the global assessments but comparing the diary data *Urtica dioica* was rated only slightly higher. This study was limited by the short time frame of treatment.[11]

The potential of an *Urtica* extract (Hox alpha or IDS 30) and its active constituent 13-HOTrE to suppress the expression of metalloproteinases (enzymes involved in degradation of the matrix of joints) was examined. Researchers postulated the clinical efficacy of nettle leaf extracts in the treatment of rheumatoid arthritis was due to this suppressive effect. The results suggest that the monosubstance 13-HOTrE is one of the more active anti-inflammatory substances in IDS 30 and that it

may be a promising remedy for inflammatory joint diseases.[12]

An extract of nettle (IDS 23) was investigated for its effects on the lipopolysaccharide (LPS) stimulated secretion of proinflammatory cytokines in human whole blood of healthy volunteers. TNF-alpha and IL-1 beta concentration after LPS stimulation was significantly reduced by simultaneously given IDS 23. After 24 hours these cytokine concentrations were reduced by 50.8% and 99.7%, respectively. In contrast to described effects on arachidonic acid cascade *in vitro*, isolated nettle constituents including caffeic acid chlorogenic acid, quercetin and rutin did not influence LPS stimulated TNF-alpha, IL-1 beta and IL-6 secretion. Researchers concluded that their findings may explain the positive effects of this extract in the treatment of rheumatic diseases.[13]

Platelet hyperactivity plays an important role in arterial thrombosis and atherosclerosis. A study looked at the effects of different extracts of *Urtica dioica* on platelet aggregation and concluded that flavonoids were responsible for the anti-platelet action. Rat platelets were incubated *in vitro* with different concentrations of the tested extracts and aggregation was induced by different agonists including thrombin, epinephrine and collagen. The crude aqueous extract inhibited thrombin-induced platelet aggregation in a dose-dependent manner while the ethyl acetate extract exhibited the most anti-aggregant effect with a mean inhibition of 76%. Flavonoids isolated from the plant leaves, produced a strong inhibitory effect on thrombin-induced platelet aggregation.[14]

Immunomodulatory Activity

Research is increasingly showing potential for *Urtica dioica* to elicit immunomodulatory activity. A number of studies have found nettle to be a very widely used herb in Turkey for cancer, though no studies into the clinical effectiveness has been undertaken.[15,16,17,18]

Isolated lectins (UDA) found in nettle were shown to be promising immunomodulatory agents, having also anti-viral and fungistatic effects *in vitro*.[19]

A specific carbohydrate-binding agent found in *Urtica dioica* was able to efficiently prevent cell-to-cell human T-lymphotropic virus type 1 (HTLV-1) transmission and fully prevented HTLV-1-induced stimulation of peripheral blood mononuclear cells growth.[20]

Healthy volunteers were used to examine the effects of a nettle leaf extract (IDS 23/1) on levels of the cytokines TNF-alpha and interleukins. The cytokines were induced by stimulation with lipopolysaccharide (LPS). After 7 and 21 days ingestion *ex vivo* a decrease of LPS stimulated TNF-alpha release of 14.6 %and 24.0%, respectively, was observed. Interleukin-1 beta was also reduced by 19.2 and 39.3%. [21]

Researchers compared *Uritca* leaf extract (IDS 30) with water on disease activity of induced colitis in mice. Mice treated with IDS 30 clinically and histologically revealed fewer signs of colitis than untreated animals. Faecal IL-1beta, mucosal TNF-alpha concentrations and mononuclear cell proliferation were significantly lower in treated mice. The overall effect was thought to be due to a decrease in the Th1 response.[22]

Dendritic cells are important antigen presenting cells that play a role in the initiation of rheumatoid arthritis (RA) An *in vitro* study showed the suppressive effect of IDS 30 on the maturation of human myeloid dendritic cells, leading to reduced induction of primary T cell responses. This was thought to be a possible pathway explaining the therapeutic effect of IDS 30 on T cell mediated inflammatory diseases like RA.[23]

Antioxidant, Hepatoprotective & Chemoprotective Effects

Various animal studies have found potent hepatoprotective and chemoprotective effects of nettle, thought to be due to antioxidant activity.

Aflatoxin (AF) was used in one study to induce tissue damage. The preventive potential and antioxidant capacity of nettle was then evaluated by liver histopathological changes, measuring serum marker enzymes, antioxidant defence systems and lipid peroxidation. Administration of nettle extract restored the AF-induced imbalance towards near normal particularly in liver and almost normal histologic findings compared with degenerative changes in the untreated rats.[24]

Another study investigated the effects of the herbs *Nigella sativa* and *Urtica dioica* on lipid peroxidation,

antioxidant enzyme systems and some liver enzymes in carbon tetrachloride (CCl4)-treated rats. The CCl4 treatment for 45 days increased lipid peroxidation and liver enzymes, and decreased the antioxidant enzyme levels. Nettle treatments (alone or combined with *Nigella sativa*) decreased the elevated lipid peroxidation and liver enzyme levels and also increased the reduced antioxidant enzyme levels.[25]

Urtica treatment substantially reduced the carcinogen 3-methylcholanthrene induction of hepatic, lung, and renal cytochrome P-450 enzyme activity by 79, 42, and 50%, respectively. This reduction in CYP1A1 and CYP1A2 expression levels with *Urtica* points to a potential chemoprotective ability of *Urtica* due to the anticipated decrease in the activation of environmental chemical carcinogens.[26]

Urinary Tract Actions for BPH and Prostate Cancer

The root of nettle has been studied for its role in managing the symptoms of benign prostatic hyperplasia (BPH) and prostate cancer. Nettle root, along with other natural agents, has a place in the conservative and early treatment of BPH.[27] The possible modes of action in moderating the symptoms of BPH include interaction with SHBG receptors[28,29] and inhibition of aromatase or 5 alpha-reductase.[30] An *in vitro* study found a favourable role for nettle extract in relation to suppression of adenosine deaminase activity in cancerous prostate tissue. The researchers suggested this was the action behind the positive effects of nettle with prostate cancer.[31]

An antiproliferative effect of nettle root extract has been observed both in an *in vivo* and *in vitro* model. A significant antiproliferative effect of the extract was found in human prostatic epithelial cells, whereas stromal cell growth remained unaltered.[32,33]

Another study concluded that some hydrophobic constituents such as steroids in the stinging nettle roots inhibited the membrane Na+,K(+)-ATPase activity of the prostate, which may subsequently suppress prostate-cell metabolism and growth.[34]

A double-blind, placebo-controlled, randomized, study compared *Urtica dioica* with placebo in 620 patients. At the end of 6-month trial, un-blinding revealed that patients who initially received the placebo were switched to *Urtica dioica*. Both groups continued the medication up to 18 months. After the initial six months, 81% of the nettle group reported improvement in symptoms compared to only 16% of the placebo group.[35]

A RCT multicenter study with 246 patients for 1 year examined nettle root (Bazoton uno) and BPH symptoms. The symptom score decreased on average from 18.7 to 13.0 with a statistically significant difference compared to placebo. The median volume of residual urine changed from 35.5mL before therapy to 20.0mL and from 40.0 to 21.0mL with placebo. The number of adverse events (29/38) as well as urinary infections (3/10 events) was smaller under nettle therapy compared to placebo. Treatment with nettle was determined to be a safe therapeutic option for BPH, especially for reducing irritative symptoms and BPS-associated complications due to the postulated anti-inflammatory and antiproliferative effects of the stinging nettle extract.[36]

One study examined different doses of *Urtica dioica* root and *Pygeum africanum* on urine flow, residual urine, and nocturia . Both dosages significantly reduced symptoms and mild adverse effects that did not result in discontinuation of treatment was reported.[37]

Other studies have looked at nettle combined with saw palmetto – normally a product known as PRO 160/120 was used. One study randomised 257 patients to treatment with the herbal compound or placebo under double-blind conditions for 24 weeks. Double-blind treatment was followed by an open control period of 24 weeks during which all patients were administered the herbal compound. Assessment of the patients included a symptom self-rating questionnaire, a quality of life index as well as uroflow and sonographic parameters. Patients treated with the herbal compound exhibited a substantially higher reduction in symptoms (53%) compared to the placebo group. It applied to obstructive as well as to irritative symptoms, and to patients with moderate or severe symptoms at baseline. The tolerability of the herbal extract and long term safety was excellent.[38,39]

Other studies have compared herbal treatment with the synthetic 5-alpha-reductase inhibitor, finasteride. These trials showed equivalent efficacy

for both treatments unrelated to prostate volume. There were improvements in the International Prostate Symptom Score in both treatment groups, with no statistically significant differences. However, the safety analysis showed that more patients in the finasteride group reported adverse events than in patients treated with the herbal compound.[40]

Another prospective, randomized, double-blind clinical trial assessed the efficacy and safety of PRO 160/120, in comparison to the alpha1-adrenoceptor antagonist, tamsulosin, in lower urinary tract symptoms caused by BPH in 140 patients. Results showed 32.4% of the patients in the herb group and 27.9% in the tamsulosin group were responders. Both drugs were well tolerated, with one adverse event in 1514 treatment days for PRO 160/120 and one event in 1164 days for tamsulosin.[41]

Irritant Activity (Hyperaemic Effects)

Topical application of nettle sting has been used for many years for pain relief. An exploratory study assessed the present use of the common stinging nettle to treat joint pain. Eighteen self-selected patients using the nettle sting of *Urtica dioica* were interviewed. Information regarding patients' use of nettle therapy was elicited, including mode of application, dosage and effects. All except one respondent were sure that nettle had been very helpful and several considered themselves cured. No observed side effects were reported, except a transient urticarial rash. [42]

A small RCT evaluated the effectiveness of nettle sting for chronic knee pain, and assessed the acceptability of the method to GPs and patients, and the optimal methods for recruitment and outcome measurement. Patients were randomised to receive either treatment with *Urtica dioica*, or placebo intervention with *Urtica galeopsifolia* daily for 1 week. The main outcome measure was the WOMAC pain subscale with baseline pain scores of 9.2 and 7.9 in the two groups. The mean reduction in pain score at the end of treatment in the nettles group was 1.7 and in the controls 1.6. Patients liked the treatment mostly because it was 'natural' and the sting was acceptable and viewed only as a minor irritation.[43]

A RCT in 27 patients with osteoarthritic pain at the base of the thumb or index finger examined the effectiveness of Urtica leaf application daily for one week to the painful area. The effect of this treatment was compared with that of placebo, *Lamium album*, for one week after a five-week washout period. Observations of pain and disability were recorded for the twelve weeks of the study. After one week's treatment with nettle sting, pain scale scores and disability questionnaire showed a significantly greater effect than with the placebo herb.[44]

Indications

- Inflammatory joint disease - arthritis, tendonitis
- Neuralgia
- Allergic rhinitis
- Atopic eczema
- Inflammatory conditions of the urinary tract
- Fluid retention
- Prevention of chemical toxicity and liver damage
- Fatigue, general weakness

Energetics

Cooling, drying.

Use in Pregnancy

Use with caution in the first trimester.

Contraindications

People with known sensitivities or allergies to stinging nettle should use this herb cautiously. Local application of nettle can be irritating, and cause contact urticaria, but preparations taken internally are generally well tolerated.

Drug Interactions

Caution with lithium and warfarin. Monitor with antidiabetic and antihypertensive drugs.

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	45%
Weekly Dosage:	15 to 80mL

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