WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 15, 847-863. Review Article ISSN 2277– 7105

THERAPEUTIC AND NUTRITIONAL POTENTIAL OF *URTICA DIOICA LINN*

Rawat Suman*[1], Mishra H.S.[2], Agarwal A.K.[3], Ranjna[4], Kumar A.[5]

[1,4,5]PG, [2]Lecturer, [3]Professor & HOD, L.H. State Ayurveda College, Pilibhit, Uttar Pradesh.

Article Received on
21 July 2023,

Revised on 11 August 2023,
Accepted on 01 Sept. 2023,

DOI: 10.20959/wjpr202315-29420

***Corresponding Author**
Rawat Suman
PG, Lecturer, Professor & HOD, L.H. State Ayurveda College, Pilibhit, Uttar Pradesh.
sumanjaintwal@gmail.com,

ABSTRACT

Urtica dioica Linn. is high altitude plant found in Himalayan region of India. This herb has been used as culinary delicacy in many food cultures since centuries but in last few decades, this plant has been well researched for its probable therapeutic properties. At the same time, it has a promising nutritional potential. *Ayurveda* a millennial old science of traditional medicine of India now popular world over has vague reference of *vrischikaalii* which literally means a plant inflicting pain like scorpion sting. Trichomes present on surface of almost all parts of *U. dioica* inflict scorpion sting like pain on contact with bare skin due to presence of some specific chemicals. Present paper aims at exploration of all textual references from classical texts of Ayurveda up to contemporary scientific publication to workout classical identity of this potential herb and establish this herb available in abundance in main stream therapeutics in Ayurveda.

KEYWORDS: Ayurveda, *Urtica dioica*, stinging nettle, *bicchu ghas.*

INTRODUCTION

Medicinal plants are the plants which exert medicinal therapeutic effects on human body as well as animal life. All forms of life derive their source of energy from plants. Since the dawn of human civilization, medicinal plants have been indispensable source of remedies and food for human life. Plants are essential part of traditional form of medicinal systems called Ayurveda. Plants are common source of medicines that are easily accessible, economical and free from prospective side effects. In Indian local health tradition, healers use around 2500 plant species for various health ailments.[1] According to World Health Organization reports, around 4 billion tribal people use herbal medicines for their wellbeing.[2]

In botanical name of Stinging nettle '*Urtica dioica* Linn.', term "urtica" in Latin means "to burn" and is referred to burning sensation that occurs when skin is brushed against fine hairs (trichomes) of plant. "Dioica" in Latin means "two houses" and refers to stinging nettle having male and female flowers in one plant depending on subspecies. In English word "nettle" is derived from Anglo Saxon word "noedl" which means needle referring to fine trichomes that act like hypodermic needles and inject mixture of irritant chemical substances into skin.

Urtica dioica, locally known as *bicchoo ghas* has rich ethnomedicinal history. Along with its pharmacological and therapeutic properties, it is eaten as vegetable by local folks. This plant has been accounted for various pharmacological activities like antioxidant,[3] anti-inflammatory, antiulcer,[4] anticolitis, antiviral,[5] anticancer,[6] antifungal.[4,7,8] Young leaves are cooked and eaten as nutritious potherb. Additionally, *Urtica dioica* had also been used as a source of bast fibres for textiles and is sometimes used in cosmetics. A peculiarity of this plant lies in its ability to cause various cutaneous reactions.

METHODOLOGY

To investigate therapeutic and nutritional properties of herb *urtica dioica L.* all available online databases, online and offline books were referred and consulted. Research websites and databases like Researchgate, PUBMED, SCOPUS were scrutinized for subject pertaining to pharmacological properties investigated for herb *urtica dioica L.* To evaluate and study classical aspect of *Urtica dioica L.,* if any all classical texts available in institutional library were also explored.

OBSERVATIONS

Distribution - *Urtica dioica* is native of Europe but now grows in many parts of Temperate Asia, Europe, New Zealand, North Africa (Luke sowa et al., 2017). Family of nettles (urticaceae) is a group which is commonly found in tropical and subtropical regions of both hemispheres (Vogl and Hartl 2003). In India, stinging nettle is found in Himalayas, from Pakistan to South-west China. Urtica found growing in Kashmir, Uttarakhand, Himachal and most of North Eastern hilly terrains. It is perennial herb that can be seen in moist shady woodland, thickets, mountain slopes along streams and roadsides generally in deep rich soil.

Morphology: It grows about 2 meters (6.5ft) in height. Its leaves are serrated; they have flat surfaces covered with biting villi. Leaves are pointed, 2.54-5.08 cm wide and 5.08-15.24 cm

long (sansal,2017; karakas,2003), borne oppositely along the stem. Both stems and leaves are covered with numerous stinging and non-stinging trichomes (plant hairs). Trichomes are in leaf from march to November, in flower from May to October and seeds ripen from June to October[9].Plant can be monoecious or dioecious, depending on subspecies. The tiny green or white flowers are seen in leaf axis. Fruits are small achenes and plant produces numerous seeds. Flowering season of *Urtica dioica* is between June to September (Blumenthal et. al., 2000; review of Natural Products, 2011) and seeds ripen from June to October.

Propagation - The plant can spread vegetatively with its yellow creeping rhizomes and often forming diverse colonies in wastelands and open deserted areas.

Stinging activity- Trichomes (plant hairs) present on stems and leaves of stinging nettle can cause pruritus, irritation and minute blisters on bare skin (Vogl and Hartl 2003; Lust 1983; Huxley 1992; Cronquist et al 1981). Stinging trichomes of leaves and stems have bulbous tips that break off when brushed against bare skin, revealing needle like tubes that pierce the skin. They inject mix of acetylcholine, formic acid, histamine, serotonin causing itchy, burning rash in humans and other animals that can last up to 12 hours. This defense mechanism is effective deterrent against most large herbivores, though the plant is important source of food for several butterfly species and aphids.

Fig. 1: Trichomes of *Urtica Dioica.*

Fig. 2: Nettle Leaves.

Nutritional Potential

In popular traditions, *Urtica dioica* leaves are eaten raw and blanched, gently fried or steamed in many foodstuffs such as pesto, sauces, soups, purees, cookies, gelatins and jams. Dried herb is processed for capsules, tablets, teas and other preparations. Targeted studies favored the use of *Urtica dioica* to produce curd for fresh cheese.[10] Proteins (3.7%), dietary

fibres (6.4%) and low-calorie content (45.7% Kcal/100g) offer *Urtica dioica* shoots as nutritionally valid source of vit A and C, Calcium, iron, sodium and fatty acids.[11]

Nutritional facts of cooked *Urtica.*

Contents	Daily Requirement (%)	Value
Vitamin B1 (Thiamine)	0	0.0 mg
Vitamin B3 (Niacin)	2	0.4 mg
Choline	3	17.4 mg
Vitamin B6	8	0.1 mg
Vitamin B2	12	0.2 mg
Vitamin A	67	2011.0 U
Vitamin K	416	498.6 µg
MINERALS		
Selenium	1	0.3 µg
Zinc	2	0.3 mg
Phosphorus	7	71.0 mg
Copper	8	0.1 mg
Iron	9	1.6 mg
Magnesium	14	57.0 mg
Maganese	34	0.8 mg
Calcium	37	481.0 mg
CALORIES		
Carbohydrates	2	7 gm
Fibre	24	7 gm
Protein	5	2.4 gm

Source: Nutrient optimizer, 2022; Nutrient value.org, 2022

Despite being wholesome, leaves are easily digested and high in mineral (especially in iron), vitamin C and vitamin A. *Urtica dioica* is both used as medicine as well as food in many countries including Mediterranean region and South East Asia because of its widespread habitat and conjointly exceptional biological properties. Green tea processed from leaves of *Urtica dioica* is being successfully marketed in international herbal tree markets. This tea is popularly being used to cure hay fever, diabetes, gout, and arthritis. Dried plant is also used as livestock feed. Heating or cooking fresh leaves renders them safe for consumption, which is why it can safely be eaten after cooking.

Urica dioica* vis-à-vis *Vrishikali

Vrischikaali is said to have *Tikta rasa*, *Vaatshaamaka* (SS.Su.39.7) and *Tridoshashaamaka* properties (CS.Vi.8.158). It is said to be wound cleansing *(vranshodhana)* and is used in worm infestation *(krimi nashak)*, skin diseases, poisoning, asthma *(shwas)*, cough *(kasa)*,

anaemia *(pandu)*, insanity*(unmada)*and epilepsy*(apasmara)*. Some classical references mentioned in classical texts of Ayurveda regarding *vrischikaali* have been listed below –

Formulations	Indications	References
Mahapaishaachik ghrita	*Unmada, apasmara, chaturthik jwara, grahonmada chikitsa*	CS.Ci.9.48 AH.U.6.36
Palankashaadi taila	*Apasmara*	CS.Ci.10.34
As *pradhaman nasya dravya*	*Apasmara*	CS.Ci.10.45
As *parisheka* and *paan dravya*	*Udara chikitsa*	CS.Ci.13.109 AH.Ci.15.49
Vyoshaadi ghrita	*Mritikka bhakshanjanya pandu*	CS.Ci.16.20 AH.Ci.16.37
Content of *Vidaarigandhaadi gana*	*pitta vaat nashak, gulma, angmarda, urdwa shwas* and *kaasa naashaka*	SS.Su.38.4 AH.Su.15.9
Content of *arkaadi gana*	*Kapha meda nashak, krimi kushtha nashak, vrana shodhana*	SS.Su.38.16 AH.Su.15.28
Content of *vaat shaamaka varga*		SS.Su.39.7
As a *Madhur dravya*		SS.Su.42.18
Content of *vaatnaashak kwatha*	*Vaat dhushit stanya*	AH.U.2.10
Ghrita yoga	*Mrittika bhakshanjanya roga*	AH.U.2.76
As a *gharshana dravya*	*Dantvidradhi*	AH.U.22.34

Urtica dioica is not mentioned in *Ayurvedic* literature clearly. However, a vague reference to *Vrischikaali* had been made by learned sages and *Nighantu* writers. Till date, exact identity of *Vrishchikaali* could not be established. Some Ayurvedic experts believe *vrishchikaali* is probably *Tragia involucrata*, some others consider *Urtica dioica* as potential source of *vrischikaali*. However, *vaathara* properties and *tikta rasa* of *vrischikaali* suggest *Urtica dioica* to be more appropriate source of *vrischikaali* (SS.Su.39.7, 42.11).

Therapeutic Potential

Ethnomedicinal Uses

1. *Urtica dioica* as a whole plant extract was principally used in traditional medicine of oriental Morocco as an anti- hypertensive remedy (j. ethnopharmacol., 58 (1997).
2. *Urtica dioica* is used to treat stomachache in Turkish folk medicine.[12]
3. Decoction of leaves and stalks taken in moderate quantities are used as a cure for minor skin problems. When dried, leaves are often used to relieve asthma and similar bronchial troubles by inhalation.[13]
4. Balkan countries use the leaves in form of infusion as a remedy for treatment of ailments like diarrhoea, vaginal discharge, internal and external bleeding.[14]

5. The ancient Egyptians apparently used the infusion of nettle for relief of lumbago and arthritis.[15]
6. The exceptional nutritional values of leaves were reaped by consuming them as tonic in preparation of soups, and several dishes for strengthening the body.[16-18]
7. In Indian traditional folklore, *Urtica dioica* decoction is used for treatment of eczema, nosebleeds, uterine hemorrhages.[18]
8. Fresh stinging nettle leaves were applied to arthritic joints, rheumatic disorders in a process called urtification , which is said to increase local blood flow.
9. In Venezuela, *Urtica dioica* paste was applied over Syphillis wounds, its decoction used to increase perspiration and decrease body temperature.
10. *Urtica dioica* root has been used in prostatic hyperplasia for a long time.
11. Greek doctors Pedanious Dioscorides and Galen detailed that *Urtica dioica* had diuretic and purgative properties and was helpful for treatment of asthma, pleurisy and spleen sickness.
12. The leaves decoction was utilized as weight reduction aid.[19]

Pharmacologically Active Metabolites

Pharmacological actions of the drugs may be attributed to bioactive phytochemicals / other constituents present in fruits, vegetables, grains and other plant foods that have been linked to altering / reducing risk of major chronic diseases. The most important active compounds of leaves of *Urtica dioica* are sterols (beta-sitosterol, hydroxysitosterol) and flavonoids (rutin, kaempferol, quercetin,). Moreover, leaves contain minerals (calcium, potassium), tannins, acids (salicylic acid, malic acid, caffeine acid) and amines (histamine).[20] In nettle leaves, the presence of numerous active compounds for instance caffeine acid derivatives, ceramides, nine forms of carotenoids, essential fatty acids, vitamin, phytosterols, glycosides and proteins have been confirmed.[21]

The roots of stinging nettle contain mixture of water soluble compounds, including lectins, phenolics and sterols.[22] The roots are reported to contains polysaccharides (glucans, glucogalacturonans, arabinogalactan acid) in large quantities.

Seeds and leaves of *Urtica dioica* contain minerals, vitamins and amino acids. According to determination of proximate composition minerals, amino acids, vitamins contents, results have been shown that nettle can supply 90-100% of vitamin A (including Vitamin A and beta carotene) and is good source of dietary iron, calcium, protein. In fresh or processed state

nettle has high protein, low calorie, source of essential nutrient minerals and vitamins particularly in vegetarian, diabetes or other specialized diets.[23]

Application of *Urtica dioica* in various industrial, pharmaceutical industries is due to varied number of phytochemical constituents found in the plant. High concentration of chlorogenic and 2-o caffeomalic acid are found in nettle leaves. High quantity of flavonoids and anthocyanins are present in nettle stalks. Phenolic metabolites in nettle are crucial with regards to their biological properties (antioxidant and anti -radical).[24]

Pharmacological Properties (Preclinical Studies)

Antioxidant Activity

It had been reported that ethyl acetate, water, ethanol extracts of *Urtica dioica* have antioxidant potential by using reducing power, superoxide anion scavenging, DPPH activity, metal chelating activity, scavenging of hydroxide peroxide methods (Gulcin et al, 2004; Khare et al.,2012; Ghaima et al,2003; Bourgeois et al;2016). In another study, TAS (total antioxidant status) and TOS (total oxidant status) of *Urtica dioica L.* plant were determined. TAS value of plant extract were determined 7.817±0.314 and TOS value to be 10.866±0.404 suggesting that plant extract had high antioxidant potential.[25]

Wound Healing Properties

In vivo, wound healing experiments were carried out by researchers to corroborate whether *Urtica dioica L.* extract is suitable for wound healing. Wound healing experiments in rat models were conducted. Rats were treated with two concentrations of the extract (i.e.200 and 400µg per dose). Wound closure was accelerated in U.D.L. extract treated rats. wound closure between treated and non treated wounds was satisfying significant for $p<0.001$. In control, wound persistent inflammations was apparent by macroscopic observations for several days. While no signs of inflammation could be observed in wound treated with extract from day 2. By applying the ointment wounds healed in shorter period (9-10 days) compared to control wounds that healed in 13 -15 days. This can be due to anti-inflammatory effect, enhancement of cell proliferation and migration in ointment treated wounds.[26]

Anti Microbial Properties

Extracts of *Urtica dioica L.* were tested for antibacterial activity against various gram positive and gram negative bacteria. Baccillus Subtilis IP5832, Lactobacillus plantarum, Psedomonas aerugiona and E. coli isolated from food and urine samples. Ampicillin,

erythromycin, ciprofloxacin, and gentamycin were used as positive control. The results showed that *Urtica dioica L.* has weak antimicrobial activity since MIC (minimum inhibitory control), and MBC (minimum bacterial concentration) of extract ranged from 9.05 to more than 149.93mg^{-1}.[27]

Anti Epileptic Activity

In this study anticonvulsant effect of different doses of *Urtica dioica L.* in PTZ (pentylenetetrazole) and MES (maximal electroshock) models of seizures in experimental animals were studied. *Urtica dioica L.* extract at dose level (200mg/kg) showed maximum protection against penylenetetrazole induced seizures in experimental animals. However, *Urtica dioica* extract (100mg/kg) exhibited significant increase in latency to myoclonic jerks. On other hand maximal electroshock model showed protection with *Urtica dioica* extract (200mg/kg) against tonic hind limb extension. The antioxidant *Urtica dioica* extract showed protective effect against PTZ and MEZ induced seizures exhibiting its potential use in experimental animals. The plant extract also produced significant decrease in phenobarbitone sleeping time test by decreasing the sleep latency. The onset of sleep caused by *Urtica dioica* extract suggest its central depressant activity.[28]

Various experimental observation suggest flavonoids to be responsible for antiepileptic activity, through modulatory GABA receptor - Cl^- channel complexes due to similarity with benzodiazepenes.[29,30] In present study, phytochemical screening showed presence of phenolic compounds and flavonoids as phytoconstituents.

Anti Cancerous Activities

Cytotoxic activity of *Urtica dioica L.* was widely tested by in vitro MTT assay and trypan blue viability exclusion dye assay (to evaluate the number of live cells). The cellular and molecular mechanism of toxicity were analyzed using DNA fragmentation assay, tunel test (to detect type of cell death apoptosis or necrosis), quantitative real time PCR (to quantify apoptosis and metastasis related mRNA levels), western blotting (to quantify apoptosis related levels) and flow cytometry (to analyze cell cycle distribution apoptosis).

In an animal study by Telo et al. (2017), the effects of *Urtica dioica* in N. Methyl N. nitro source induced rat models of breast cancer were investigated. Aqueous extract of *Urtica dioica* ,50g/kg powdered was added into foods of rats for 5 months. The lipid peroxidation, the antioxidant enzymatic activities and formation of mammary gland tumor was evaluated.

Urtica dioica administration decreased levels of lipid peroxidation, and increased catalase antioxidant enzymatic activity in rats affected with mammary tumors. Results demonstrated decrease in formation of breast cancer with a decrease in number of cancer masses.

Cardiovascular Activity

Study was performed on anaesthesized male wistar rats that received a continuous intravenous perfusion during 1.25 hours of an aqueous extract of aerial part *Urtica dioica* L. at low dose of 4mg/kg/h or at high dose of 24mg/kg/hr or furoseamide (control diuretic) at dose of 2mg/kg/hr. As compared to control period in each rat, the arterial blood pressure was decreased proportionally to the dose of perfusion of plant extract (15 and 38%, $p < 0.001$) respectively. These effects were accompanied by correlative increase of diuresis (11 and 84%, $p<0.001$, respectively) and natriuresis (28-143%, $p<0.001$respectively). In rats perfused by furosemide, the arterial blood pressure was decreased by28% ($p<0.001$). The diuresis and natriuresis were also increased proportionally in this case (85 and 155%, $P<0.001$ respectively) Nevertheless, the hypotensive action of *Urtica dioica* were reversible during recovery periods in about one hour with lower dose of plant extract and furosemide , while the effect of higher dose was persistent, indicating a possible side effect .As a result , an acute hypotensive action on cardiovascular system was observed .Moreover, diuretic and natriuretic effects were also observed, suggesting an action on renal function .Finally the plant extract seems to have toxic effect at higher doses.[31]

Anti Rheumatic activity

Cytokines particularly TNF (tissue necrosis factor) are major pathogenic factor in rheumatoid diseases and are elevated in synovial fluids.[32] In rheumatoid arthritis elevated activation of NF-KB has been detected in synoviocytes and endothelial cells.[33,34,35,36] In a study effect of *Urtica dioica* leaf extract on activation of NF-KB was evaluated. *Urtica dioica* extracts are used as an adjuvant remedy in RA with proven therapeutic efficacy. Previously, it was shown that *Urtica dioica* extracts inhibits the expression of several cytokines as well as eicosanoides formation in the stimulated peripheral blood cells.[37,38] study demonstrated that standardized extract of *Urtica dioica* leaves potently suppresses activation of NF-KB in response to several stimuli by inhibiting the proteolytic degradation of its inhibitor IKB-α.[39] Another transcription factor which has been implicated in pathogenesis of RA is activator protein 1 (AP-1). It is suggested that AP-1 activation may be responsible for synovial hyperplasia in rheumatoid arthritis. *Urtica dioica* extracts exerted inhibitory effect on activation of AP-

1.[40,41] It clearly suggests that antirheumatic effect of *Urtica dioica* extract may be attributed to its ability to inhibit proinflammatory transcription factors.

Cholesterol Lowering Activity

Male rats were fed on high cholesterol diet (10ml/kg) for four weeks followed by administration of *Urtica dioica* extract (100 or 300mg) or 10mg/kg lovastatin supplementation to study the hypocholesterolemic effects of *Urtica dioica* on plasma lipid levels, hepatic enzyme activities and liver histopathological changes. It was found that *Urtica dioica* extract at 100mg/kg and 300mg/kg significantly reduced the levels of total cholesterol (TC), and low density lipoprotein cholesterol (LDL-C), and also markedly reduced liver enzymes and weight in animals with increased cholesterol diet. Hematoxylin and eosin staining showed that in the 100mg/kg extract of *Urtica dioica* group, the appearance of liver cells was similar to control group, the steatosis and inflammation were not found. In the 300mg/kg extract of *Urtica dioica* group mild steatosis was observed but mononuclear inflammatory infiltration was not found.[42] A hypercholesterolemic diet causes an increase in oxidative in the liver, resulted in increase in ALT and AST activities, inducing fatty liver. Anti inflammatory effects and antioxidative effects of *Urtica dioica* extract had already been documented in multiple studies before. These properties might aid in hepatoprotective nature of *Urtica dioica* extract. Muergo et al, has explained several mechanisms about cholesterol reducing activity of plant sterols. It was reported that plant sterols which are structurally similar to cholesterol could displace cholesterol from mixed micelle, since they are more hydrophobic than cholesterol. This replacement causes reduction in micellar cholesterol concentration and consequently decrease in cholesterol absorption.[43]Thus it is possible that *Urtica dioica* extract could decrease storage of cholesterol through this mechanism. However, further studies are needed to establish the exact mechanism.

Anti Leishmaniasis activity

Neglected parasitic diseases (NTD) like cutaneous leishmaniasis (CL) are responsible for causing high mortality and morbidity rates in developing countries. This disease is one of the most important opportunistic infection in HIV infected individuals. The inhibitory concentration (IC50), cytotoxic concentration (CC50) and effective concentration (EC50) of *Urtica dioica* extract were assessed in order to determine its anti- leshmanial activity. results demonstrated optimal concentration of extract for reducing the promastigotes and amastigotes growth were 3500 and 6000µg/ml respectively. These doses killed half of both forms of

parasite. Results indicated that the extract has a potent action against Leishmaniasis major promastigotes and amastigotes via modulation of immune responses, having no toxicity for host macrophages.

The efficacy of *Urtica dioica* extract was determined for the treatment of mice infected with Leishmaniasis Major. After treatment with *Urtica dioica* extract, all the treatment groups showed remarkably smaller C.L. lesions in comparison with untreated group and other control group. It was established that the aqueous extract treatment considerably reduced the Leishmaniasis Major replication and effectively killed them.[44]

Antiageing and Antioxidant Activity

Nettle extracts are being used in cosmetics because of its rejuvenating effect on skin health. Using an experimental design approach and a clustering analysis, a link between phytochemical constituents of *Urtica dioica* extract and their biological activities were established. The analysis showed anti-aging potential of *Urtica dioica* extract by inhibition of enzyme activities such as elastase and collagenase. Enzymes elastase and collagenase are responsible for loss of skin elasticity leading to wrinkles.[45] Among molecules present in *Urtica dioica* extract, urosolic acid and quercetin are most interesting for development of antiaging potential.[46] Urosolic acid mainly accumulated in roots is well known elastase inhibitor.[47] whereas quercetin mainly accumulated in leaves is prominent antioxidant.[48] The deduced antiaging models predicting the inhibitory effect of each extract on collagenase and elastase activities were confident and statistically significant.

Hepatoprotective Activity

30 Adult male wistar albino rats were divided into three groups sham group (Gp1), control group (Gp 2) and *Urtica dioica* group (Gp 3). All rats were exposed to hepatic ischemia for 60 min, followed by 60 min of reperfusion. In group 2, a total of 2ml/kg 0.9% saline solution was given intraperitoneally. in Group 3, a total of 2ml/kg *Urtica dioica* was given intraperitoneally. At the end of procedure, liver tissues and blood samples were taken from all rats. Serum aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, ceruloplasmin, catalase, paraoxonase, arylesterase and lipid hyperoxide levels were measured. Liver tissue histopathologies were evaluated by light microscopy.

As a result, the study found serum aspartate aminotransferase, alanine aminotransferase and lactate dehydrogenase levels were significantly higher in Group 2 than in Group 1 and

significantly lower Group 3 than Group 2. Also, Group 2 had higher serum lipid hyperoxides and ceruloplasmin levels but lower catalase, paraoxonase and arylesterase levels than Group 1. In group 3, serum lipid hyperoxides and ceruloplasmin levels were significantly lower and catalase, paraoxonase and arylesterase levels were higher in than those in group 2. Histopathological examination showed that liver tissue damage was significantly decreased in Group 3 as compared to Group 2. All the results showed that *Urtica dioica* has protective action on liver in hepatic ischemia reperfusion injured rats.[49]

Clinical Studies

Antidiabetic Activity of *Urtica Dioica L.*

Aqueous extract of nettle showed strong glucose lowering effect and the results indicate that it promotes intestinal glucose absorption.[50] leaves extract of *Urtica dioica L.* showed increase in FIRI, blood glucose and insulin, decrease in lepin and no effect on HDL,LDL,LDL/HDL ratio, VLDL, ALP and ALT. Decrease in serum glucose, insulin, LDL,HDL,LDL/HDL ratio VLDL,ALP and ALT .Increase in serum TG,VLDL and AST.[51] *Urtica dioica L.* leaves extract increase insulin secretion α amylase and α glucosidase inhibitory activity, reduction in intestinal glucose absorption and enhancement of insulin secretion by Langerhans, proliferation of β cells, protective activities of β cells of langerhans, enhancing glucose utilization.[52-56]

Treatment of Benign Prostate Hypertrophy Using *Urtica Dioica* L.

Urtica dioica L. root contains sterols, flavonoids, tannins, acids, minerals, lectin, polysaccharides, ceramides, mono-terpenoids, fatty triterpene and phenylpropane. These phytochemical constituents inhibit prostate growth, inhibit the connection of sex hormone binding globulin, inhibits TNFα activity, has anti-inflammatory and anti-proliferative action.

Clinical trials suggest benefit of stinging nettle extract for men with milder forms of BPH.[57,58] The effectiveness of root extract (600mg,2 times per day,120 weeks) was demonstrated in the multicenter study of 4051 patients in various stages of BPH.[59] Friesen reported the results in multicenter long term study of 4980 patients who received nettle extract for 224 days on average, at doses 600mg twice per day for three months then 600mg daily during remaining time.[58] The extract improved urinary symptoms associated with BPH in 78% of patients after three months and 91% patients after six months. The diurinal and nocturnal urinary frequency as well as mean urine output improved. Nettle root can be used for 6-12months as its long term use is possible without any serious adverse effects.[61]

CONCLUSION

Vachaspatyam is modern Sanskrit dictionary written in 19th century by *Vachaspati Taranath Bhattacharya ji.* Description as given in *vachaspatyam* clearly defines *vrischikaali* as a medicinal plant that causes *vrischika damsha vedna* (scorpion bite like pain sensation) when bare skin is brushed against the plant, *Urtica dioica* is one such herb that causes stinging sensation when fresh leaves are touched by skin. As stated by eminent scholars of *Ayurveda,* other probable sources of *vrischikaali* like *Tragia involucarata, Girardia hetrophylla, Pergularia extensa* does not possess stinging activity as implied by the etymological derivation of *vrischikaali* or its English name stinging nettle. Therefore, these plants should not be considered probable source of classical drug *vrischikaali.*

Ethnomedicinal claims suggest use of *urtica dioica* infusion in lumbago and Arthritis (Namazi N et.al. 2012) and *vrischikaali* is mentioned as *vaatasamshaman varga* (SS.Su.39.7) in Ayurvedic classical texts. In local health tradition, Balkan countries use the leaves in form of infusion as a remedy for treatment of diarrhoea, vaginal discharge, internal and external bleeding. (Shabani M. et al 2015) and *vrischikaali* has been mentioned as having *raktapittahara* property in *Raja Nighantu*.[62] Keeping some of these references in mind it can be safely deduced that *vrischikaali* mentioned in classical *Ayurvedic* texts can be *Urtica dioica* Linn.

Natural products based medicines are basis of synthetic chemicals based pharmaceutical industry. Approximately 70,000 species of plants are used in modern and traditional medicine systems. Still various plants in nature are underutilized and limited to tribal population, are in need of exploration.

Present review is an attempt to consolidate all available literature regarding phytochemical, pre-clinical, clinical studies regarding *Urtica dioica* from various databases. Most of therapeutic potential of *Urtica dioica* seem to derive from its rich antioxidant property. However, most of the studies stated in this review are pre- clinical studies, in which various extracts of *Urtica dioica* have been tested for its varied therapeutic potential. More such clinical studies and targeted studies are needed to generate robust empirical evidence which can be used to promote better physical health in general population.

REFERENCES

1. Zaved T.,Riaz S.,Uzair M. et.al.Biological activity of *Terminalia arjuna* on human pathogenic microorganisms.Pakistan journal of pharmaceutical Research, 2016; 02: 23-27.
2. Eswarappa R.S.,Subramaiyah Y.L.,Austin R.S.et al.Antioxidant Activities of leaf galls extracts of *Terminalia chebula* (gaertn.) retz.(combretaceae).Acta Sci. pol. Technol. Ailment, 2015; 14(2): 97-105.
3. Mavi A,Terzi Z,Ozgen U,Yildrim A,Coksun M. Antioxidant properties of some medicinal plants .Biol Pharm Bull, 2004; 7: 702-5.
4. Miraj S,Kiani S. Der Pharm Lett., 2016; 229-37.
5. Krystofova O, Adam V, Babula P, Zehnalek J, Beklovs M, Havel L et al. Effects of various doses of selenite on stinging nettle (Urtica dioica L).Int J Health Res Public Health, 2010; 7: 3804-15.
6. Miraj S,Kiani S.Der Pharm Lett., 2016; 166-169.
7. Miraj S,Kiani S.Der Pharm Lett., 2016; 135-138.
8. Keivani S,Miraj S.Der Pharm Lett., 2016; 102-6.
9. J. Asgarpanah, R. Mohajerami, Phytochemistry and pharmacological properties of *Urtica dioica* L, J.Medicin. Plant. Res., 2012; 46: 5714-5719.
10. Law B.A., Tamine A.I., Technology of cheese making 2nd ed.; Wiley Blackwell: London,UK, 2010; 512.
11. Rutto L.K.; Xu,Y.; Ramirez E; Brandt M., Mineral Properties and dietary value of raw and processed stinging nettle (*Urtica dioica* L.) int. J. Food Sci., 2013; 857120.
12. Yildrim N, Turkoglu S, Ince O, Ince M. Cell Mol Biol Sci., 2012; 1882-8.
13. Aktas C, Erboga M, Fidano Erboga Z, Bozdemir Donmez Y, Topeu B, Gurel A. Andrologia, 2016.
14. Shabani M, Miraj S, Rafieian-kohpayei M, Namjoo A.R., Adv Biomed Re, 2015; 4.
15. Namazi N, Tarighat A, Bahrami A. Pak J Biol Sci., 2012; 15(2): 98.
16. Cetinus E, Kiline M, Inanc F, Kurutas EB, Buzkan N. J Exp Med., 2005; 205(3): 215-21.
17. Simancas B, Juvay M, Cotado A, Munne-Bosch S.J.Photochem. Photobiol., 2016; 156: 22-8.
18. Irgin C, Corekci B, Ozan F, Halicioglu K, Topas O, Yildrim AB. Arch Oral Biol., 2016; 69: 13-8.

19. Schackebaei D, Godini A, Abolghazi M, Majnouni M, Hesari M. Protection of ischemic and reperfused rat heart by aqueous extract of *Urtica dioica* .Iran Cardiovasc Res J, 2010; 4: 107-11.
20. All kangari. O vitalone A, what do we know about phytotherapy of Benign prostate hyperplasia Endocrinol. Metab. Clin.N.Am, 1994; 4: 798-807.
21. N.D.Virgilioa, E.G.Parazogloub, Z. janakauskienec, S.D. Lonardo, M.Praczyke. The potential of stinging nettle (*Urtica dioica L.*) as a crop with multiple uses. Ind Crops Prohad, 2015; 68: 42-49.
22. Fagelman E.; Lowe, F.C., Herbal medications in treatment of benign prostate hyperplasia .Urol.clin.N.Am, 2002; 29.
23. L.K.Rutto,Y.Xu, E. ramirez , M. Brandt, mineral properties and dietary value of raw and processed Stinging nettle (*Urtica dioica* L.). int. J. Food. Sci., 2013.
24. P. Pinelli, F. Leri, P. vignolini, L. bacci, S. Baronti, A. Romain, Extraction and HPLC analysis of phenolic compounds in leaves, stalks, and textile fibres of *Urtica dioica* L.,J. Agric. Food. Chem, 2008; 56: 9127-9132.
25. Mohammed FS, Uysal et al total antioxidant and oxidant status of *Urtica dioica* (nettle). Kadirli uygulamani Buimer Dergisi, 2021; 1(12): 109-115.
26. Kasouni A. chatimitakos T, Stalikas C, et al. The unexplored wound healing activity of *Urtica dioica linn.* extract: an in vitro and in vivo study. Molecules, 2021; 26: 6248.
27. Kukrić ZZ, Topalić-Trivunović LN, Kukavica BM, Matoš SB, Pavičić SS, Boroja MM, Savić AV. Characterization of antioxidant and antimicrobial activities of nettle leaves (Urtica dioica L.). Acta periodica technologica, 2012; (43): 257-72.
28. Loshali A, Joshi BC, Sundriyal A. et al.Antiepileptic effects of antioxidant potent extract from *Urtica dioica* L. root on petylenetetrazole and maximal electroshock induced seizure model.Heliyon, 2021; 7: e06195.
29. Choudhary N., Bijjen K.R., Kalia A.N. Antiepileptic potential of flavonoids fraction from the leaves of Anisomelles Malabarica, J. Ethnopharmacol, 2011; 135(2): 238-242.
30. H.G.Park, S.Y.Yoon, J.Y.Choi, G.S.Loer, J.H.Choi, C.Y.Shin et al., Anticonvulsant effect of wogonin isolated from Scutella riabaicalensis, Eur. J. Pharmacol, 2007; 574(3).: 112-19.
31. Tahri A.,yamani S.,et al.; Acute Antidiuretic, natriceutical and hypotensive effects of a continuous perfusion of aqueous extract of *Urtica dioica* in rat, Journal of ethnopharmacology, Nov 2000; 73: 1-2: 95-100.
32. Elliot M.J. t, Maini R.N., Feldmann M., Kalden J.R., et al., Lancet, 1994; 1105-1110.

33. Handel M.L., Mc morrow L.B. et al., 1995; 38: 583-591.
34. Marok R., Winyard P.G. et al., Arthritis Rheum., 1996; 39: 583-591.
35. Fujisawa K., Aono H., Hasunuma T. et al., Arthiritis Rheum, 1996; 39: 197-203.
36. Miyazawa K., Mori A. et al., Am. J. Pathol, 1998; 152: 793-803.
37. Obertretis O., Ruttkowski T., Teucher T. et al. Arzheim-forsch /Drug Res., 1996; 46: 389-394.
38. Teucher T., Obertretis B., Ruttkowski T. et al. Arzneim-Forsch/Drug Res., 1996; 46: 906-910.
39. Riehemann k, Behnke B, Schulze Osthoff K, plant extracts from stinging nettle (*Urtica dioica*), an antirheumatic remedy, inhibits the proinflammatory transcription factor NF-KB. FEBS letters, 1998; 442(1): 89-94.
40. Asahara H., Fujisawa K. et al., Arthritis Rheum., 1997; 40: 912-918.
41. Shiozawa S., Shimizu K., Tanaka K., Hino.K., J.Clin.invest, 1997; 99: 1210-1216.
42. Nassiri ASL, Zaman soltani , Abbasie ,et al., Effects of *Urtica dioica* extract on lipid profile in cholestrolemic rats, J.Chin.Inter.Med, 2009; 7(5): 428-433.
43. Merguo S, Higashi K, Hase T, Honda Y, Otsuka et al., Solubilization of phytosterols in diacylglycerol versus triacylglyecerol improves the serum cholesterol lowering effect Eur. J.Clin.Nut., 2001; 55(7): 513-517.
44. Badirzadeha, heidari-Kharaji M, Faleh omraniv et al.,Antileishmanial activity of *Urtica dioica* L. against zoonotic cutaneous Leishmaniais PLOS. Neglected Tropical Disease, 2020; 14(1): e0007853.
45. Witte haute J., Mackle S., et al Inhibitory effects of polyphenols from grape pomace extract on collagenase and elastase activity, Fitoterapia, march, 2015; 101: 179-187.
46. Otles S., Yalcim,B. Phenolic compounds analysis of root, stalk and leaves of nettle, Sci. World Journal, 2012; 1-12.
47. Ying Q-L, Rine hart A.R., Simon S.R., Cheronis J.C. Inhibition of human leucocytes elastase by urosolic site for pentacyclic triterpenes , Biochemical Journal.Vol 277,issue 2, 1991; 521-526.
48. Boots A.W., Wilms L.C., et al. In vitro and ex vivo anti-inflammatory activity of quercetin in healthy volunteers, Nutrition, 2008; 24: 703-710.
49. Kandis H, Karapolat S, Yildirim U et al. Effects of *Urtica dioica* on hepatic ischemia reperfusion injury in rats .clinics, 2010; 65(12): 1357-1361.
50. Goodarzi MT, Jamshid K, Panah M.H) Antidiabetes effects of the aqueous extract of *Urtica dioica* on high fructose fed rats, 2011; 44: S334.

51. Ahangarpour A, mohm.M,Dianat M. Antidiabetic effect of hydro alcohol *Urtica dioica* leaf extract in male rats with fructose induced insulin resistance, 2012; 37: 181-186.
52. Sasan TA, Goodarzi MT, Jamshid K, Panah M.H. Antidiabetes effects of the aqueous extract of *Urtica dioica* on high fructose fed rats, 2011; 44: S334.
53. Domola MS, Vu V, Robson Doucette CA, Sweeney G, Wheeler MB. Insulin Mimetics in U.D: Structural and computation analysis of *Urtica dioica* extract, 2010; 24(2): S175-182.
54. Bnouham M, Meshfour Fz, Ziyyat A, Aziz M, Lessyer A, et al Antidiabetic effect of some medicinal plant of Oriental Morrocco in neonatal non insulin dependent DM rats, Hum. Exp. Toxicol, 2010; 29: 865-871.
55. Golaipur MJ,Ghafari S,Kouri V,Kestkar AA. Proliferation of beta cells of pancreas in Diabetic rats treated with *Urtica dioica*.Int.J.Morphol, 2010; 28: 399-404.
56. Fazeli SA,Ghravvi AM,Ghafari S,Jahan Shahi M,Golalipur MJ Effects of *Urtica dioica* on CA3 hippocampal pyramidal cell loss in young diabetic rats. Neur. Regen.Res., 2010; 901-905.
57. Volobel H;Herzog R;Rutishauser G;Kreis H.Results of study on effectiveness of ERU(extraction radiculis urticae) capsules in conservative treatment of Benign Prostate Hyperplasia.Urologe.A, 2010; 1985: 24,49-51.
58. Koch E; Biber A, Parmakologische Wirkungen Von Sabat and Urtikae extrakten als Gundlage fur eine rationale medikamentose therapie der benignen prostahyperplasic. urologe B, 1994; 34: 95-100.
59. Stahl H.P,Die Therapie Prostischer Nykturie.Z.Fur Algemeine Med, 1984; 60: 128-132.
60. Freisen A,Statistiche Analyse einer Multi zentre-Langzeitstudie Mit ERP,Benigne prostate hyperplasie II.j.Klin.Exp.Uraz, 1988; 19: 121-130.
61. Dhouibi,R;Affes,H;Ben salem,Hammami S;Sahnoun Z; Screening of pharmacological uses of *Urtica dioica* and other benefits .Prog. Biophys.Mol.Biol., 2020; 150: 67-77.
62. Tripathi I.,1st edition, *Rajanighantu* by Pt.Narhari, Dravyaguna prakaashika (Hindi commentory),Varanasi, krishnadas Academy, 1982; 273.