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# A review on nettle leaf and its pharmacological & phytochemical aspects

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**Abstract**
Stinging nettles can be originated all over the world. Plant hairs situated on the leaves and stems contain a number of chemicals, which can cause a stinging reaction and painful irritation when brought into interaction with human skin. However, stinging nettles have a number of health profits and have been used therapeutically since at least the times of Ancient Greece. Studies have shown that all parts of the nettle have antioxidant, antimicrobial and pro-health capabilities. Maximum nettle medicines are made from the flowers, stems and leaves, but roots are also used in pharmacology & They possess various pharmacological activities. This valuable plant has been used most usually as a diuretic and for treating painful muscles and joints, eczema, gout and anaemia. Nettles may be used as a vegetable, in juice, tea and as an ingredient in many dishes. The use of stinging nettles as a feed component could also completely affect the health of poultry and animal productivity. However, despite these proven benefits, the nettle is still an undervalued plant. The leaves and root extract of stinging possess various activities like hypoglycaemic, anti-inflammatory, antiproliferative, antioxidant, hypolipemic, Hepatoprotective, antirheumatic, antineoplastic, antiviral activity and antibacterial activity.

**Keywords:** Stinging nettles, Anti-Inflammatory, Hepatoprotective, Anti-Neoplastic, Antioxidant, Hypolipemic, Immunomodulatory activity, Anti- Microbial activity

## Introduction

Nettle, or stinging nettle, is a perennial plant growing in temperate and tropical wasteland areas around the world. It grows 2 to 4 meters high and produces pointed leaves and white to yellowish flowers and it belongs to the family of Urticaceaea. The genus name Urtica comes from the Latin verb urere, meaning 'to burn,' because of these stinging hairs. The species name dioica means 'two houses' because the plant usually contains either male or female flowers. Nettle has a well-known reputation for giving a savage sting when the skin touches the hairs and bristles on the leaves and stems. In the last few years, Urtica dioica L., has been accepted as a healing plant because of its considerable effects on human health in many countries all over the world. For over 2000-year nettle has been used as a natural remedy for its therapeutic properties. However, it was until beginning of the 20th century in which its medical 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. Most of the indications from traditional medicine have been validated and new properties have been discovered. Moreover, nettles are reported to be of high nutritional value, with high levels of minerals and vitamins [1].

The leaves (Figure 1) and stems (Figure 3) are very hairy with non-stinging hairs and also bear many stinging hairs or trichomes (Figure 2), whose tips come off when touched, transforming the hair into a needle that will inject several chemicals including acetylcholine, histamine, 5-HT (serotonin), moroidin, leukotrienes and possibly formic acid. After contacting human skin, the irritant is released and produces pain, wheals or a stinging sensation which may last for even more than 12 h. The burning property of the juice is dissipated by heat, enabling the young shoots of the Nettle, when boiled, to be eaten as a pot-herb [5].

The herb is a well-known medicinal herb that is used as a leafy vegetable as a nutritious human diet (containing minerals, flavones, amino acids, vitamins, tannins etc.) in various parts of the world. Many functional cosmeceuticals like shampoos, toothpaste and creams are prepared from the leaf extract of nettle. The nettle fibres are also being used for the production of new textile of natural origin. Its leaves and roots extracts are used in rheumatic and allergic (seasonal) conditions. Apart from these it is also used in early stage of benign prostatic hyperplasia (in reducing the urinary problems) and in diabetes (for controlling blood glucose levels) [8].

**Fig 1:** Nettle Leaf

Urtica dioica L. (family Urticaceae), a herb commonly known as stinging nettle, has been used since time immemorial against a variety of diseases. In Latin the name Urtica is derived from the "uro" meaning "to burn" or "urere", meaning to sting. Stinging nettle's species name dioica in Latin means for "two houses" (from Greek word oikia, meaning house) because the plant is of dioica nature, bearing either male or female flowers on separate plants. In folk lore, the fresh herb had been used for treating arthritic or paralytic limbs by stimulating blood circulation and bringing warmth to the affected sites (the treatment is known as "urication"). The urication or rubefaction effect of the herb had been used in folk lore for the treatment of rheumatism, and muscular paralysis [9].

**Fig 2:** Urtica dioica L. Trichomes

**Plant Description**

U. dioica is originally from the colder regions of northern Europe and Asia, today this herbaceous shrub grows all over the world. Stinging nettle grows well in nitrogen-rich soil, blooms between June and September of every year, and reaches nearly 3 feet high. The stem is erect and green, the leaves are opposite, cordate at the base, oblong or ovate, finely toothed, dark green above and paler beneath. The flowers are in Reddish-brown to greenish-white colour. The small, green, dioecious flowers occur as racemes in the axils of the upper leaves. Usually, the plant has either male or female flowers, in separate inflorescences, hence the specific name of the plant, dioica. U. dioica flowers from May to September every year [6].

**Fig 3:** Urtica dioica L. Stem

Nettles are considered weeds due to their rapid growth and soil coverage. However, there are economic and ecological reasons for cultivating stinging nettles. According to Dreyer and Müssing, nettles can improve soils over-fertilized with nitrogen and phosphate. They can also promote the biodiversity of local flora and fauna. Over 40 species of insect are supported by nettles. U. dioica can reduce heavy metal content in soil. Urtica spp. can be used to produce new high-quality agricultural raw materials for the dyeing, textile and energy sectors. Due to their content of tough fibres, nettles were used in Germany and Austria to make textiles during the First World War. Despite these benefits, most stinging nettles are wild harvested. Primary producers of stinging nettles include Eastern Germany, the former USSR, Bulgaria, the former Yugoslavia, Hungary and Albania [7].

## Botanical Survey

**Table 1:** Botanical Survey of Urtica dioica L. (10)

| | | |
|---|---|---|
| **1.** | **Roots** | Extensive underground network of hard winter rhizomes, fibrous roots produced along with rhizomes. |
| **2.** | **Stem** | Unbranched, and grow from 60 - 150 cm high covered with bristly stinging hairs slender and approximately square in cross section. |
| **3.** | **Leaves** | Opposite, toothed, pointed stipules (small leaf-like appendages) occur at the base of the leaf, but senesce early. Leaf stalks are ¼ to 2/3 the length of the leaf, |
| **4.** | **Flowers** | Tiny, greenish-white flowers monoecious or dioecious in axillary cymose clusters, hanging panicles |
| **5.** | **Dioecious** | Perigone has 4 tepals, 4 stamens and 1 ovary with brush like stigma. |
| **6.** | **Monoecious** | Male flower consists of only stamens, perianth of 4 segments. Stamens curve inward in bud stage and grow back at end of flowering for anthers to fling out the pollen |
| **7.** | **Fruit** | Stinging nettle produces a small, dry, oval shaped, 1 seeded fruit (achene) that is yellow to greyish-tan. Fruits are clustered along drooping flower spikes, |
| **8.** | **Seeds** | Erect, Albumen scanty, Cotyledons rounded |

**Fig 4:** Whole Nettle Plant

## Taxonomical Description

**Table 2:** Taxonomical Description of Urtica dioica L. (14)

| | | |
|---|---|---|
| **1** | Kingdom- | Plantae - Plants |
| **2** | Subkingdom- | Tracheobionta - Vascular plants |
| **3** | Superdivision- | Spermatophyta - Seed plants |
| **4** | Division- | Magnoliophyta - Flowering plants |
| **5** | Class- | Magnoliopsida - Dicotyledons |
| **6** | Subclass- | Hamamelidae |
| **7** | Order- | Urticales |
| **8** | Family- | Urticaceae - Nettle family |
| **9** | Genus- | Urtica L. |
| **10** | Species- Urtica dioica L., - | stinging nettle P |

### Phytochemical Composition of Nettle Plant

Different factors affect the chemical composition of nettle plants, such as the variety, genotype, climate, soil, vegetative stage, harvest time, storage, processing and treatment [11-13]. Stinging nettles are a rich source of nutrients. A comprehensive proximate analysis showed that harvested upgrowths contained approximately 90% moisture, up to 3.7% proteins, 0.6% fat, 2.1% ash, 6.4% dietary fibre and 7.1% carbohydrates [10]. On the other hand, nettle leaf powders contain on average 30% proteins, 4% fats, 40% non-nitrogen compounds, 10% fibre and 15% ash. [17].

**Table 3:** Phytochemical Composition of Nettle Plant (11)

| | | |
|---|---|---|
| **1** | Moisture (%) | 7.04 ± 0.77 |
| **2** | Crude protein (%) | 33.77 ± 0.35 |
| **3** | Crude fibre (%) | 9.08 ± 0.14 |
| **4** | Crude fat (%) | 3.55 ± 0.06 |
| **5** | Total ash (%) | 16.21 ± 0.54 |
| **6** | Carbohydrate (%) | 37.39 ± 0.72 |
| **7** | Calcium (mg/100 g) | 168.77 ± 1.47 |
| **8** | Iron (mg/100 g) | 227.89 ± 0.21 |
| **9** | Tannins (%) | 0.93 ± 0.01 |
| **10** | Polyphenols (mg GAE/g) | 128.75 ± 0.21 |
| **11** | Carotenoids (µg/g, db) | 3496.67 ± 0.56 |
| **12** | Caloric value (kcal/100 g) | 307.24 ± 0.13 |

In a study of nettles by Rafajlovska *et al.*, (higher quantities of proteins were found in the leaves than in the stems and roots. The content of proteins in the leaves ranged from 16.08 ± 0.38–26.89 ± 0.39%, depending on the source of the sample. The highest protein contents in the stem and roots were 14.54 ± 0.27% and 10.89 ± 0.11%, respectively. Other studies of nettle composition have found that the plants contain a significant number of biologically-active compounds. The nettle leaves contain terpenoids, carotenoids including β-carotene, neoxanthin, violaxanthin, lutein and lycopene, fatty acids, especially palmitic, cis-9,12-linoleic and α-linolenic acids, different polyphenolic compounds, essential amino acids, chlorophyll, vitamins, tannins, carbohydrates, sterols, polysaccharides, isolectins and minerals, the most important of which is iron [8].

**Phytochemistry**

The seeds and leaves of U. dioica contain vitamins, minerals and amino acids. Chemical interest in U. dioica was stimulated by reports that they cause irritation when comes in contact with skin. The leaves of U. dioica possess sharp spines with stinging hairs that contains histamine and formic acid, which causes irritation. Many compounds were previously isolated by different researchers on U. dioica, viz., phytosterols, lignans, carotenoids, fatty acids, phenolics etc. [4].

GC-MS analysis shows the presence of 43 compounds. Fatty-acid esters (C14:0, C16:0, C18:1, C18:2, C18:3, C19:2, etc.), 9-oxononanoic, hydroxycinnamic, and vanillic acids, free fatty acids, and vanillin, eugenol, apiol, squalene, etc. made up most of the 36 identified compounds. In addition to the aforementioned 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-phenylmethyl substituents in addition to 5, 10-diethoxy-2, 3, 7, 8- tetrahydro-1H,6H- dipyrrolo[1,2-a;1′,2′-d] pyrazine (III) [12].

Amino acid analysis shows dominating presence of aspartic acid, asparagines, glutamic acid, alanine, and threonine in homeopathic matrix tincture of Urtica dioica. Histidine was also identified in the tincture, indicating that the amino acid is in bound form 19. Arginine, isoleucine and leucine dominated among the free amino acids [20].

An unusual lectin has been isolated from Urtica dioica L. rhizomes. It is a small (8.5 kDa) monomeric protein with high contents of glycine, cysteine and tryptophan 21. Aspartic acid and Alanine amino acids were isolated from the root extract 19. Polar extracts of the stinging nettle (Urtica dioica L.) roots were screened to have lignans (+)- neoolivil, (-)- secoi solariciresinol, dehydrodiconiferyl alcohol, isolariciresinol, pinoresinol, and 3, 4-divanillyltetrahydrofuran. These compounds were isolated from Urtica roots 22. Root extract of Urtica fissa isolated 8 known steroidal compounds β-silosterol, daucosterol, palamitic acid, stigmasterol, α-spinasterol, potassium nitrate, cholestrine-5, 22- enyl- 3β-alcohol, stigmasterol-3-o-β-D-glucopyranoside and phenols found in small traces only [14].

The leaves of U. dioica are being used a s herbal tea for the treatment of different ailments, such as hypertension, benign prostatic hyperplasia etc. the leaves were reported to contain caffeic acid, chlorogenic acid, high content of chlorophyll and other pigments.26 Phytochemical literature on U. dioica gave a weak indication for the presence of alkaloids, there are no reports published elsewhere [23].

The leaves of U. dioica were used in animal husbandry traditionally, various reports indicated the carotenoids and chlorophyll are used to improve full productive of animals. The traditional methods for extraction from plant material include steam distillation, Soxhlet percolation using organic solvents, perhaps these procedures have lots of disadvantages such as degradation, loss of biologically active compounds, duration etc. Sovova *et al* utilized supercritical fluid extraction using liquid CO2 in order to isolate carotenoids and chlorophyll from the leaves of U. dioica. 35 HPLC analysis of extracts resulted maximum yields of chlorophyll a, chlorophyll b, beta carotene, and lutein. This report evidenced the presence of abundant chlorophyll and beta carotene in the leaves of U. dioica. [22].

**1. In Aerial Part**

**a. Flavonoids**

Quercetin-3-O-rutinoside (rutin), kaempferol-3-O-rutinoside and isorhamnetin-3-O-glucoside, Organic acids: Caffeic acid and its esters, ferulic acid, chlorogenic, citric, fumaric and phosphoric acids (up to 1.8%) [17].

**b. Essential oil**

Carvacrol (0.30%), carvone (9.0%), naphthalene (8.9%), (E)-anethol (4.7%), hexahydrofarnesyl acetone (31.20%), α -ionone (4.04%), (E)-geranyl acetone (2.9%), (E)-β-ionone (2.8%), phytol (11.20%), ester (14.7%), free alcohol (2%), ketones (38.5%), Farnesyl acetone (1.26%) [17].

**c. Minerals and trace elements:**

Calcium (853-1050mg/ 100g), Potassium (532-613mg/100g), Magnesium (175mg/100g), Phosphorus (50-265mg/100g), Iron (2-200mg/100g), Sodium (16-58mg/100g), Sulphur, Zinc, Manganese, Copper, Nickel and Selenium [22].

**d. Vitamins**

Vitamin A (retinol), vitamin B2 (riboflavin), vitamin B5 (pantothenic acid), vitamin B9 (folic acid), vitamin K (phylloquinone) (Vitamin B & K- 0.16-0.64 mg/100 g of dried material), vitamin C (ascorbic acid) (20-60mg/100g of dried material) [17].

**e. Other constituents**

Amino acids, glucokinnins, chlorophyll (0.08-0.3 % in fresh leaves and 0.6-1 % in dry leaves), Tannin and carotenoids [17].

**2. In Root Part**

**a. Acidic polysaccharides**

Glucans, arabinogalactans and rhamnogalacturonans, Flavonoids: myricetin, quercetin, kaempferol, quercetin 3-O-rutinoside (rutin), kaempferol-3-O-rutinoside and isorhamnetin. [22].

**b. Minerals and trace elements**

Calcium, Magnesium, Zinc, Manganese and Copper.

**c. Lectins**

Urtica dioica agglutinin (UDA), consisting of a single-chain polypeptide made of 89 amino acids and rich in glycines, cysteines and tryptophans.

**d. Phytosterols**

β-sitosterol; β-sitosterol-3-O-β-glucoside, (6'-O-palmitoyl)-sitosterol-3-O-β-D-glucoside; 7β-hydroxysitosterol; 7α-hydroxysitosterol; 7βhydroxysitosterol-β-D-glucoside; 7α-hydroxysitosterol-β-glucoside; 24R-ethyl-5α-cholestane-3β,6α diol; stigmasterol, campesterol, stigmast-4-en-3-on, hecogenin, [17].

**e. Lignans:**

Neo-olivil, secoisolariciresinol, dehydrodiconiferyl alcohol, isolariciresinol, pinoresinol, and 3,4 divanillyltetrahydrofuran, Coumarins: Scopoletin.

**3. In fruits (seeds)**

**a. Fixed oil**

Saturated and unsaturated fatty acids [6.8%, 1.1%, 3.6%, 20.2%, 12.4% of lipid fraction of C16:0 (Palmitic), C18:0 (Stearic), C18:1 (Oleic), C18:2 (Linoleic), C18:3 (Linolenic)].

**b. Carotenoids**

β-carotene (61%), hydroxy-α-carotene (0.9%), lutein epoxide (13.1 %) and violaxantin (14.7%), Polysaccharides. [28].

Stinging nettle also contains 1-1.2% fat in fresh plants & 48.81% in dry plants. Lower fat content is found in the whole dry young plants (3.37%) and dry adult leaves (2.92%).

**Pharmacological Aspects**

U. dioica plant and its parts thereof are a source of traditional medicines with many important pharmacological effects. The leaf, flower, seed and root contain many types of chemical constituents like flavonoids, phenols, polysaccharides, chlorophyll, amino acids, carotenoids, lignans, lectin, minerals, tannins and vitamins. On the basis of literature and research it has reported that the nettle have various activities such as anti-oxidant, anti-diabetic, anti-inflammatory, anti-carcinogenic, analgesic, antiviral antiulcer, immune-stimulation, anti-proliferative, anti-bacterial, hepatoprotective, anti-fungal etc. In folk medicine, it is used as a purgative, diuretic, expectorant, haemostatic and vermifuge. Moreover, it is used for the treatment of rheumatism, haemorrhoids, hyperthyroidism, bronchitis, eczema, rheumatoid arthritis, hay fever, urinary tract infection, bursitis, alzheimer's, asthma, gingivitis, kidney stones, prostate enlargement and cancer. The juice is believed to stimulate the digestive system and promotes breast milk in nursing mothers. Nettle also used as hair product to control dandruff, eczema and natural colour of hair. It helps to stimulate hair growth activity [26].

**1. Anti-diabetic**

The hydroalcoholic extract of U. 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 hyperglycaemia. U. dioica leaves results in reduction in the level of blood glucose and glycated haemoglobin during streptozotocin (STZ)-induced diabetes. Hydroalcoholic extract of U. dioica leaves shows reduction in dexamethasone induced diabetes and its associated complications such as depressive like behaviour and cognitive dysfunction, hyperglycaemia, plasma corticosterone and oxidative stress. The aqueous extract of plant 250 mg/kg has shown a significant glucose lowering effect against alloxan induced diabetes in rats 32. The fructose induced insulin resistance in male rats has been shown to decrease serum glucose level on administration of hydro- alcoholic leaf extract 49. Urtica dioica has been tested for the alpha amylase inhibition activity and 60% inhibition is seen in 2 mg/ml aqueous extract of plant. Farzami *et al*., 2003, have reported the enhancement in the induction of insulin secretion by a component of U. dioica leaves extract in perfused Islets of Langerhans and its *in vivo* effects in normal and streptozotocin diabetic rats. The cold methanolic extract of leaves of Urtica dioica and Urtica pilulifera (250 mg/kg) has also shown significant antihyperglycemic effect in alloxan induced diabetes [35, 36].

**2. Antiarthritic Activity**

Methanolic extract of the root of Urtica dioica has been used as a remedy for rheumatoid arthritis due to suppression of cytokine production. Methanolic leaf extract of U. pilulifera had analysed for antiarthritic activity as it inhabits the CFA induced paw swelling, skin lesions and articular deformity by suppressing inflammatory nuclear factor NF-κB in rats [42].

**3. 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 aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin level and malonyldehyde (MDA) and also by the increase in level of superoxide dismutase (SOD) level. 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. 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 [43].

**4. Anti-inflammatory**

U. 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 7. Seed oil extract of U. dioica had a weak anti-inflammatory effect in rats, had no analgesic effects in mice and is non-toxic. At the dosage concentration of 200 and 400 mg/kg, the Methanolic extract of plant has been shown to inhibit the abdominal twitches induced by acetic acid and paw edema induced by carrageenan. On infusion of Urtica dioica leaf supplements N- Methyl- D- aspartate (NMDA) injection has been reported to show brain lesion and subsequent inflammation in wistar rats significantly reducing the nuclear factor kappa B (NF- kB) binding activity to DNA showing a significant anti-inflammatory effect 56 and this activity is also found prevalent in the ethanolic extract of Urtica fissa. The extract of Urtica dioica have been screened to have anti-inflammatory activity due to inhibition of pro-inflammatory

transcription factor NF-κB due to presence of high phenolic contents and this activity is found in ethanolic extract of U. urens due to presence of Chlorigenic acid. [37].

**5. Anti-Neoplastic activity**

Aqueous extract of U. dioica leaves were evaluated with anti-cancer activity in LNCaP treated prostrate carcinoma cell line 58. The extract shows significant reduction in LNCaP cell viability in a dose dependent manner, thus shows cytotoxic effect using MTT Assay 57. The extract has been used as complementary and alternative therapies during and after the chemotherapy treatment of cancer patients. 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). [38].

**6. Antioxidant**

The hydro-alcoholic extract of U. dioica showed positive in-vitro antioxidant activity. Ferulic acid is detected as a potential antioxidant present in the species using HPTLC. It has antioxidant, antimicrobial, antiulcer and analgesic properties. Its extract shows *in vitro* inhibition of several key inflammatory events that cause the symptoms of seasonal allergies [12].

**7. Antiarthritic Activity**

Methanolic extract of the root of Urtica dioica has been used as a remedy for rheumatoid arthritis due to suppression of cytokine production. Methanolic leaf extract of U. pilulifera had analyzed for antiarthritic activity as it inhabits the CFA induced paw swelling, skin lesions and articular deformity by suppressing inflammatory nuclear factor NF-κB in rats. [42].

**8. Antimicrobial**

Gulcin *et al*. studied antimicrobial activity of aqueous extract of U. dioica against nine different microbial (P. aeruginosa, Proteus mirabilis, E. coli, S. aureus, Citrobacter koseri, S. pneumonia, Enterobacter aerogenes, M. luteus, S. epidermidis) and one yeast species (Candida albicans). The extract exhibited antimicrobial activity against all tested microorganisms, with highest activity against S. aureus bacteria. C. albicans causes the most of the clinical yeast infections like mouth infections. The study concluded that all concentrations of the extract showed antimicrobial activity against gram-positive and gram-negative bacteria in comparison to miconazole nitrate, amoxicillin clavulanic acid, ofloxacin, and netilmicin (screened using macrodilution method). Ali *et al*. studied the methanolic extract of Sambucus ebulus and U. dioica L. for antimicrobial effect on 16 skins and wound infections isolates of methicillin resistant Staphylococcus aureus. The Methicillin Resistant S. aureus (MRSA) pathogen is a worldwide major problem and for treatment of a common infections associate with this pathogen various types of effective antibiotics are used in both hospitals and communities. The study concluded that the both extracts showed antibacterial activity against MRSA isolates and can be used as natural antimicrobial/antiseptic [41].

**9. Anti- hyperlipidemic Activity**

The plant exhibits potential antihyperlipidemic activity as it lowers the concentrations of lipids and lipoproteins in blood. The dose of 150 mg/kg of the aqueous extract when supplemented for 30 days to rats feeding on normal or high fat diet, improved the blood lipid profile. The extract resulted to decrease in total cholesterol, and decreases the ratios of low density/high density cholesterol (LDL/HDL) ratios by lowering the content of LDL and plasma total apo- protein B The dose of 100 and 300 mg/kg of the ethanolic extract of the plant has shown significant reduction in the level of total cholesterol and LDL level in hypercholesterolemic rats [40].

**10. Immunomodulatory activity:**

In this study, the immunomodulatory activities of the total flavonoid fraction and the isolated major flavonoid glycosides were investigated by *in vitro* tests. The neutrophils play the primary role as an effector or killer cell for many types of infections (Stites, 1987). Defects in neutrophil defence, particularly chemotaxis, phagocytosis and intracellular killing activity, were found to be associated with a variety of infectious complications (Lehrer *et al*. 1988). Optimal host defence against infection is understood to be the high capacity of neutrophils to respond by chemotaxis. Chemotaxis is initiated by the migration of the phagocytic cells in response to chemotactic stimuli, causing them to migrate in the direction of increasing concentration of the attractant (Wagner and Jurcic, 1991). Neutrophils can sense the chemotactic substances at nanomolar concentrations and move towards them. Zymosan is accepted as a chemoattractant agent in many *in vivo* and *in vitro* bioassays. The immune cells and mediators are directly involved in the processing of antigens, removal of microorganisms by phagocytosis, lysis of bacteria, viruses or tumour cells. Many malignant diseases are caused by a decreased number or function of immune competent cells (Wagner and Jurcic, 1991). The antitumoral activity of quercetin has been reported by the Natural Cancer Institute, indicating an increase in the life span of mice implanted with P388 leukaemia (Armand *et al*., 1988). The results of our study suggest that the immune stimulatory flavonoid glycosides may be responsible for the traditional anticancer use of the aerial parts of Urtica dioica, although the immune system has a complex structure and further *in vivo* studies using different activity pathways are needed to confirm the hypothesis [39].

**Conclusion**

In this review we conclude that the bioactive compounds isolated from the Urtica plant have been reported to show various medicinal, antiproliferative, and antimicrobial activities. 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, arthritis, Skin diseases, etc. 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 bioactive compounds isolated from the plant will help in designing new drugs and other

pharmaceutical compounds to fight against widespread diseases like cancer, arthritis, Skin diseases, etc. In addition, Urtica dioica and all its parts have a broad spectrum of activity. It has been used as a folk medicine for various ailments. Moreover, it works as a functional food. In many parts of the world, it is taken as a leafy vegetable with a variety of medical applications. Being rich in flavones, organic acids and sterols it is a potential candidate for exploring the lead molecule for various diseases.

**References**


1. Wgner H, Willer F, Kreher B. Biologically active compounds from the aqueous extract of Urtica dioica. Planta Med. 1989; 55(5):452-4.
2. Upton R. Stinging nettles leaf (Urtica dioica L.): Extraordinary vegetable medicine. J Herb. Med. 2013; 3:9-38.
3. Rafajlovska V, Kavrakovski Z, Simonovska J, Srbinoska M. Determination of protein and mineral contents in stinging nettle. Quality Life. 2013; 4(1-2):26- 30.
4. Shi A, He P, Rong A, Zhang J. Nutritional Components in the young leaves and stems of Urtica cannabina L. from inner Magnolia, Food Research and Development. 2007; 05:46.
5. Gubin KV, Hanina MA. Study of Chemical Composition of Urtica cannabina L. From Western Siberia, Chemistry of plant raw material. 2009; 2:89-92.
6. Zhang H, Guo X, Han Y, Dong N. Extraction and identification of saponins from Urtica augustifolia leaves, Chinese Journal of Food Science, 2008, 1.
7. Shilpi J, Khushbu S, Parashar A, Diksha G. A drug: Urtica dioica, Journal of Drug Discovery and Therapeutics. 2017; 5(2):17-22.
8. Kumar A, Bisht AS, Joshi S, Juyal D. Pharmacognosical and pphytochemical study of a plan Urtica parviflora Roxb- A review, Journal of Pharmacognosy aand phyto chemistry. 2017; 6(3):42-45.
9. Ji TF, Liu CH, Wang AG, Yang JB, Su YL, Yuan L, *et al*. Studies on the chemical constituents of Urtica dioica L. grown in Tibet Autonomous Region, Zhong Yao Cai. 2007; 30:662-4.
10. Ellnain-Wojtaszek M, Bylka W, Kowalewski Z. Flavanoids compounds in Urtica dioica L. Herba Pol. 1986; 32:131-7.
11. Bucar F, Britzmann B, Streit B, Weigend M. LC-PDA-MS-profiles of phenolic compounds in extracts aerial parts of Urtica species, Planta Med. 2016; 72:152.
12. Telo S, Halifeoglu I, Ozercan IH. Effect of stinging nettle (Urtica dioica L.) on antioxidant enzyme activities in rat model of mammary gland cancer, Iranian Journal of Pharmaceutical research. 2017; 16:164-170.
13. Aishan H, Baba M, Iwasaki N, Kuang H, Okuyama T. The constituents of Urtica cannabina used in uighar medicine, Pharmacological biology. 2010; 48(5):577-83.
14. Kan Y, Orhan I, Koca U, Özcelik B, Aslan S, Kartal M. Fatty Acid Profile and Antimicrobial Effect of the Seed Oils of Urtica dioica and U. pilulifera, Turkish Journal of Pharmaceutical Sciences. 2009; 6(1):21-30.
15. Korani B, Mirzapour A, Moghadamnia AA, Khafri S, Neamati N, Parsian H. The effect of Urtica dioica hydro-alcoholic extract on glycemic Inex and AMP-Activated protein Kinase levels in Diabetic Patients: A randomized single- Blind Clinical trial, Iran Red Crescent Med Journal, 2016, 19(3).
16. Akbay P, Basaran AA, Undeger U, Basaran N. *In vitro* immunomodulatory activity of flavonoid glycosides from Urtica dioica, Phytother Res. 2003; 17:34-7.
17. Asgarpanah J, Mohajerani R. Phytochemistry and Pharmacological properties of Urtica dioica L., Journal of medicinal plants research. 2012; 6(46):5714-5719.
18. Akg€ul A. Spies Science and Technology. Association Food Technology, Publ. No: 15. Ankara, Turkey, 1993.
19. Baytop T. Therapy with Plant in Turkey. Istanbul University, Faculty of Pharmacy (Second press). Nobel Medicine Bookstores, Istanbul, Turkey, 1989.
20. Wetherilt H. Isırgan Otu Yaprak Ve Tohumlarının Besleyici €ozelliklerive Antit €um €ore Etkileri. PhD Thesis, (Turkish). Hacettepe University. Graduate Institute of Health Science, Ankara, Turkey, 1989.
21. Does MP, Ng DK, Dekker HL, Peumans WJ, Houterman PM, Van Damme EJ, *et al*. Characterization of Urtica dioica agglutinin isolectins and the encoding gene family. Plant Mol Biol. 1999; 39(2):335-47.
22. Le Moal MA, Truffa-Bachi P. Urtica dioica agglutinin, a new mitogen for murine T lymphocytes: unaltered interleukin-1 production but late interleukin 2-mediated proliferation. Cell Immunol. 1988; 115(1):24-35.
23. Wagner H, Willer F, Kreher B. Biologically active compounds from the aqueous extract of Urtica dioica. Planta Med. 1989; 55(5):452-4.
24. Stinging Nettle-Urtica dioica-Montana Plant Life. Available in http://montana. plant-life.org/species/urtica_dioica.htm.
25. Bombardelli E, Morazzoni P. Urtica dioica L. Fitoterapia. 1997; 68:387-402.
26. Urtica Dioica. Available in http://findmeacure.com/2015/06/06/urtica-dioica.
27. Ji HF, Li XJ, Zhang HY. Natural products and drug discovery. Can thousands of years of ancient medical knowledge lead us to new and powerful drug combinations in the fight against cancer and dementia? EMBO Rep. 2009; 10(3):194-200.
28. Nahata A, Dixit VK. Evaluation of 5 α -reductase inhibitory activity of certain herbs useful as antiandrogens. Andrologia. 2014; 46(6):592-601.
29. Testai L, Chericoni S, Calderone V, Nencioni G, Nieri P, Morelli I, *et al*. Cardiovascular effects of Urtica dioica L. (Urticaceae) roots extracts: *in vitro* and *in vivo* pharmacological studies. J Ethnopharmacol. 2002; 81:105-9.
30. Tahri A, Yamani S, Legssyer A, Aziz M, Mekhfi H, Bnouham M, *et al*. Acute diuretic, natriuretic and hypotensive effects of a continuous perfusion of aqueous extract of Urtica dioica in the rat. J Ethnopharmacol. 2000; 73:95-100.
31. Alberte RS, Roschek WP, Li Dan. Anti-inflammatory and anti-allergic extracts from nettle. US Patent 20100009927 A1, 2010.
32. Revell C. Method and composition for the treatment of benign prostate hypertrophy and prevention of the cancer. US Patent US6482447B2, 2002.
33. Stass D. Composition for treating hair and scalp and method for preparing same. US Patent 7205009 B2, 2007.
34. Fogel D. Herbal compositions for the treatment of diabetes and/or conditions associated therewith. EP Patent 2170360 A2, 2010.
35. Qujeq D, Davary S, Moazzi Z, Mahjoub S. Effect of

Urtica dioica leaf extract on activities of nucleoside diphosphate kinase and acetyl coenzyme, a carboxylase, in normal and hyperglycemic rats. African J Pharm Pharmacol. 2011; 5(6):792-6.
36. Rahimzadeh M, Jahanshahi S, Moein S, Moein MR. Evaluation of alpha-amylase inhibition by Urtica dioica and Juglans regia extracts. Iran J Basic Med Sci. 2014; 17(6):465-9.
37. Johnson TA, Sohn J, Inman WD, Bjeldanes LF, Rayburn K. Lipophilic stinging nettle extracts possess potent anti-inflammatory activity, are not cytotoxic and may be superior to traditional tinctures for treating inflammatory disorders. Phytomedicine. 2013; 20(2):143-7.
38. Kocasli S, Demircan Z. Herbal product use by cancer patients in both the pre and post-surgery periods and during chemotherapy, African Journal Tradit. Complement Altern. Med. 2017; 14(2):325-333.
39. Akbay P, Basaran AA, Undeger U, Basaran N. *In vitro* immunomodulatory activity of flavonoid glycosides from Urtica dioica L. Phytother Res. 2003; 17(1):34-7. Doi: 10.1002/ptr.1068. PMID: 12557244.
40. Daher CF, Baroody KG, Baroody GM. Effect of Urtica dioica extract intake upon blood lipid profile in the rats, Fitoterapia. 2006; 77:183-8.
41. Gulcina I, Kufrevioglua IOOktayb M, Buyukokurogluc ME. Antioxidant, antimicrobial, antiulcer and analgesic activities of nettle (Urtica dioica L.). J Ethnopharmacol. 2004; 90:205-15.
42. Abudoleh S, Disi A, Qunaibi E, Aburjai T. Anti-Arthritic Activity of the Methanolic Leaf Extract of Urtica pilulifera L. on Albino Rats, American Journal of Pharmacology and Toxicology. 2011; 6(1):27-32.
43. Sidana J, Deswal G, Nain P, Arora K. Liver toxicity and hepatoprotective herbs, Int J Pharm Sci Rev Res. 2011; 9:121-61.