



REVIEW ARTICLE

Pharmacological Properties and Therapeutic Potential of *Urtica dioica* : A Comprehensive Review

Sharon Barachel Papang¹, Kedovilie Kuotsu¹, Sanskar Pradhan¹, Jyoti Timsina¹, Suikriti Sharma², Ananya Bhattacharjee^{3,*}

¹Himalayan Pharmacy Institute, Rangpo, Majhitar, 737136, East Sikkim, India

²Assistant Professor, Pharmacology Department, Himalayan Pharmacy Institute, Rangpo, Majhitar, 737136, East Sikkim, India

³Associate Professor, Pharmacology Department, Himalayan Pharmacy Institute, Rangpo, Majhitar, 737136, East Sikkim, India

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* Corresponding author.

Ananya Bhattacharjee
mouroland@gmail.com

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ABSTRACT

Urtica dioica, commonly known as stinging nettle, is a perennial herbaceous plant with a rich history of traditional medicinal use. This review aims to provide a comprehensive overview of its phytochemical composition, pharmacological effects, and potential therapeutic applications. A thorough analysis of existing literature reveals that *Urtica dioica* possesses a diverse array of bioactive compounds, including phenolic compounds, flavonoids, terpenoids, and lignans, which contribute to its extensive pharmacological profile. The plant's medicinal properties include antioxidant, anti-inflammatory, antimicrobial, anticancer, and cardioprotective activities, among others. Scientific studies have validated many of its traditional uses and highlighted its potential in managing conditions such as diabetes, arthritis, liver disorders, and neurodegenerative diseases. With its therapeutic versatility and low toxicity, *Urtica dioica* represents a promising candidate for further research and development in natural medicine.

Keywords: *Urtica dioica* Stinging nettle; Nettle leaf; Bichu butti; Sisnu

INTRODUCTION

Urtica dioica, commonly known as stinging nettle, is a perennial herbaceous plant belonging to the Urticaceae family. It is characterised by its stinging hairs, which can cause skin irritation upon contact. The plant is native to Europe, Asia, North Africa, and North America, thriving in moist, nutrient-rich soils across these regions.¹ Traditionally, *U. dioica* has been utilised for its nutritional and medicinal properties. Young leaves are consumed as a nutritious vegetable, rich in proteins, vitamins, and minerals. Medicinally, various parts of the plant have been employed to treat ailments such as arthritis, rheumatism, and allergic rhinitis.²

Phytochemical analysis has identified a diverse array of bioactive compounds in *U. dioica*, including phenolic compounds, flavonoids, terpenoids, and lignans. These constituents contribute to the plant's extensive pharmacological profile, which encompasses antiviral, antimicrobial, anticancer, antioxidant, anti-inflammatory, and cardioprotective activities.³

Taxonomical classification^{4,5}

- Domain – Eukarya
- Kingdom – Plantae (plants)
- Subkingdom – Tracheobionta (vascular plants)
- Superdivision – Spermatophyta (seed plants)
- Division/Phylum – Magnoliophyta/Anthophyta/Angiosperms (flowering plants)
- Class – Magliopsida (dicotyledons)
- Subclass – Hamamelidae
- Order – Urticales
- Family – Urticaceae
- Genus – *Urtica*
- Species – *Urtica dioica*

Common names

- English: stinging nettle, nettle leaf, common nettle, stinging bramble^{5,6} burning nettle, lesser nettle, or dwarf nettle⁷ big string nettle⁸ nettle, tall nettle,

- slender nettle, greater nettle⁹
- Hindi: Bichu butti
- Sanskrit: Vrishchhiyaa shaaka
- Unani: Anjuraa
- Nepal: Sisnu²
- Kumaon: Shisuun⁶
- Kashmiri: Soi¹⁰
- Garhwal: Kandali⁶
- Assamese: Chorati¹¹
- Kannada: Churachi¹¹

BOTANICAL DESCRIPTION

Urtica species is a nitrophilous perennial herbaceous plant. It can grow up to 1-2 m in height, depending on the soil conditions. They have long stoloniferous rhizomes, that are cylindrical in shape, tapering and can sometimes be branched.^{7,12} The root is irregularly twisted and appears greyish-brown in colour. It has a thickness of about 5mm and is hollow in cross section.¹² The stinging hairs are 1 mm long. It is thick at the base and tapered to such an extent that the ends appear as a fine, sharp point. The hairs are few to numerous and point the upward direction.¹³

Stem can be green, reddish or yellowish. They are erect, hollow to solid, fibrous and tough, and covered by stinging hairs and trichomes. The stem may be simple or branched, having a blunt square shape with four vertical grooves.^{7,12,13}

The soft green leaves are 3-15 cm long. The leaves are connected to the stem with a petiole, which is shorter than half of the leaf blade. They may be lobed or unlobed but are not separated into leaflets. They are simple, stipulate, opposite, serrated, oblong, or ovate. Both leaf surfaces are covered with fine trichomes: shorter simple hairs which are mixed with longer rigid hairs (the ones that sting) and with cystoliths. In the European variety (*Urtica galeopsifolia*), the stinging hairs are absent.^{7,12-14}

Flowers are small, reddish-brown to greenish-white in colour. They are radially symmetrical with a length of 1.5-20cm and 0.6-12 cm broad. They are dioecious, occurring as racemes in the axils of the upper leaves. The staminate flowers have 4-5 long tepals, 4 stamens that protrude and flat filaments. The pistillate flowers have 4 short tepals that are sparsely pubescent, esetulose, ovoid and single-celled.^{12,13}

Flowering and fruiting time is from June to October.¹⁵ The androecium is made up of four elements, surrounded by the same quantity of hairy tepals, and a vestigial pistil in the middle. The gynaecium is made up of hairy pistils covered by two pairs of unequal tepals. Pollen is released when the tepals on the staminate flowers open, allowing the inward-curved stamens to move outwards. Pollination takes place, mostly by wind.¹⁶ Pollination leads to the formation of fruits, which contain only one seed, which completely fills the fruit. The seed, either brown or olive, has an elliptical shape.⁷

Fruit is dry and does not split open when ripe (achene). The length is 1-1.4 mm, and width is 0.7-0.9 mm. The fruits

are smooth and have a very thin wall.¹²

Inflorescences is panicles, each 2-8 cm long from the upper leaf axils, the female ones are curved, whereas male ones are patent.^{7,12}

The flowers are grouped into clusters on four branching stems found in the leaf axils. The female flowers are curved, while the male flowers spread out.⁷



Fig. 1: *Urtica dioica* plant



Fig. 2: Leaf of *Urtica dioica*



Fig. 3: Labelled parts of *Urtica dioica*



Fig. 4: Flower and roots of *Urtica dioica*

Habitat

Urtica dioica grows in temperate and tropical wasteland areas around the world.¹⁴

This herb is available in many South Asian Countries. In the Indian subcontinent specifically, it is found growing in temperate and sub-tropical Himalayas, from Kashmir to Sikkim between 1200 to 3500 m above sea level. It is also found in Assam, Arunachal Pradesh and Himachal Pradesh.^{12,17}

It is also found in temperate regions like Europe (more in northern than in southern Europe), Asia, North Africa and North America (Canada, USA and Mexico with the exception of Hawaii) It is found in altitudes as high as 1800 metres.^{7,12}

In Nepal, it is known as Sisnu and is reported to be distributed in moist areas in locations with an altitude of about 500–4500 m.⁹

TRADITIONAL USES

Both the roots and flowers of the plant are eaten as a vegetable, either in soups or as a pot herb. It is also used to treat arthritis and joint pain by applying fresh leaves directly to the skin. The root paste is used for minor bone fractures and dislocations. A decoction made from the roots and seeds help with diarrhea and cough. Additionally, a curry made from young shoots is given to women during childbirth.¹⁸

PHYTOCONSTITUENT OF *URTICA DIOICA*

Various parts of the plant, including leaves, roots, seeds, and stalks, contain many important phytoconstituents that contribute to its pharmacological properties. Some are:

1. **Aerial Parts (Leaves and Stems):** It mainly contains flavonoids (quercetin, kaempferol, rutin, isorhamnetin), which possess antioxidant, anti-inflammatory, and anti-allergic property. Phenolic acids (caffeic acid, chlorogenic acid, ferulic acid) have antioxidant, neuroprotective, and hepatoprotective property. Lignans (secoisolariciresinol, matairesinol) contribute to estrogenic activity, anti-cancer, and anti-inflammatory activity. Tannins mainly contain astringent, antimicrobial, anti-diarrheal property. Terpenoids (β -sitosterol,

stigmasterol) has Anti-inflammatory, and cholesterol-lowering effect. Carotenoids (lutein, β -carotene) are important for vision protection. Vitamins (A, C, K) and minerals (iron, magnesium, calcium) provides nutritional benefits, and hematopoietic effects.

2. **Roots:** The roots are rich in Sterols (β -sitosterol, campesterol, stigmasterol) are useful for Benign prostatic hyperplasia (BPH) treatment and has an anti-inflammatory effect. Coumarins have anticoagulant, vasodilatory effects. Polysaccharides possess Immunomodulatory and anti-inflammatory effect. Lectins are known for their Anti-cancer, immune-modulating effect.
3. **Seeds:** It mainly contains Fatty acids (linoleic acid, α -linolenic acid, palmitic acid) which has its importance in Cardioprotective activity. Tocopherols (Vitamin E) mainly possess antioxidant, skin protective action. Lignans have Phytoestrogenic activity, neuroprotective effect.
4. **Flowers:** It contains flavonoids (quercetin, kaempferol), mainly has anti-allergic and antioxidant property. Essential oils (β -caryophyllene, α -pinene) possess Anti-inflammatory, antimicrobial effects.^{13,19}

PHARMACOLOGICAL ACTIVITY

Immuno-modulatory activity

The methanolic extract of *Urtica dioica* was found to have notable immunomodulatory effects. Its key compound, *Urtica dioica* agglutinin (UDA) was found to stimulate T-lymphocytes uniquely, enhancing lymphocyte growth, cytokine secretion, and reducing nitric oxide production. Flavonoids in *Urtica dioica* boost intracellular killing activity, as shown by the NBT reduction test, and influence immune cell movement (Boyden Migration Chamber). UDA also acts as a mitogen for T-cells, triggering delayed interleukin-2 proliferation while maintaining interleukin-1 levels, highlighting its potential as a natural immune booster.¹⁵

Anti-aging property

The ethanolic extract of *Urtica dioica* has antioxidant properties that help fight aging by reducing oxidative stress and free radical damage. These effects may be beneficial for age-related diseases. It also has anti-inflammatory properties that help reduce chronic inflammation, a major cause of ageing. Additionally, its haemostatic effects support skin health and tissue regeneration, making it useful for anti-ageing treatments.²⁰

Wound healing property

The methanolic extract of *Urtica dioica* helps in wound healing; bleeding, promoting cell movement and growth, fighting

bacteria, and influencing important healing pathways. By reducing inflammation and oxidative damage, the extracts create a good environment for tissue repair. Their ability to control bleeding is important for starting the healing process. They also speed up wound healing through several mechanisms, include reducing inflammation and oxidative stress, and stopping healing by helping cells grow, move, and form new blood vessels. Some studies suggest that its extracts can affect cell growth, including slowing down the growth of certain cancer cells. Additionally, they help prevent infections, which is essential for proper wound healing. *Urtica dioica* extracts also influence key biological pathways, like the TGF- β /BMP pathway, which plays a major role in healing wounds.²⁰

Hepatoprotective property

The ethanolic extract of *Urtica dioica* was found to protect the liver by reducing harmful oxidation and boosting antioxidant enzymes. It also supports the immune system and reduces inflammation, which may contribute to its liver-protecting effects. Overall, UD works in multiple ways to prevent liver damage and other related issues.²⁰

Antimicrobial activity

In a study, the evaluation of the anti-microbial activity of *Urtica dioica* on different microbial species was carried out. Cultures of the test microorganisms were prepared and incubated. 250 μ g of the water extract of *Urtica dioica* was infused into a 6 mm diameter filter paper disc. These paper discs were then placed on the cultures. The zones of growth inhibition around the discs were measured and recorded. Clear inhibition zones around the discs indicated the presence of antimicrobial activity.

Results showed that all concentrations of the extract of stinging nettle have antibacterial activity against the Gram-positive and gram-negative bacteria when compared with standard and strong antimicrobial compounds such as miconazole nitrate, amoxicillin clavulanic acid, ofloxacin, and netilmicin.²¹

Anti-allergic activity

The bioactives DL-methyl-m-tyrosine, isopropyl- β -D-thiogalactopyranoside, deoxyharringtonine 4-shogaol, piperine, 8-dehydrogingerone and phosphatidylcholine are identified in the aqueous and ethanolic (20, 40, 60 and 80%) extract of *Urtica dioica* leaves, which is responsible for the anti-rhinitis activity.

Urtica dioica extract slowed several inflammatory events that cause the symptoms of allergic rhinitis. These include- 1. the antagonist and negative agonist activity against the Histamine-1 receptor, 2. the inhibition of mast cell tryptase, 3. inhibition of Cyclooxygenase-1, Cyclooxygenase-2, and 4. hematopoietic Prostaglandin D2 synthase HPGDS inhibi-

tion.

In an in vitro study, GeneBLAzer™ H1-NFATbla HEK 293T cells were used and the effect of *Urtica* extract to H1 receptor was analysed. The extract exhibited inhibitory activity with an IC50 value of 251 μ g/mL. The positive control, tripolidine, a H1 receptor antagonist, demonstrated an IC50 value of 19 nM. Similarly, the extract inhibited tryptase with an IC50 of 172 μ g/mL, while the tryptase inhibitor protamine had an IC50 value of 103 μ M. For Cox-1 and Cox-2, the inhibitors showed IC50 values of 48 nM and 1.2 μ M, respectively, while the extract exhibited IC50 values of 160 μ g/mL and 275 μ g/mL for these enzymes.²²

Cardioprotective activity

The *Urtica dioica* aqueous extract contains phenolic compounds such as caffeic and malic acid, which are known to have antioxidant properties, scavenging abilities and lipid peroxidation stabilisation, which play a key role in protecting against ischemia-reperfusion injury.

Wistar rat hearts were used for the study. They were cannulated and perfused with Krebs solution at 37°C through the aorta. Baseline data was collected after a 20–30 minute stabilization period. The hearts then underwent 40 minutes of ischemia followed by 45 minutes of reperfusion. Damage from ischemia was assessed by comparing cardiac parameters before and after ischemia. The procedure was done for a control group and for a tested group similarly, but *Urtica dioica* extract (200 μ g/ml) was added to the Krebs solution 10 minutes before ischemia and 10 minutes after reperfusion in the tested group. Cardiac performance was similar in both the control and test groups during the baseline period but after reperfusion following ischemia, both groups experienced ischemia-reperfusion injury and a decrease in cardiac performance compared to baseline. However, the decline in cardiac performance was less in the test group compared to the control. Additionally, the test group experienced less damage and a more pronounced recovery in cardiac function. The left ventricular diastolic pressure after reperfusion was significantly lower in the test group (38.93 \pm 4.06 mm Hg) compared to the control group (51.35 \pm 2.3 mm Hg), further supporting the lower cardiac damage in the test group.²³

Nephroprotective activity

In a male rabbit model, a 95% ethanol extract of *Urtica dioica* demonstrated therapeutic efficacy against gentamicin-induced nephrotoxicity when administered at 100 mg/kg body weight per day (orally). Through the enhancement of glutathione levels and the reduction of malondialdehyde levels, the extract exhibits potent antioxidant activity. Furthermore, it aids in regulating serum creatinine and blood urea nitrogen levels.¹³

Analgesic activity

Stinging nettle, or *Urtica dioica*, has been used traditionally for various health purposes, and some research indicates it might help with pain. Essentially, studies, primarily on animals, suggest that ethanolic extract from the plant can reduce pain responses. This pain relief is likely due to the plant's natural compounds, such as flavonoids and other phenolic compounds, which can reduce inflammation, a common cause of pain.²⁴

Antiendometriosis activity

The methanol extract of the aerial parts of *Urtica dioica* demonstrated an anti-endometriosis effect in a surgery-induced endometriosis rat model at a dosage of 100 mg/kg b.wt./day body weight per day, administered orally. This effect was evidenced by a reduction in volumes, adhesion scores, adhesion levels of TNF- α , VEGF, and IL-6 IL-6, supported by histopathological outcomes findings.¹³

Antiviral activity

The water-based extract of *Urtica dioica* fresh bark effectively eliminated the Petaluma virus (FIV-Pet) that infected the Crandell feline kidney cell line (CrFK). It achieved this by inhibiting viral replication and reducing the formation of syncytia at low doses (0.5–1 g/ml) in a dose-dependent manner.¹³

Anti-inflammatory activity

Ethanolic extract of *Urtica dioica* has been shown to suppress cyclooxygenase (COX) and lipoxygenase, which stimulate pro-inflammatory mediators such as prostaglandins and leukotrienes, inhibit TNF-kappa activation in human T lymphocytes, macrophages, and epithelial cells, and lower levels of pro-inflammatory cytokines TNF- α and IL-1. Additionally, in canine articular chondrocytes, nettle leaf extract downregulated NF- κ B targets, such as COX-2 and MMPs, and reduced IL-1 β -induced NF- κ B activation. Additionally, it decreased LPS-induced NO levels in macrophages. Additionally, *U. dioica* has been shown in clinical trials to have an anti-inflammatory impact in inflammatory bowel illness and rheumatoid arthritis.²⁰

Hypotensive activity

The aqueous extract of *Urtica dioica* has been shown to exert a hypotensive effect, demonstrating a beneficial inotropic effect associated with a significant reduction in heart rate while not affecting cardiac pressure. However, blood pressure has been observed to decrease by 15% and 38%, respectively, when the aqueous extract is continuously infused intravenously at doses of 4 mg/kg/h and 24 mg/kg/h.²⁵

Antioxidant activity

Strong antioxidant qualities and ROS scavenging capabilities of *Urtica dioica* extracts, especially the polyphenol-enriched extract, can guard against oxidative stress and the cellular damage it causes. Their safety for possible usage as food additives or dietary supplements is further demonstrated by the fact that they do not cause cytotoxicity to normal human colon epithelial cells.²⁶

Diuretics and anti-urolithiatic activity

In rabbits, *Urtica dioica* (aqueous extract) exhibits both natriuretic and diuretic effects, while the potassium (K+) levels remain unchanged. Furthermore, *Urtica dioica* has demonstrated efficacy against urinary tract infections. Notably, the aerial portion (methanol extract) possesses antiurolithiatic properties, effectively suppressing elevated creatinine and calcium levels in the urine while significantly reducing calcium and oxalate deposits in the kidneys. Additionally, *Urtica dentata* (n-butanol extract) also exhibits antiurolithiatic properties, inhibits calcium oxalate deposition, and protects renal tissue from damage caused by kidney stones, as observed in a rat model.¹³

Anthelmintic activity

A study conducted in vivo demonstrated that Swiss albino mice naturally infected with *Aspicularis tetraptera* exhibited anthelmintic activity when administered a daily oral dose of a methanolic extract derived from the leaves and seeds of *Urtica dioica* (175 mg/ml).¹³

Neuroprotective activity

Neuroprotective efficacy of medicinal plants can be achieved by exhibiting various mechanisms such as antioxidant activity, inhibition of inflammation and preventing accumulation of polyubiquitinated protein aggregates in brain and enhancing protective signaling. Plant organs such as leave, stems, bark, roots, flowers, seeds and fruits has been used as alternative and complementary therapy. Medicinal herbs contain mixture of active components or phytochemicals like flavonoids, alkaloids, isoprenoids, polyphenols and tannins etc. herbs which are rich in antioxidants also have neuroprotective properties.²⁷

It has been demonstrated that ethanolic extract of *U. dioica* has provided neuroprotective activity via modulation of different inflammatory and biochemical markers (TNF- α , IL-1 β , NF-kB, GSH, CAT, etc.) and highlights the significant potential in the management of neuroinflammation.

According to numerous computational, in vitro, in vivo, and clinical investigations, *U. dioica* represents a promising herb with neuroprotective potential, especially for neurodegenerative disorders associated with diabetes and AD.²⁸

Antifungal activity

Urtica dioica ethanol extracts have demonstrated inhibitory effects on several plant pathogenic fungi, including *Rhizoctonia solani*, *Alternaria alternata*, *Fusarium oxysporum*, and *Fusarium solani*. The extracts exhibited significant efficacy against *A. alternata* and *R. solani*, suggesting their potential as natural alternatives to commercial fungicides in agricultural applications.²⁹

Another study also indicated that *U. dioica* leaf extracts have strong antifungal efficacy against diseases such as *Chaetomium globosum*, implying potential applications in ethnopharmacology.³⁰

Anticancer activity

Researchers utilised *Urtica dioica* leaf extract to biosynthesise selenium nanoparticles (SeNPs) in an environmentally friendly manner. These SeNPs exhibited significant anticancer activity against the HepG2 liver cancer cell line while demonstrating minimal cytotoxic effects on normal Vero cells, highlighting their potential for therapeutic applications.³¹

The dichloromethane extract of *U. dioica* has shown cytotoxic and apoptotic properties in MDA-MB-468 human breast adenocarcinoma cells. This indicates the extract's capability to trigger cell death in breast cancer cells, presenting a potential therapeutic option.³²

Antidiabetic activity

The extracts from *Urtica dioica* have been shown to inhibit enzymes responsible for carbohydrate breakdown, such as α -glucosidase and α -amylase. This inhibition helps to regulate blood glucose levels after meals by slowing the absorption of glucose and the digestion of carbohydrates.³³

250 mg/kg of plant aqueous extract has demonstrated a notable glucose-lowering impact against alloxan-induced rats with diabetes. It has been demonstrated that giving hydro-alcoholic leaf extract to male rats with fructose-induced insulin resistance lowers their serum glucose levels. Both normal and streptozotocin-induced diabetic rats received the leaf extract in perfused islets of Langerhans, which significantly increased insulin secretion and lowered blood sugar levels. In diabetes caused by alloxan, the cold methanolic extract of leaves (250 mg/kg) has also demonstrated a strong antihyperglycemic action.³⁴

Contradictions, comparisons and gaps in existing studies of *Urtica dioica*

Extensive research consistently identifies strong antioxidant capacity in *Urtica dioica* attributed to its flavonoids and phenolic compounds. However, comparative studies reveal that while *Urtica dioica* is potent, it is sometimes less effective than recognized antioxidants like *Murraya koenigii* (curry

leaf) or turmeric, depending on the extraction method and plant part analyzed. In some assays, nettle extracts outperformed other vegetables and standards, while in others, their activity was intermediate or lower.^{9,35}

In the context of anti-inflammatory and antimicrobial activities, *Urtica dioica* shows broad-spectrum effects. However, antimicrobial efficacy is typically less pronounced than that of standard antibiotics such as amoxicillin-clavulanic acid or ofloxacin. The effectiveness also heavily depends on the extraction solvent and assay conditions.⁹

Results regarding clinical benefits—especially for analgesic, anti-arthritic, or glycemic control actions—are inconsistent: while some small human studies and animal trials report improvements in pain and inflammation, larger or more rigorous studies often fail to replicate these benefits or find only modest effects compared to placebo. Discrepancies are likely due to differences in extract preparation, dosing, patient selection, and study endpoints.^{9,36}

Long-term safety data, as well as information on interactions with conventional drugs, use in special populations (children, pregnant women, elderly), and optimal dosing—all remain insufficiently studied.⁸

CONCLUSION

Medicinal plants have been valuable in treating various diseases at their root cause since the dawn of human civilization, often offering therapeutic benefits with minimal side effects.³⁷ *Urtica dioica* (stinging nettle) is a widely distributed medicinal plant with a rich history of traditional use and a strong phytochemical foundation. Its diverse bioactive compounds contribute to a broad range of pharmacological effects, including antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. Scientific studies have validated many of its traditional uses and highlighted its potential in managing conditions such as diabetes, arthritis, liver disorders, and neurodegenerative diseases. Given its therapeutic versatility and low toxicity, *Urtica dioica* represents a promising candidate for further research and development in natural medicine. Continued studies, particularly clinical trials, are essential to fully harness its medicinal potential and ensure its safe integration into modern healthcare.

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