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Review Article

HIGHLIGHTS ON NUTRITIONAL AND THERAPEUTIC VALUE OF STINGING NETTLE (*URTICA DIOICA*)

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ABSTRACT

Urtica dioica L. is a herbaceous plant belonging to the family of Urticaceae that has been used for centuries against a variety of diseases. Thanks to its high content of nutriments and bioactive compounds like poly phenols, vitamins and minerals, nettle possesses a great nutritional value and a large number of pharmacological effects, including anti-proliferative, anti-inflammatory, antioxidant, analgesic, immunostimulatory, anti-infectious, hypotensive, antiulcer activities and cardiovascular disease prevention. Stinging nettle is considered safe and has been shown to be side effects free, when taken by mouth of up to 18 gram per day. The most common stinging nettle preparations usually include the crude dried powder, dry extract, infusion (herbal tea), decoction or fresh juice. Stinging nettle root is mainly used for mictional disorders related to benign prostatic hyperplasia while the leaves are used for arthritis, rheumatism and allergic rhinitis. This up to date review highlights the current knowledge and scientific advances concerning *Urtica dioica*.

Keywords: *Urtica dioica*, Polyphenols, Urtica Dioica Agglutinin (UDA), Benign prostatic hyperplasia, Rheumatism.

INTRODUCTION

Nettle has been used for over 2,000 y as a natural remedy for its therapeutic properties. However, it was until the beginning of the 20th century that its medicinal importance was largely studied and dramatically enhanced, beginning with the determination of the chemical structure of the main chemically active agents and their pharmacological properties. It should be stressed that most of the indications from traditional medicine have been validated and new properties have been discovered. Moreover, given its balanced protein composition and its high content of minerals and vitamins, nettle has also been shown to be of great nutritional interest.

In Morocco, these medical and nutritional data remain poorly explored, and the use of nettle is being increasingly neglected both in the culinary field and in the medical and veterinary areas.

This work highlights the current knowledge and scientific advances concerning *Urtica dioica*. We begin with a botanical and a phytochemical study of the plant and its traditional medical uses in Morocco. We then look in detail at its nutritional and medical properties and we describe, at last, its methods of preparation and use, its toxicity and the use precautions.

Botanical study

Native to Eurasia, nettle was widely distributed throughout all the temperate regions of the world. It is now found in Europe (more in northern than in southern Europe), in northern Africa, in Asia and in northern and southern America where it's also largely widespread [1]. Table 1 summarizes the most known common names of *Urtica dioica*.

Nettle is a herbaceous plant, 1 to 2m tall and perennial with rhizomes. It belongs to the Urticaceae family in the Rosales order and the genus *Urtica* characterized by unicellular stinging hairs. The erect stems are strong, hairy, mostly unbranched and quadrangular. They are green in young plants and purple/reddish in older ones. The leaves are opposite, egg-shaped, elongated, with a strongly serrated margin and a pointed tip (fig. 1). The leaves and stems are very hairy and bear many stinging hairs whose tips come off when touched, transforming the hair into a needle that injects a stinging liquid. The nettle is dioecious with separate male and female plants that flower from June to September. The flowers are unisexual, small, and are arranged in clusters on slender, branched spikes formed in the leaf axils. Female flowers are greenish and have a unilocular ovary with a solitary ovule bearing one style with a brush-like stigma. Male flowers are yellowish and composed of 4 stamens, with long elastic filaments, which are bent inwards in the bud. Stinging nettle produces oval-shaped achenes (one-seeded fruits) containing tiny dark brown or almost black seeds. The root system is composed of a taproot which branches into fine rootlets allowing the tuft nettle to expand [1, 2].

Traditional medicinal uses

In Morocco, all parts of the plant are used in traditional medicine. The whole plant is used as a diuretic, anti-hypertensive, anti-diabetic, hemostatic, anti-asthenia, antianemic, antispasmodic, antirheumatic and as a remedy for headaches and chills [3, 4]. Nettle is also used to treat spleen, renal and dermal disorders [5]. The seeds are administered orally for their aphrodisiac and galactagogue effects and other traditional uses against tuberculosis and kidney stones have been described [6]. External uses include the treatment of aphthae, hemorrhoids, scabies and pruritus [4].

Table 1: Common names of *Urtica Dioica* all around the world

Latin name	*Urtica dioïca L. Syn*
English names	Nettle; Common nettle; Stinging nettle; Tall nettle; Slender nettle; Greater nettle.
French names	Ortie dioïque; Grande ortie; Ortie piquante; Ortie élevée.
Arabic names	الحريكة; القراص (Hourriga; Kerrass)
Spanish names	Ortiga; Ortiga gran; Ortiga grossa; Ortiga major; Ortiga inayor.
German names	Brennesslbatter; Brennessel-kraut; Nesslkraut; Haarnesselkraut.

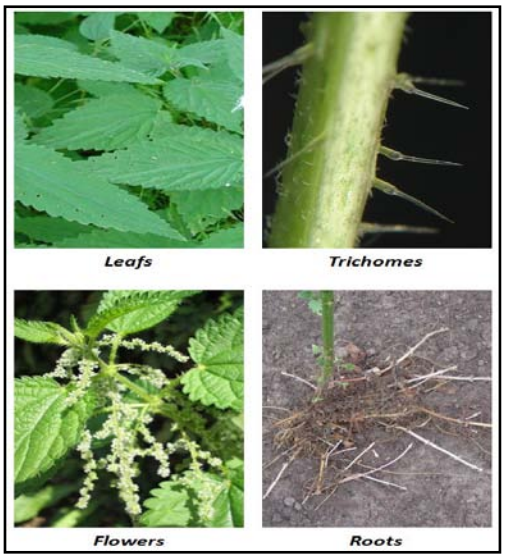

Fig. 1: *Urtica dioica,* botanical aspects (Pictures from Wikipedia. Permission granted to copy, distribute and/or modify under the terms of the GNU Free Documentation License)

Phytochemical study

The leaves of nettle are rich in flavonoids, as well as phenolic compounds, organic acids, vitamins and minerals. The root contains lectins, polysaccharides, sterols and lignans. The stinging action is due to the liquid contained in nettle's hairs. This liquid contains at least three compounds that could be the cause of its allergic reactions: acetylcholine, histamine and serotonin [2, 7].

Nettles secondary metabolites have marked pharmacological properties. The main flavonoids are quercetin, kaempferol and rutin. These flavonoids have antioxidant and anti-inflammatory properties that may limit oxidative damage responsible for some chronic diseases such as cancer, cardiovascular diseases and degenerative diseases. They have many other effects, such as the inhibition of lipid peroxidation of liver mitochondria and blood cells and have also been shown to have hypoglycemic, antibacterial and antiviral properties [8-10]. The most active flavonoid is quercetin. It has strong antioxidant and anti-inflammatory actions [11]. It is not only capable of reducing the incidence of mammary tumors in rats [12, 13] but it also has anti-tumor activity against prostate cancer [14]. Its anti-ulcerogenic activity has also been demonstrated [15, 16]. The antioxidant activity of rutin is similar to that of quercetin [17-19]. In addition, it has anti-inflammatory, anti-cancer properties and reduces the cytotoxicity of oxidized bad cholesterol (LDL) [20, 21]. Tannins, caffeic acid, ferulic acid and coumarins also have antioxidant activity and may protect cells against damage caused by free radicals [22, 23].

Nettle root contains a lectin called *Urtica dioica* Agglutinin (UDA). This lectin is somewhat unique. It has a low molecular weight (8 to 9 kDa) and consists of a single polypeptide chain of less than 100 amino acids [24]. The UDA has immunomodulatory activity and appears to limit the autoimmune manifestations [25]. Table 2 summarizes the chemical composition of nettle's main parts.

Nutritional value

Nettle leaves are rich in protein, fat, carbohydrates, vitamins, minerals and trace elements. Proteins make up of 30% of the dry mass [31]. Furthermore, the protein content of the leaves widely covers the needs of amino acids, especially the essential amino acids for humans [33, 38]. Content of mineral substances is about 20% of the dry mass [31, 45]. Nettle is rich in iron, zinc, magnesium, calcium, phosphorus and potassium. Leaves content of cobalt, nickel, molybdenum and selenium have also been determined [32]. The proportions of different compounds given in the literature are different. The origin and time of sample collection may be responsible for that. The maximum and minimum levels of various compounds are shown in tables 3 and 4.

Table 2: Chemical composition of *Urtica dioica*

Part used	Chemical composition	References
Aerial parts	Flavonoids: Quercetin-3-O-rutinoside (rutin), kaempferol-3-O-rutinoside and isorhamnetin-3-O-glucoside.	[26-28]
	Organic acids: Caffeic acid and its esters, ferulic acid, chlorogenic, citric, fumaric and phosphoric acids.	[26, 29]
	Essential oil: Carvacol, carvone, naphthalene, (E)-anethol, hexahydrofarnesyl acetone, (E)-geranyl acetone, (E)-β-ionone and phytol.	[30]
	Minerals and trace elements: Calcium, Potassium, Magnesium, Phosphorus, Iron, Sulphur, Zinc, Manganese, Copper, Nickel and Selenium.	[31-37]
	Vitamins: vitamin A (retinol), vitamin B2 (riboflavin), vitamin B5 (pantothenic acid), vitamin B9 (folic acid), vitamin C (ascorbic acid), vitamin K (phylloquinone).	[33, 38]
	Other constituents: Tannins, chlorophyll and carotenoids.	[38]
Root	Acidic polysaccharides: glucans, arabinogalactans and rhamnogalacturonans.	[39]
	Flavonoids: myricetin, quercetin, kaempferol, quercetin-3-O-rutinoside (rutin), kaempferol-3-O-rutinoside and isorhamnetin.	[40]
	Minerals and trace elements: Calcium, Magnesium, Zinc, Manganese and Copper.	[34]
	Lectins: *Urtica dioica* agglutinin (UDA), consisting of a single-chain polypeptide made of 89 amino acids and rich in glycines, cysteines and tryptophans.	[24, 41]
	Phytosterols: β-sitosterol; β-sitosterol-3-O-β-glucoside, (6'-O-palmitoyl)-sitosterol-3-O-β-D-glucoside; 7β–hydroxysitosterol; 7α-hydroxysitosterol; 7β-hydroxysitosterol-β-D-glucoside; 7α-hydroxysitosterol-β-glucoside; 24R-ethyl-5α-cholestane-3β,6α-diol; stigmasterol, campesterol, stigmast-4-en-3-on, hecogenin.	[27, 39]
	Lignans: neo-olivil, secoisolariciresinol, dehydrodiconiferyl alcohol, isolariciresinol, pinoresinol, and 3,4-divanillyltetrahydrofuran.	[42, 43]
	Coumarins: Scopoletin	[39, 43]
Fruit (seeds)	Fixed oil: saturated and unsaturated fatty acids.	[44]
	Carotenoids: β-carotene, lutein and violaxantin.	
	Polysaccharides.	

The vitamin composition is very varied. It contains both fat-soluble vitamins A, D, E and K, and also significant amounts of water-soluble vitamins, such as vitamin C and the B vitamins (B1, B2, B3, B9). Wetherilt found that 100g of fresh leaves contained 0.0l mg vitamin B1 (thiamine), 0.23 mg of vitamin B2 (riboflavin), 0.62 g of vitamin B3 (Niacin), 0.068 mg vitamin B6, 238 mg of vitamin C, 5 mg of pro-vitamin A (β-carotene) and 14.4 mg of vitamin E (α-tocopherol) [38].

This richness in nutrients gives the nettle valuable nutritional and also pharmacological properties. Trace elements and vitamins strengthen

the immune system and allow the body to better resist bacterial and viral infections. The simultaneous presence in nettle of vitamins B1, C, E, iron, zinc, selenium and manganese contributes to its anti-oxidant qualities. Nettle has also a remineralizing action, thanks to the presence of calcium, potassium, silicon and iron. It would be beneficial in osteoarthritis and osteoporosis. The high potassium content is another indicator of the protective power of nettle leaves against cardiovascular disease. The iron content and also the presence of vitamin C, which increases the bioavailability of iron makes that nettle is indicated for the treatment of anemia. Additionally, the magnesium intake it provides reduces the incidence of all forms of stress while zinc has an anti-inflammatory action.

Another asset of the nettle is chlorophyll. The nettles leaves contain a significant amount of chlorophyll, around 4.8 mg per gram of dry leaves [46]. This chlorophyll promotes cleansing and detoxification, it cleanses the digestive system and fights bloating and bad breath. In addition, chlorophyll promotes regeneration of cells and activates wounds healing.

Finally, thanks to their high content of protein, essential amino acids, vitamins and iron, nettle leaves can be an important nutritional supplement. Therefore, they can be a good remedy for the treatment of protein-energy malnutrition in malnourished children, pregnant women, convalescents and the elderly.

Table 3: Nutritional composition of fresh leaves of stinging nettle [31, 33-36]

Nutritional constituent	Min (%)	Max (%)
Water	65	90
Proteins	4.3	8.9
Ashes	3.4	18.9
Carbohydrates	7.1	16.5
Lipids	0.7	2
Fibers	3.6	5.3
Calories (kcal/100g)	57	99.7

Table 4: Content of mineral and trace elements (mg/100 g of dry matter) [31-37]

Minerals and trace elements		mg/100 g of dry matter	
		Min	Max
Minerals	Calcium	113.2	5090
	Magnesium	0.22	3560
	Phosphorus	29	75
	Potassium	532	917.2
	Sodium	5.5	16
Trace elements	Cobalt	0.0084	0.018
	Copper	0.52	1.747
	Iron	3.4	30.30
	Manganese	0.768	5.784
	Molybdenum	0.4265	-
	Nickel	0.0732	-
	Selenium	0.0027	0.0074
	Zinc	0.9	3.033

Pharmacological properties

Antiproliferative activity

Many research works show that nettle root's components can interfere with several mechanisms involved in the pathogenesis of benign prostatic hyperplasia. The antiproliferative effect on prostate cancer cells of UDA and the methanolic alcoholic root extracts has been demonstrated *in vivo* and *in vitro* [45, 47, 48].

Lignans from root extract not only inhibit the binding of androgens to their transporter proteins SHBG (Sex Hormone Binding Globulin), but also the binding of these proteins to the membrane receptors of the prostate, thereby inhibiting their proliferative activity on prostate tissues [42, 45, 49].

The root extract reduces the production of estrogen by aromatase inhibition, thereby decreasing the conversion of androgens to estrogens [50]. Also, it was mentioned that root extracts inhibit the enzymatic activity of the membrane of prostate cells, which would stop its growth [45, 51]. Clinical studies on a root extracts showed a significant improvement of the symptoms of benign prostatic hypertrophy [52-54].

Anti-inflammatory activity

Scientific research has highlighted the nettle's ability to decrease the inflammatory response, through multiple mechanisms whose consequences are the reduction of synthesis of lipid mediators and proinflammatory cytokines. Indeed, leaf extracts inhibit the biosynthesis of arachidonic acid cascade enzymes, in particular the cyclo oxygenases COX-1 and COX-2, thereby blocking the biosynthesis of prostaglandins and thromboxanes [55].

In addition, an inhibitory effect was demonstrated on the NF-kappa B (nuclear factor kappa-light-chain-enhancer of activated B cells) system involved in immune, inflammatory and antiapoptotic responses [56,57] and the PAF (Platelet Activating Factor) [55]. Furthermore, several studies have shown that the extract of the leaves reduces the release of Interleukins IL-2 and IL-1β, Interferon γ (IFN γ) and Tumour Necrosis Factors TNF-α and TNF-κ [58,59].

Therefore, the anti-inflammatory effect of nettle leaves suggest that it may be useful in acute inflammatory diseases but also in chronic diseases, like rheumatoid arthritis.

The aqueous extract of nettle roots also has anti-inflammatory activity. Wagner had shown that a polysaccharide fraction of this extract has an inhibitory effect on the induced rat paw oedema, comparable to that of indomethacin [60]. The anti-inflammatory effect is related to the inhibition of cyclo oxygenases and lipoxygenases, and to cytokines production.

Antioxidant activity

Extracts of nettle have a neutralizing role of reactive oxygen species (ROS). Their antiradical activity on the superoxide anion O2 °-, the hydroxyl radical OH ° and nitric oxide radical NO ° was determined by spectrophotometry. Numerous studies have shown that the methanolic and ethanolic extracts of leaves have a remarkable antioxidant effect on the 1,1-diphenyl-2-picrylhydrazyl radical (DPPH) [9, 61-63].

Chelation of ferrous iron was evaluated using ferrozine, which forms a red chromophore with the residual iron (FeII-Ferrozine) having an absorption maximum at 562 nm. The absorbance obtained shows that nettle has a significant chelating activity of the ferrous ions [63].

Another study conducted on rats treated with carbon tetrachloride (CCl_4), showed that nettle decreased lipid peroxidation and increased the activity of the antioxidant defense system playing thus a protective role against hepatotoxicity. This antioxidant activity is essentially correlated to the phenolic compounds content [9, 64].

Immunomodulatory activity

Many studies indicate that flavonoids are able to modulate the immune system. This modulatory effect of the aerial parts of nettle was studied on mice, using an ethanolic extract at two different doses (50 and 100 mg/kg), taken orally for 14 d. The activities of enzymes such as cytochrome P450, lactate dehydrogenase (LDH) and NADPH-cytochrome P450 reductase showed a significant decrease while the antioxidant enzymes showed a significant increase. In addition, the plant has also shown a modulatory effect on enzymes of the kidney, lung and stomach, such as glutathione-S-transferase, superoxide dismutase and catalase [65].

Quercetin-3-O-rutinoside, kaempherol-3-O-rutinoside and isorhamnetin-3-O-glucoside present in the aerial parts of the nettle contributes to the immunomodulatory activity [2, 66].

Furthermore, the immunomodulatory effect of the UDA isolated from the roots, has been demonstrated in several studies that elucidate their action on T cells, macrophages, thymocytes and on the release of TNFα [60].

Analgesic and antinociceptive properties

In addition to its anti-inflammatory action, the nettle has an analgesic effect, proved *in vivo* in rats and mice. The aqueous extract of the leaves at the dose of 1200 mg/kg is capable of reducing the thermal stimulation in the hot plate test at 55 °C and causes a greater resistance to pain [67].

The antinociceptive effect of the hydroalcoholic extract of nettle leaves was evaluated through the acetic-acid writhing test and formalin-induced paw licking test. The results obtained show that the hydroalcoholic extract significantly reduces in a dose-dependent manner the nociceptive response in mice and rats. Flavonoids, the caffeoyl malic acid and the caffeic acid could be responsible for these analgesic properties [56].

Antiulcer properties

The protective effect of the nettle against gastric ulcers is dose dependent. The aqueous extract of aerial parts, at doses of 50 and 200 mg/kg protected rats against gastric ulcer, with significant protection rates ranging from 67.7 to 77.8%. Moreover, this extract showed analgesic activity against gastric dilatation caused by acetic acid [63].

Anti-infective properties

The antibacterial properties of various extracts of *Urtica dioica* against different bacterial strains were identified by several studies. In a study conducted on nine bacteria: *Citrobacter koseri*, *Enterobacter aerogenes*, *Escherichia coli*, *Micrococcus luteus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pneumoniae*, the aqueous extract of aerial parts inhibited the growth of all these bacteria except some strains of *Pseudomonas aeruginosa* [63].

Another study on 38 microorganisms brought evidence of the bactericidal effect of organic extracts of the aerial parts. These extracts inhibited the growth of *Acinetobacter calcoaceticus*, *Bacillus cereus*, *Bacillus spizizenii*, *Bacillus subtilis*, *Citrobacter freundii*, *Entrobacter aerogenes*, *Erwinia sp.*, *Escherichia coli*, *Klebsiella pneumoniae*, *Micrococcus sp.*, *Saccharomyces cerevisiae*, *Salmonella paratyphi* B, *Serratia marcescens*, Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Vibrio parahaemolyticus*. Phenolic compounds in the nettle would be responsible for this antibacterial effect [68].

The antiviral activity of the nettle was evaluated *in vitro* [69]. The selective and powerful inhibitory action of UDA on the intracellular replication of HIV (HIV-l and HIV-2), respiratory syncytial virus (RSV), and cytomegalovirus (CMV), was well elucidated [70].

The antimycotic activity on some pathogenic fungi (*Alternaria alternata*, *Aspergillus flavus*, Candida albicans, Ceratcystis ulmi, Fusarium oxysporum, Fusarium solani, Phoma exigua, *Phytophthora carotovora*, *Porphyromonas gingivalis*, *Microsporum cookei*, *Microsporum gypseum*, *Saccharomyces cerevisiae*, *Trichoderma viride*, *Trichophyton mentagophytes* and *Rizoctonia solani*) was also confirmed [63, 71].

Antidiabetic activity

A study conducted to evluate the anti-diabetic activity *in vivo* showed the hypoglycemic effect of aqueous extracts of leaves of nettle on diabetic rats. These results are explained by the inhibition of the intestinal absorption of glucose [72].

Furthermore, studies performed on the islets of Langerhans have demonstrated the stimulatory action of nettle on insulin secretion, accompanied by a decrease in blood sugar. Tests performed on normal and diabetic rats after intra peritoneal injection of aqueous extracts confirmed this result [73].

Antihypertensive action

Intravenous injections of an aqueous extract of the aerial parts of the nettle, using two concentrations: 4 and 24 mg/kg/h resulted in a blood pressure drop of 15% and 38% proportionally to the administered dose. This decrease was correlated with an increase in diuresis and natriuresis. However, the hypotensive effect was reversible after one hour if a low concentration (4 mg/kg/h) had been used, while it persisted when using a high concentration (24 mg/kg/h) [74].

Moreover, root extracts tested on isolated pieces of vaso constricted aorta showed a relaxant activity. This vasodilator effect is due to the release of the endothelial nitrogen oxide, potassium channel opening and a negative inotropic action [75].

Effect on platelet aggregation

Several studies indicate that extracts of nettle strongly inhibit platelet aggregation. The inhibitory effect of the aqueous extract of the leaves on platelet aggregation induced by thrombin was clearly demonstrated. Flavonoids are the main compounds involved in this activity [76, 77].

Action on hyperlipidemia and atherosclerosis

Daily administration of aqueous extract of *Urtica dioica* at 150 mg/kg for 30 d, either as part of a normal or high fat diet, caused a reduction in serum lipids and lipoproteins. Significant decreases in cholesterol and LDL/HDL ratio (Low Density/High Density Lipoproteins) were observed [77].

Similarly, administration of an ethanolic extract to hypercholesterolemic rats, using doses of 100 mg/kg and 300 mg/kg, was responsible for the decreased of cholesterol and LDL levels [78, 79].

Anti allergic activity

The anti-allergenic activity of the nettle is mainly due to two mechanisms. In addition to its inhibition of histamine H1 receptors, nettle inhibits tryptase, consequently reducing mast cell degranulation and the release of proinflammatory cytokines [55].

In a randomized double-blind study with allergic patients having allergic rhinitis, an improvement in symptoms was observed after one week of treatment [80].

Toxicity

Toxicological studies have shown that the LD50 (median lethal dose) of the aqueous extract of the leaves administered intraperitoneally in mice is 3.5g/Kg [72]. While the LD50 of the hydro-alcoholic extract of the leaves administered orally is 5.77 g/Kg [56].

Toxicity studies carried out on the roots have shown that the LD50 values obtained after intravenous injection of an aqueous extract and an infusion of the roots to rats are respectively 1.721 g/kg and 1.929 g/kg [81].

Whereas the LD50 of hydro-alcoholic extracts administered intraperitoneally is 600 mg/Kg [82]. The toxic dose of the fixed oil of nettle seeds is greater than 12.8 ml/kg [83]. For chronic oral application in rats, the DL50 was 1.31g/kg (table 5).

Table 5: LD50 of different *Urtica dioica* extracts

	Extracts	Animals tested	Administration routes	LD50 (mg/kg)	References
Leaves	Hydo-alcoholic	Mice	Oral	5770	[56]
	Aqueous	Mice	Intraperitoneal	3500	[72]
Root	Hydo-alcoholic	Rats	Intraperitoneal	600	[82]
	Aqueous	Rats	Intravenous	1721	[81]
	Infusion	Rats	Intravenous	1929	[81]
	Infusion	Rats	Oral	>1310	[81]
Seeds	Fixed oil	Mice	Intraperitoneal	>12.8	[83]

Modes of use and use precautions

Nettle is used by oral and local routes. The most frequently used preparations in herbal medicine are the total dry powder, dry extracts, infusions, decoctions and the fresh nettle juice.

Orally, aerial parts are used as diuretics and also in the treatment of arthritis, rheumatism and gout. Nettle teas are also used in the treatment of rhinitis and seasonal allergies [84].

Thanks to their high content of iron and trace elements, nettle leaves infusions, tinctures or fresh juices are prescribed to treat anemia and also for asthenia, convalescence and demineralization states. In association with the marigold (*Calendula officinalis*) and curled dock (*Rumex crispus*), nettle leaves are used for the treatment of chronic skin conditions such as eczema, psoriasis and hives [85]. Nettle fresh juice has a hemostatic effect on the skin and nasal bleeding. It also overcomes the heavy periods or menorrhagias by reducing their flow [85].

Used in mouthwash, nettle is also effective against oral infections such as aphtha, gingivitis and tonsillitis [86]. External preparations like fresh nettle poultices are used in cases of acne and to alleviate arthritic and rheumatic pain [86].

Nettle preparations are also applied externally in hair care against dandruff and oily hair. Furthermore, the nettle roots, alone or associated with saw palmetto (*Serenoa repens*), are used as teas or extracts in mictional disorders due to benign prostatic hyperplasia [85].

The adherence to dosage recommendations is essential. The recommended adult dosage of the dried aerial parts is 1.2 to 18g per day. For fresh juice, the recommended dose is 15 to 45 ml per day. Dosages for the dried root preparations are 0.3 to 24g per day. Recommended dosages and frequency of administration for each type of preparations are shown in table 6.

Table 6: Recommended doses of *Urtica dioica* extracts

Parts used	Preparation	Recommended doses	References
Dried aerial parts	Dry powder	6 à 12 g, per day	[87]
		8 à 12 g, 2 à 3 times daily	[84]
		2 à 5 g, 3 times daily	[88]
		3 à 6 g, 3 times daily	[89]
	Infusion	6 à 12 g, per day	[87]
		3 à 5 g, 1 à 3 times daily	[84]
		2 à 5 g, 3 times daily	[88]
		3 à 6 g, 3 times daily	[89]
	Decoction	2 à 5 g, 3 times daily	[88]
	Liquid extract	6 à 12 g, per day	[87]
	(Dry weight equivalent)	2 à 5 g, 3 times daily	[84]
		2 à 4 g, 3 times daily	[89]
	Tincture	1.4 à 2.8 g, per day	[87]
	(Dry weight equivalent)	0.5 à 1g, 3 times daily	[90]
		0.4 à 1.2g, 3 times daily	[88]
Fresh aerial parts	Fresh juice	15 ml, 1 à 3 times daily	[84]
	Dry powder	0.3 à 0.6 g, per day	[91]
		4 à 6 g, per day	[87]
	Infusion	4 à 6 g, per day	[87]
		4 à 6 g, 3 à 4 times daily	[84]
	Decoction	4 à 6 g, per day	[87]
		4 à 6 g, 3 à 4 times daily	[84]
	Liquid extract	1.5 à 7.5 g, per day	[87]
	(Dry weight equivalent)	4.5 à 7.5 g, per day	[84]
		1 à 1.5g, 3 times daily	[88]
	Dry extract	2.1 à 8.4 g, per day	[84]
	(Dry weight equivalent)	4.5 à 12.1 g, per day	[88]
Dried roots	Tincture	3 g, per day	[84]
	(Dry weight equivalent)	0.5 à 1g, 3 times daily	[90]
		1 à 1.5g, 3 à 4 times daily	[88]

Despite having anti allergic properties, nettle may cause allergies in sensitive people. Some rare hypersensitivity reactions like hives, itching, edema, oliguria and gastralgia have been reported [92, 93].

Furthermore, the use of nettle orally is contraindicated in pregnant women because of the risk of abortion [94] and in children under 12 because of a lack of clinical studies in this area [1].

CONCLUSION

Notorious for its unpleasant irritant effects, stinging nettle is actually rich in vitamins and minerals and possesses many medicinal properties. During the last decades, several studies have focused on the pharmacological properties and the analysis of the chemical composition of this plant.

Although its potential benefits are still not entirely defined, many studies have strengthened its claimed indications from traditional medicine. Conducted *in vitro* and *in vivo* in animals, these studies have indeed approved many of the nettle pharmacological effects as antiproliferative, anti-inflammatory, anti-oxidant, analgesic, anti-ulcer, immunostimulating, anti-infectious, anti-hypertensive and also as protective against cardiovascular diseases.

In addition, and in regard to its richness in protein, minerals and vitamins, the stinging nettle provides a proven great nutritional value.

In the perspective of a large medical use, several clinical trials conducted in humans, confirmed these pharmacological and nutritional properties. And many toxicological studies proved that nettle can be considered safe since significant doses, administered orally in humans, showed no side effects.

CONFLICT OF INTERESTS

Declared None

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