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A Review on Stinging Nettle Root

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***ABSTRACT**: Urtica dioica L. is an herbaceous plant belonging to the family of Urticaceae that has been used for centuries against a variety of disease. This up to date review highlights the current knowledge and scientific advances concerning Urtica dioica. Stinging nettle is named for the fine silica-rich hairs that cover its stems & leaves; A solid base supports a single elongated cell with a brittle tip. When the tip is broken, the exposed sharp point penetrates the skin and pressure injects toxins i.e mixture of Acetylcholine, Formic acid, Histamine and Serotonin. 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[1].Stinging nettle root is used for urination problems i.e., painful urination. The plant is commonly used in herbal medicine and can be cooked and eaten as a nutritious protherb. This nettle plants as very good source of energy and proteins, high fiber, and a range of health benefitting bioactive compounds.*
***KEYWORDS**: Utrica dioica, Sting, Silica-rich hairs, protherb.*

I. INTRODUCTION:

Urtica dioica is commonly known as stinging nettle. It is found in many cooler temperate parts of the world - Europe, Asia, Africa, New Zealand etc. It is widespread in northern Europe and less spread in North Africa where it is restricted by its need for moist soil. Different sub-species or varieties have different distribution. The plant boats pretty, heart-shaped leaves and yellow or pink flowers but the stem is tiny, stiff hairs that release chemicals when touched. The leaves, stem or root from the nettle plant can be crushed and made into powders, tinctures, creams, teas and more. Stinging nettle is an herbaceous plant and often grows to about 2 metres (6.5 feet) in height. The plant can spread vegetatively with its yellow creeping rhizomes and often forms dense colonies. The toothed leaves are borne oppositely along the stem and both the stems and leaves are covered with numerous stinging and non-stinging trichomes (plant hairs). The plant can be dioecious (an individual produces only female or male flowers) or monoecious (an individual bears both male and female flowers), depending on the sub-species. The tiny green or white flowers are borne in dense whorled clusters in the leaf axils and stem tips and are wind-pollinated. The fruits are small achenes, and the plants produce copious amounts of seeds. Stinging nettle has a long history of use as a medicinal herb and is still used in folk medicine for a wide array of disorders, though there is limited clinical evidence supporting its efficacy. The rootstock is used as a diuretic and as an herbal treatment for benign prostatic hyperplasia and other urinary disorders. Tea made from the leaves has been used to treat hay fever, diabetes, gout, arthritis whereas fresh stinging leaves are sometimes applied to arthritic joints in a process known as utrification, which is said to stimulate blood flow. Topical creams have been developed for joint pain and various skin ailments including eczema and dandruff [2-5].

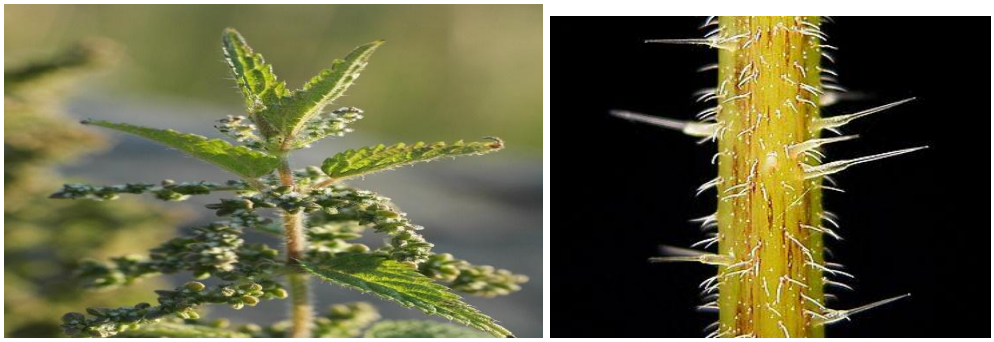

Fig. 1 Stinging nettle, closeup defensive hairs

Scientific classification (Toxonomic tree) [6]

Domain	: Eukaryota
Kingdom	: Plantae
Phylum	: Spermatophyta
Sub phylum	: Angiospermae
Class	: Dicotyledonae
Order	: Urticales
Family	:Uriticaceae
Genus	: Urtica
Species	: Urtica dioica

Three family members of nettle*:*

1. **Stinging nettle**

Fig. 2- Stinging nettle (*Urtica diocia*)

Probably the most commonly known and recognized member of the Nettle family (Urticaceae) is stinging nettle (*Urtica dioica*). Many folks know of its medicinal and edible qualities and enjoy foraging for it. Stinging nettle can be found throughout North America, Europe, Asia and North Africa. The leaves of stinging nettle are rough.

2. **Wood Nettle**

Fig. 3- Wood nettle (*Laportea Canadensis*)

Less well known is Wood nettle. The scientific name of wood nettle is Laportea Canadensis. It is native to the eastern half of North America. It too is prized by foragers as food and medicine. The leaves of wood nettle are rough.

3. Clear Wood:

Fig. 4: Clearweed (*Pilea pumila*)

The third plant to review in the nettle family is clearweed (*Pilea pumila*) — also found in eastern North America. It is edible and people have foraged and eaten this plant — mistakenly thinking they were harvesting stinging nettle.

All three plants are in the Nettle Family and each has been assigned to a different genus (Urtica, Laportea and Pilea). When we look at the leaves, we can see how very similar they are in shape. Clearweed's leaves are smooth and somewhat glossy while both stinging nettle and wood nettle have "rougher" looking leaves.

II.PHARMACOGNOSTIC STUDY:

Urtica dioica is a dioecious, herbaceous, perennial plant, 1 to 2 m (3 to 7 ft) tall in the summer and dying down to the ground in winter. It has widely spreading rhizomes and stolons, which are bright yellow, as are the roots. The soft, green leaves are 3 to 15 cm (1 to 6 in) long and are borne oppositely on an erect, wiry, green stem. The leaves have a strongly serrated margin, a cordate base, and an acuminate tip with a terminal leaf tooth longer than adjacent laterals. It bears small, greenish or brownish, numerous flowers in dense axillary inflorescences. The leaves and stems are very hairy with non-stinging hairs, and in most subspecies, also bear many stinging hairs (trichomes or spicules), whose tips come off when touched, transforming the hair into a needle that can inject several chemicals causing a painful sting or paresthesia, giving the species its common names: stinging nettle, burn nettle, burn weed, or burn hazel. Both the leaves and stems are covered with erect and bristly glandular hairs that contain acetylcholine, formic acid, 5-hydroxytryptamine and histamine. The plant causes skin irritation if touched without gloves.[7]

***Macroscopical Studies**:*

Fig. 5- Parts of *Uritica dioica* Linn. 1) Whole plant;2) flowers 3) Trichomes 4) Roots 5) leaf

Macroscopical studies revealed that root is branched taproot, rounded with wiry rootlets, 1-1.5 cm thick and brown in colour; leaves are long-petioled, elliptic to broadly ovate in shape, green in colour and incised-dentate. Leaf is totally morphologically different from closely related species of Utrica i.e., *Utrica dioica* (leaves uneven and more robust); stem is 0.5-1 cm thick, green in colour rounded and branched.[8]

Microscopical Description:

Leaves:

Transverse section of the *Utrica dioica* leaf has been reported to have a layer of upper and lower epidermis embedded with stomata; stomata are present more on the lower side, the cells of the upper being larger in size than that of the lower one, enclosed with striated cuticle, unicellular to multicellular. Non-glandular trichomes with unicellular stalk and cylindrical unicellular head are prominent, meristele shows radially arranged rows of vessels and an arc of phloem, 3-5 rows of collenchymatous tissue lie underneath, lamina shows a row of palisade underneath the upper epidermis. Mesophyll is occupied by 5-6 row of spongy parenchyma.

Stem:

Transverse section of dicot stem is quadratic with prominent corners; several vascular bundles are located with prominent corners; several vascular bundles are located at each corner; between bundles the cells are thickened and pitted; fiber caps with an irregular outline occur outside of the phloem; fiber cell walls are slightly thickened, with a large cell lumen; small calcium oxalate cluster crystals 10-20µm diameter are present in parenchyma; pith parenchymatous with central cavity.

Rhizome*:*

The transverse section of rhizome has been reported to consist of cork, cortex, pericycle, vascular bundle and pith. The cork comprises of brown thin walled cells and cortex composed of tangentially elongated parenchymatic cells. The pericycle region consists of fibers in a small group as well as single; elongated fibers with thick lignified walls. However, pericycle fibres in the secondary phloem region are large in size and having a cluster crystal of calcium oxalate. The vascular tissue separated by wide medullary rays. The secondary phloem mainly comprises of parenchymatous cells whereas secondary xylem is dense and lignified, the lignified and non-lignified tissues of secondary xylem are separated by medullary rays; lignified cells of secondary xylem have medullary thickened walls and several simple pith. Pith is composed of rounded non-lignified parenchyma.

Root:

The transverse section of root has shown cork, phelloderm and vascular bundle having primary xylem in the center. The cork is thin walled and phelloderm is very narrow. The vascular bundle consisting of secondary phloem and xylem with an alternating zone of lignified and non-lignified parenchymatous cells separated by medullary rays as in the rhizomes. The Centre consisting of strand of primary xylem with occasional small vessels [9-12].

Phytochemistry:

The major chemical constituents of *Utrica dioica* are flavonoids, tannins, volatile compounds, fatty acids, polysaccharides, isolectins, sterols, terpenes, protein, vitamins and minerals [13-15]. GC-MS analysis shows the presence of 43 compounds. Fatty- acid esters (C14:0, C16:0, C18:2, C18:3, C19:2 etc.,) 9-oxononanoic acid, hydroxycinnamic acid, vanillic acids, free fatty acids and vanillin, eugenol, apiol, squalene etc., made up most of the 36 identified compounds. In addition to the mentioned compounds pyrazine and pyrazole derivatives were detected for the first time in studied samples of HMT. These included 4-ethyl-4,5-dihydro-5- propyl-1H-pyrazol-1-carboxaldehyde isomers (I) and derivatives of hexahydropyrrolo-[1,2-a] pyrazin-1,4-dione (II) with 3- alkyl and 3- phenyl methyl substituents in addition to 5,10 –diethoxy-2,3,7,8-tetrahydro-1H, 6H-dipyrrolo [1,2-a] pyrazine (III)[16] .

Amino acid analysis shows dominating presence of aspartic acid, asparagines, glutamic acid, alanine and threonine in homeopathic matrix tincture of *Utrica dioica*. Histidine was also identified in the tincture, indicating that the amino acid is in bound form[16]. Arginine, isoleucine and leucine dominated among the free amino acids. An unusual lectin has been isolated from *Utrica dioica*. Aspartic acid and alanine amino acids were isolated from the root extract. Polar extracts of the roots of the stinging nettle were screened to have lignans (+)-neoolivil (-)- secoisolariciresinol, dehydrodiconiferyl alcohol, isolariciresinol, pinoresinol etc.,

About nine types of carotenoids were isolated from the phytochemical analysis of leaves at different maturity stages which are lutein, lutein isomers, β-carotene and β-carotene isomers were the major carotenoids found at every level of maturity [18].

***Major constituents of Nettle**:*

VITAMINS : Vit-A, C and K as well as several B vitamins.
MINERALS : Calcium, iron, magnesium, potassium, sodium
AMINO ACIDS : Essential amino acids
POLYPHENOLS : Quercetin, Coumarin, flavonoids
PIGMENTS : Beta-carotene, lutein, luteoxanthin.

Benefits:

Nettle treat enlarged prostate symptoms, aid blood sugar control, Natural diuretic, Wound and burn healing, reduce inflammation, treat hay fever and lower blood pressure.[18]

III. PHARMACOLOGICAL EFFECTS*:*

Anti-diabetic:

The hydroalcoholic extract of *Utrica dioica* leaves prevents from severity of diabetes by preventing severe increase in blood glucose concentration and also regenerates β-cells, if used before induction of hyperglycemia[19]. *Utrica dioica* leaves results in reduction in the level of blood glucose and glycated haemoglobin during streptozocin (STZ) - induced diabetes [20]. The leaves show reduction in dexamethasone induced diabetes and its complications such as depressive like behavior and cognitive dysfunction, hyperglycemia, plasma corticosterone and oxidative stress [21].

***Anti-inflammatory**:*

Utrica dioica has been reported to increase total antioxidant capacity and reduce inflammatory stress. The two most prevalent active chemical agents found in the stinging nettle are formic acid (methanolic acid) and histamine (1H-Imidazole-4-ethanamine; 2- (4- Imidazolyl ethylamine; 4- (2- Aminoethyl)- 1H- imidazole) which function as an anti-inflammatory agent [22,23].

***Anti-cancerous**:*

Aqueous extract of *U. dioica* leaves were evaluated with anti-cancer activity in LNCaP treated prostrate carcinoma cell line [25]. The extract shows significant reduction in LNCaP cell viability in a dose dependent manner, thus shows cytotoxic effect using MTT Assay [24]. The extract has been used as complementary and alternative therapies during and after the chemotherapic treatment of cancer patients [26].

Leaf extract of *U. pilulifera* has been analyzed for its use in cancer treatment as it increases protein concentration and reduces the lipids in lipidemic liver and remodels the phospholipids compositions showing its potential to be used in treatment of cancer diseases. Aerial part of *Urtica pilulifera* extract shows highest cytotoxicity against breast infection, about 85% of the cells were found dead at the concentration of 500 µg/ml due to presence of phenolic compounds (phenolic compounds are known to inhibit mutagenesis in humans) [27].

The aqueous extract of plant has been investigated for cytotoxic activity against MCF‐ 7, MDA‐ 231 breast cancer cell lines by using the XTT cell cytotoxicity assay. On MCF‐ 7 cells; IC50 value at 48th hr was 34 µg/ml increasing the concentration of aqueous extract to 29.2 µg/ml has been observed to decrease MDA‐ 231 cell viability to 43% [28].

The aqueous extract of the *Urtica dioica* roots has been analyzed in vitro for the cytotoxic effect and its anticancerous activity against acute myelogenous leukemia cell line [29].

***Anti-oxidant**:*

The hydro-alcoholic extract of *Utrica dioica* showed positive in-vitro anti-oxidant activity. Ferulic acid is detected as a potential antioxidant present in the species using HPTLC. It has antioxidant, antimicrobial, antiulcer and analgesic properties [31,32].

***Anti-arthritic**:*

Methanolic extract of the root of *Utrica dioica* has been used as a remedy for rheumatoid arthritis due to suppression of cytokine production [31].

Hepatoprotective activity:

Hepatoprotection or anti-hepatotoxicity is the ability to prevent damage to the liver, prevent the liver affections prophilactically and maintains balance in liver enzymes. The leaves extract of plant shows maximum hepatoprotective activity at dose of 400 mg/kg concluded by the decreased level of serum alanine transaminase (ALT), aspartate amino-transferase (AST), alkaline phosphatase (ALP), total bilirubin level and malonyldehyde (MDA) and also by the increase in level of superoxide dismutase (SOD) level[32,33].

The seed extract of *Urtica dioica* has also shown hepoatoprotective protective activity against ischemia‐ reperfusion induced hepatotoxicity and it exhibited hepatoprotective effect by increasing the activity

of paraoxonase, aryl-esterase and liver tissue catalase activity[34].The plant extract has shown significant hepatoprotective effect in isolated rat hepatocytes (in vitro) and in rabbits (in vivo) reduces the chances of hepatocellular degeneration and necrotic changes in CCl4 induced hepatotoxicity[35,36].

Antimicrobial Activity:

Hexane extract of *U. dioica* is analyzed to have antimicrobial activity against a multi drug resistant bacterium - Mycobacterium smegmatis. It is also assessed for having potential anti-microbial activity against all the tested bacterial strains and its minimum inhibitory concentration (MIC) value was 125, 15.62, 31.25, 250, 31.25, 125 and 7.81 µg/ml against Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Shigella flexneri and Salmonella typhi, respectively. Aqueous extract from the leaves of *U. dioica* showed antibacterial activity against bacterias like Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermis, E. coli and various other gram positive and gram-negative bacteria [37,38].

Anti-hyperlipedimic activity:

The plant has very potent anti-hyperlipedimic activity as it lowers the level of lipids and lipoproteins in blood. The aqueous extract 150 mg/kg given for 30 days to rats feed on normal or high fat diet, improved the blood lipid profile. The significant decreases in total cholesterol, low density/high density cholesterol (ldl/sdl) ratios via lower concentration of ldl and plasma total apo-protein has been observed. The ethanolic extract of the plant at dose 100 and 300 mg/kg has shown significant reduction in the level of total cholesterol and LDL level in hyper-cholesterolemic rats [39-41].

Anti-viral activity*:*

Antiviral activity is exhibited by the root of *U. dioica* against HIV-1, HIV-2, CMV, RSV and flu virus. N-acetyl glucosamine specific lectin from *U. dioica* is screened for having a strong anti- HIV activity, as it has high binding affinity towards HUT-8 cells, CD4+ and Molt-4 cells, the cells which are the binding sites for HIV-1 and HIV-2 virus [42].

Cardiovasular activity*:*

U.dioica aortic rings with intact endothelial layer, the vasorelaxant effect was abolished by L-NAME, a NO-biosynthesis inhibitor, and ODQ, a guanylate cyclase inhibitor. Furthermore, potassium channel blockers (TEA, 4-aminopyridine, quinine, but not glybenclamide) antagonized the vasodilator action of the purified fraction F1W of *U. dioica*. The same fraction produced a marked decrease of inotropic activity, in spontaneously beating atria of guinea-pig, and a marked, but transient, hypotensive activity on the blood pressure of anaesthetized rats. It is concluded that *U. dioica* can produce hypotensive responses, through a vasorelaxing effect mediated by the release of endothelial nitric oxide and the opening of potassium channels, and through a negative inotropic action.[43]

Immunomodulatory activity:

The immunomodulatory and antiinflammatory activities of aqueous *Urtica dioica* extract were investigated for their effect on the mitogenic response of murine splenocytes and nitric oxide production by murine peritoneal macrophages in vitro. It was found that this extract stimulated the proliferation of T-lymphocytes and suppressed NO production in lipopolysaccharide-stimulated macrophages without affecting cell viability.[44]

Anthelmintic activity*:*

The methanolic extract of leaves exhibited potent anthelmintic activity which has been investigated using earth worms and the results revealed a dose dependent increase in anthelmintic activity of the extract at dose 25, 50 and 100 mg/ml [32].

Precautions*:*

- It should not be given in pregnancy and breast-feeding condition.
- Nettle should not be taken during diabetes because it lowers the blood glucose levels.
- Nettle should not be given in people suffering with kidney problems [45].

Interactions:

- Anti-hypertensive drugs +nettle-
  Nettle when taken along with the anti-hypertensive drugs causes B.P to go too low
- Sedatives+ nettle-

The above ground parts of nettle were produces sleepiness. So, if we take nettle along with sedatives it causes too much of sleepiness.

- Warfarin +nettle-

  Nettle is an anti-coagulant. So, if we take nettle in combination with warfarin it decreases the effectiveness of warfarin.

IV. CONCLUSION:

This review highlights the up to date current knowledge and scientific advances concerning *Urtica dioica.L.* The pharmacognestical, macroscopical and microscopical studies reveals that the plant consists of leaves, root, stem and rhizomes. The leaves and stems are covered with erect and bristly glandular hairs that contain acetylcholine, formic acid, 5-hydroxytryptamine and histamine. Phytochemical studies on the plant revealed presence of various chemical compounds like phytosterols, saponins, flavonoids, tannins, proteins and amino-acids that showed beneficial potential of the plant to get commercially cultivated and get used for the natural drugs and medicine. Presence of Vitamins, phenolic compounds, macro and micro-elements, tannin, flavonoids, sterols, fatty acids, carotenoids, chlorophylls, accorded the plant to get utilized in different ways.

The pharmacological studies review that anti-inflammatory, antioxidant, analgesic, immunostimulatory, anti-infectious, Anti diabetic activity, Hypotensive, Anticancer activities, cardiovascular disease, anti hyperlipediemic, hepatoprotective, Antiarthritic and Anthelmintic activity. So, the bioactive compounds isolated from the plant will help in designing new drugs and other pharmaceutical compounds to fight against widespread diseases like cancer, HIV, Arthritis, Skin diseases, etc.

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