Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2022; 11(3): 169-173
Received: 12-02-2022
Accepted: 20-04-2022

Niraj Giri Goswami
Devsthali Vidyapeeth College of Pharmacy, Rudrapur, Uttarakhand, India

Manju Koli
Assistant Professor, Department of Pharmacy, Invertis, Bareilly, Uttar Pradesh, India

Anil Singh
Devsthali Vidyapeeth, College of Pharmacy, Uttarakhand, India

Deepak Giri
DSB Campus, Kumaon University, Nainital, Uttarakhand, India

Corresponding Author:
Niraj Giri Goswami
Devsthali Vidyapeeth College of Pharmacy, Rudrapur, Uttarakhand, India

Urtica dioica: An undervalued herb a comprehensive review

Niraj Giri Goswami, Manju Koli, Anil Singh and Deepak Giri

Abstract
Urtica dioica is a perennial plant which grows on distributed sites, in garden or in the forests. The herb has a very large history of medicinal usage. The subtropical and tropical regions were the area in which the stinging nettle was most applied as a remedy for curing a variety of diseases. A variety of chemicals such as agglutinins, carotenoids, flavonoids, lignans, terpenoids and phenolic compounds were isolated from the herb. The active ingredients and metabolite extracted from the plant are found to have a variety of pharmacological action. It is a clear estimation that the future is showing interest in the use of natural products and therapies. Many studies showed that the plant and its active constituents possess several pharmacological activities such as anti-inflammatory, hypoglycaemic and anti-oxidative activities. A comprehensive analysis is needed to provide more information and facts about this undervalued herb. This review will provide detailed information on *Urtica dioica* plant and its various pharmacological uses. This review also consists of collection of various case studies conducted in different parts of the world which can be beneficial for the scientists working on this plant. This review provides detailed data of chemical ingredients and their pharmacological actions which could bring new drug with a lot more potential.

Keywords: Stinging nettle, herbs, medicinal use, case study, anti-inflammatory

Introduction
Stinging nettle is a unique plant having various medicinal uses. Apart from its medical application it was also used in textile industries before the introduction of cotton. In the 19th century, Europe cultivated stinging nettle until the 2nd world war. During the world wars alternative for cotton was taken up as the fibre nettle. Industries were set up in European countries such as Germany and Austria [1]. However the industries could not grow well and were completely destroyed during the 2nd world war. Medicinal plants having the quality to cure and treat the illness provides an opportunity to take one more step ahead in the human welfare and healthcare programs. *Urtica dioica* (stinging nettle) is a special medicinal flowering plant with stinging hair. It belongs to the family Urticaceae (Genus–Urtica L; class–dicotyledons) [2]. It is found abundantly in colder regions such as Europe, Asia, North America and some parts of North Africa [3]. Stinging Nettle blooms well between the month of June and September in a nitrogen –rich soil [4].

Nomenclature [5]

Kingdom: Plantae	Division: Magnoliopsida
Sub-division: Spermatophytina	Class: Magnoliopsida
Order: Urticales	Family: Urticaceae
Genus: Urtica	Species: dioica
English name: Stinging nettle	Vernacular name: Sisun

History
The Stinging Nettle was well known from ancient period. Greeks very well knew about the clinical effect of the herb. Dioscorides describes it as diuretic, anti-tussive, tonic, digestive and wound healing aid [7]. He was the first person to describe the plant in his book. Some used it in styptic and cough while some used the herb as a material in contradiction of lung disease like tuberculosis and insomnia [8]. Greek physician such as Dioscorides in 1st century C.E and Galen testified the shoot has laxative and diuretic properties [9]. They stated that it was beneficial for asthma [10], pleurisy [11], and help in treating spleen associated ailment [12].
Germany-The nettle herb is used in German Homeopathy for the cure of Urticaria, herpes, eczema, and joint pain. Germany has licensed the nettle herb as a reference for herbal tea as antidiuretic drug [13].

Africa- Africans used in the treatment of nose bleeding, burns, extreme menstruation cramps and haemorrhage. [14].
India- the Indian Ayurvedic Pharmacopoeia has listed nettle's use in uterine haemorrhage, infantile, nose bleeding, cutaneous eruptions and psychogenic eczema. Dose- 2 to 4gm or 3 to 4ml of fluid extracts [15].
North America- Stinging nettle is also recognized as Aboriginal medicine [16]. They used as it as an anti- rheumatic drug. It is taken as muscle relieving agent during child birth.
United State- USA used the nettle herb in various dietary supplements. The herb extract was given to women during pregnancy and lactation. They also introduced herbal tonic for the treatment of allergic conditions like hay-fever and other allergies. The herb was used as clotting agent during civil war [17].

Chemical constituent
Urtica dioica consists of carotenoids, vitamins and minerals such As, Cd, Fe, Mg, Zn, Mn and Pb. The leaves of the Nettle plants comprise 1-2% flavonoids which are mainly Glycosides and Rutosides of Kaemferol, Quercetin and Isohamnetin. The medicinal plants contain water –soluble silicates in a large quantity. Seeds are rich in Linoleic acid while leaves consist of alpha-Linoleic acid as the predominant fatty acids [18].
Urtica dioica venom [19]: Tiny hollow hairs (trichomes) cover the stinging nettle [20]. On brushing against them, the fragile silica tips breaks of the hairs and they act like needles, piercing the skin which cause the nettle's venom to be injected [21]. Other constituents found in the plant include protein, fats, chlorophyll, and small amount of formic acid, serotonin, leukotrienes, acetylcholine and few nicotine particles [22].

Fig 1: *Urtica dioica* plant

Pharmacology (*In-vitro*)
Nettle leaf is considered to show various pharmacological activities. In –vitro studies were further conducted to examine the different activity of *Urtica dioica* plant [23].

Anti –inflammatory activity
The extract (IDS23, Rheuma-Hek) of nettle leaf and it's phenolic constituents were tested for their inhibitory capacity on biosynthesis of arachidonic acid metabolites by rat granulocytes (RBC -1 cell) [24]. Partial inhibitory effects were seen on the leukotrienes B4 synthesis (5 –lipoxygenase) by the isolated malic acid and the nettle leaf extract [25]. It was studied that the phenolic components exhibited diverse enzymatic target than the leaf extract (IDS23) [26]. The extract IDS23, reduced Lipopolysaccharide (LPS) stimulated release of two inflammatory cytokines- interleukin -1beta and tumour necrosis factor –alpha (TNF-alpha) in healthy human blood. Concentration of TNF –alpha was decreased by 50.8% and interleukin –concentration by 99.7% after 24 hours of administration. The extract stimulation IL-6 in the absence of Lipo-polysaccharide [27]. A test was done where 20 healthy volunteers ingested two capsules of IDS -23 (containing Nettle leaf extract) for 21 days. The Lipopolysaccharide stimulated TNFα, IL-1β, IL-6 concentrations were measured before and after 21 days [28].

Result
The stages of TNFα, TL-1 β, IL-4, IL-6 or IL-10 showed no effect as they were below detection. However, a reduction in lipopolysaccharide stimulated TNF release and interleukin-1 beta release was observed [29].

Immuno- modulatory activity
After conducting experiments, it was found out that the dried extract of Nettle (IDS 23) resulted in inhibition of lipopolysaccharide stimulated monocyte cytokine expression which indicates an immune-modulating outcome. It was concluded that the IDS23 might prevent the inflammatory barrier in autoimmune diseases like Rheumatoid arthritis. Other outcomes also exhibited the oppressive effect of IDS 30 on the human myeloid dendritic cells [30].

Inhibition of platelet aggression
Different extracts of *Urtica dioica* leaves were taken and investigated for platelet accumulation. Rat's Thrombocytes were made ready and incubated using distinct composition of the dried extracts and were introduced to agonist such as Thrombin (0.5micron/ml), Epinephrine (100 micron), ADP (10 micron) and Collagen (5mg/ml). Platelet aggregation induced by Thrombin was inhibited by the crude aqueous extract. Flavonoids extracted from the nettle leaves indicated a stress inhibitory effect on the thrombin produced platelet accumulation. These isolated flavonoids also obstructed platelet accumulation produced by collagen, ADP and epinephrine [31].
Conclusion-*Urtica dioica* shows an anti-platelet property in which flavonoids are primarily involved. The result supported conventional use of *Urtica dioica* in the management of CVS disease.

Inhibition on adenosine de-aminase activity
A substantial inhibition of adenosine de-aminase activity in prostate tissue was noticed on application of *Urtica dioica* extract.

Procedure: Some patients having prostate cancer were taken. Prostate tissues were used for the study purpose from these patients. Adenosine de-aminase (ADA) events with and without cultivation of different amount of *Urtica dioica* extracts were carried out.

Outcomes: ADA (adenosine deaminase) inhibition was observed on introduction to *Urtica dioica* extract. The inhibition can be beneficial for the patients having prostate cancer [32].

Pharmacology (*In-vivo*)
Hypoglycaemic effect
Method: Using TLC (thin layer chromatography) the water extract of *Urtica dioica* leaves was purified using different

concentration of solvent to get fragments for advanced studies. A solvent having a combination of water/isopropanol (30/70%) was found most acceptable for inceptive dissociation. Diabetic rats were taken for the study. It was found that the F1 i.e. fraction 1, increases the insulin amount into the blood serum. On conducting In-vivo studies it was observed that not only rise in insulin level of blood serum was detected in rats but a concurrent reduction of blood sugar was identified. When performed the test for glucose, the rise in insulin was 6 times during 120 minutes [33].
Conclusion: It was assumed that F1 was the active constituent in the IDS 23 dried extract and showed blood lowering effect caused by the development of insulin secreted by Langerhans Islets.

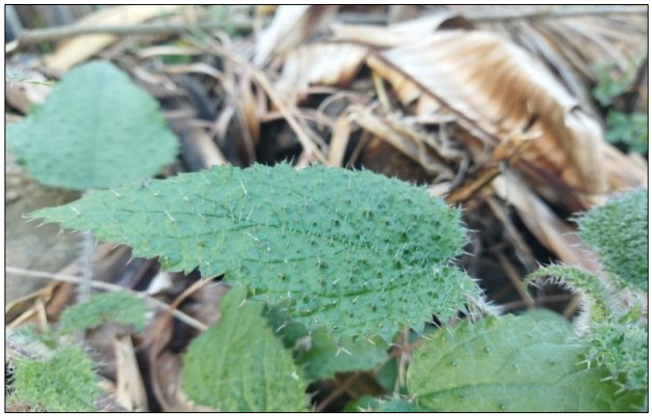

Fig 2: -Hair of *Urtica dioica*

Anti-inflammatory effect
Case 1: The rats with experimental gonarthritis induced by bovine γ-globulin and silicon atoms gave rise to a dose-dependent anti-inflammatory effect on application of extract IDS23. Body weight, meal and behaviour did not changed and death rate was restricted. The effect was much the same as diclofenac.

Case 2: The extract of nettle leaf has been utilized as a medication in Rheumatic disorder. The effect of IDS23 was investigated on disease activity of Murine colitis.
Method- Mice with colitis were examined with whichever, IDS30 or water. These mice were examined for medical indications +of colitis [34].

Result: Mice with colitis or mice treated with IDS30 showed fever indications of colitis than animals without treatment. Faecal interleukin-1β and mucosal TNF-α amount were lower in treated mice.

Conclusion: Use of IDS 30 for a long period of time was effective in the treatment of Murine colitis.

Anti-oxidative effect
In the rat brain, the effect of drug and exercise were studied for oxidative stress markers. Swimming training and the supplementation have been expected to lessen oxidative damage and maintenance of cell survival in the brain. The oxidative stress level was dignified by ESR (electron spin resonance).

Result: Supplementation of *Urtica dioica* resulted in reduced concentration of free radicals in both frontal lobe and cerebellum. Swimming however did not impact the oxidative damage [35].

Toxicology
Toxicity and antimicrobial activity of 22 aqueous plants was conducted. 6 bacteria as well as *Pseudomonas aeruginosa*, *Streptococcus pyogens*, *Escherichia coli*, *Klebsiella pneumonia*, staphylococcus epidermidis and staphylococcus aureus were used to perform antibacterial activity. Helichrysum flowers, *Tussilago farfara* leaves extract, *Solanum dulcamara* aerial parts and *Urtica dioica* leaves showed the best inhibitory activity in contrast to staphylococcus epidermis.20 plants extract out of 22 displayed toxicity in brine shrimp bioassay.
Two different dosage (50 or 100mg/kg body mass) of a water-ethanol concentrate (20-80%), extract of *Urtica dioica* leaves were given from oral route for 14 days to Swiss albino mice (8-9 weeks old). Butylated hydroxyl anisole (BHA) and distilled water served as control no unwanted side effects could be seen [36].

Clinical studies (clinical trials and case studies)
Osteoarthritis is a disorder which can seriously affect almost all synovial joints. It is characterized by regeneration and degradation of a bone and articular cartilage. Osteoarthritis, mainly of the large joints such as knees and hips considered as the main reason of the chronic infirmity in the population. Nettle leaf extracts were examined in osteoarthritis.
Three classes of drug are used in the treatment of osteoarthritis-

1. Fast-acting drugs
2. Slow-acting drugs
3. Disease-modifying drugs

Open studies
Patients with arthritic or Rheumatic complaints were given a daily dosage of 670mg (2 times) comprising a dry hydro alcoholic extract of *Urtica dioica* leaves and 5 open studies were conducted.

1. The extract preparation was tested on 152 patients with several Rheumatic, degenerative diseases. A daily dose of 1.54g of dried extract (Rheuma-Hek capsule) was given to the patients. 121 patients out of 152 were pre-tested with non-steroidal anti-inflammatory drug (NSAIDs) mainly Diclofenac. 19 patients who were not pre-treated with NSAIDs took Rheuma-Hek together with NSAIDs. Only 12 patients took Rheuma-Hek alone. When assessed by a visual analogue scale (VAS), pain symptoms in the patients taking combined therapy were improved by 70% (pain at rest by 50%; pain during movement by 51%). Patients taking only Nettle leaf extract, pain decreased by 43%. It is suggested that patients having weaker Rheumatic complaints should use the mono-therapy of Rheuma-Hek. Only 17% of physicians marked the mono-therapy with NSAIDs as good or very good, 78% of them rated the combination therapy- NSAIDs + Rheuma-Hek as good or very good. Only one patient stopped the therapy due to allergic reaction [37].
2. In the second study, 219 patients (77 men, average age-53; 142 women, average age-67) suffering from degenerative or inflammatory joint disorders were treated with Nettle leaf extract (IDS23), 2 times 2 capsules for 3 weeks. When assessed approximately one- third in 70% of the patients. Patients taking only nettle leaf extract

considered it as effective as the extract combined with NSAIDs.
3. In the result of a three week post authorization inspection study in 1528 patients (1392 Arthrose, 268 Rheumatoid arthritis) it revealed that the herbal plant product Rheuma-Hek was very well tolerated and was effective as well.
4. In another study 8955 patients suffering from osteoarthritis or rheumatoid arthritis were given 2 times 2 capsules of Nettle leaf extract of 3 weeks.

The patients were categorized into 3 groups according to the type of therapy given to them:
- Rheuma-Hek mono-therapy
- Rheuma-Hek along with NSAID combination therapy
- Rheuma-Hek along with other therapy

Result - 2754 patients (64%) were able to reduce the dose of the parallel NSAIDs. Only 7.6% of the sick people required NSAID along with Rheuma-Hek. The ache is reduced by 55% at resting mode and the pain during moving by 45%.Adverse effects were seen in 1.2% patients, complaints about Gastro-intestinal and allergic reactions.

Controlled studies
A controlled study was performed in 27 patients suffering from Osteoarthritis occurring at the base of index finger and thumb. Patients tested this nettle leaf for one week to the affected area on daily basis.

Method of application
- Nettle leaf was plucked with one hand covered by plastic bag.
- The lower surface of leaf was applied with gentle pressure to the tender area of thumb and index finger.
- The above process was continued for 30 seconds moving the hand twice.

A comparative study was made with this treatment and to dead nettle leaf (*Lamium album*). Pain and infirmity observations were noted for 12 weeks of the study. After 1 week of treatment with *Urtica dioica*, a considerable reduction in pain and disability was observed. 23 out of 27 patients reported of localized rash and slight itching. The discomfort of the nettle sting was reported by 2 pateints and 1 patient had a rash on her forearms after treatment. 1 patient discontinued the treatment due to rash on the hand and was demanding heavy gloves.
Result- Treatment with stinging nettle showed reduction of disability and pain-relieving effect after 1 week of medication. Though the sample size was small it showed a considerable result.

Clinical safety (Adverse effect)
The nettle (*Urtica dioica*) is a herb which can cause a broad range of cutaneous reaction. Any direct interaction with the nettle hair can cause itching, dermatitis and Urticaria within few seconds. Nausea, vomiting and diarrhoea were also observed.
In clinical studies, only 1.2% of the patients experienced ADRs which were mostly allergic reactions (0.13%) and gastro-intestinal complaints (0.64%). 5 clinical studies were conducted in which 10,368 patients took 70 mg, 2 times of nettle leaf extract and no serious adverse effects were reported. The occurrence of minor adverse effects was 1.2 - 2.7%. 3 patients reported of meteorism.

Use in pregnancy and lactation
Safety of this drug has yet not been established due to insufficient data. The concentrate is usually not suggested during pregnancy and lactation.

Conclusion
The pharmacological data suggests the conventional use of *Urtica dioica* leaf in treating slight articular pains such as IDS-23 which hampers the building of cytokine IL-1 β and TNF-α which plays a significant part in the pathogenesis of arthritis. NSAIDs should be restricted for the adverse effect it shows on prohibition of COX 1 and COX 2 enzyme. Nettle leaf extract being a herbal plant should be used in curing diseases like Arthritis and certain allergies and minor uterine haemorrhage. Results of clinical trials are not sufficient but more research can bring satisfactory results. However, the result supports the possibility of the conventional use in slight articular pain. Overall results showed that the nettle leaf preparations are well-tolerated and shows satisfactory results.

References

1. Koskela T. Variation in life-history traits among *Urtica dioica* populations with different history in parasitism by the holoparasitic plant *Cuscuta europaea*. Evolutionary Ecology. 2002;16(5):433-454.
2. Taylor K. Biological flora of the British Isles: *Urtica dioica* L. Journal of Ecology. 2009;97(6):1436-1458.
3. Joshi Bhuwan Chandra, Minky Mukhija, Ajudhia Nath Kalia. "Pharmacognostical review of *Urtica dioica* L." Int J of G Pharmacy. 2014;8:201-209.
4. Gülçin Ilhami, *et al*. "Antioxidant, antimicrobial, antiulcer and analgesic activities of nettle (*Urtica dioica* L.). Journal of ethno pharmacology. 2004;90(2-3):205-215.
5. Bnouham Mohamed, *et al*. "Antihyperglycemic activity of the aqueous extract of *Urtica dioica*." Fitoterapia. 2003;74(7-8):677-681.
6. Dar Sabzar Ahmad, *et al*. "Pharmacological and toxicological evaluation of *Urtica dioica*." Pharmaceutical Biology. 2013;51(2):170-180.
7. Dhouibi Raouia, *et al*. "Screening of pharmacological uses of *Urtica dioica* and others benefits." Progress in biophysics and molecular biology. 2020;150:67-77.
8. Esposito Sabrina, *et al*. "Therapeutic perspectives of molecules from *Urtica dioica* extracts for cancer treatment." Molecules. 2019;24(15):2753.
9. Olsen Carsten. "The ecology of *Urtica dioica*." Journal of Ecology. 1921;9(1):1-18.
10. Bombardelli E, Morazzoni P. "*Urtica dioica* L." Fitoterapia. 1997;68(5):387-402.
11. Safarinejad Mohammad Reza. "*Urtica dioica* for treatment of benign prostatic hyperplasia: a prospective, randomized, double-blind, placebo-controlled, crossover study." Journal of herbal pharmacotherapy. 2005;5(4):1-11.
12. Akbay P, Basaran AA, Undeger U, Basaran N. *In vitro* immunomodulatory activity of flavonoid glycosides from *Urtica dioica* L. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2003;17(1):34-37.

13. Bodros E, Baley C. Study of the tensile properties of stinging nettle fibres (*Urtica dioica*). Materials Letters. 2008;62(14):2143-2145.
14. Modarresi-Chahardehi A, Ibrahim D, Fariza-Sulaiman S, Mousavi L. Screening antimicrobial activity of various extracts of *Urtica dioica*. Revista de biologia tropical. 2012;60(4):1567-1576.
15. Upton R. Stinging nettles leaf (*Urtica dioica* L.): Extraordinary vegetable medicine. Journal of Herbal Medicine. 2013;3(1):9-38.
16. Wagner H, Willer F, Samtleben R, Boos G. "Search for the antiprostatic principle of stinging nettle (*Urtica dioica*) roots." Phytomedicine. 1994;1(3):213-224.
17. Di Virgilio N, Papazoglou EG, Jankauskiene Z, Di Lonardo S, Praczyk M, Wielgusz K. The potential of stinging nettle (*Urtica dioica* L.) as a crop with multiple uses. Industrial Crops and Products. 2015 Jun 1;68:42-9.
18. Daher CF, Baroody KG, Baroody GM. Effect of *Urtica dioica* extract intake upon blood lipid profile in the rats. Fitoterapia. 2006;77(3):183-188.
19. 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. Journal of Ethno pharmacology. 2002;81(1):105-109.
20. Lahigi SH, Amini K, Moradi P, Asaadi K. Investigating the chemical composition of different parts extracts of bipod nettle *Urtica dioica* L. in Tonekabon region. Physiology. 2011;2(1):337-340.
21. Vogl CR, Hartl A. Production and processing of organically grown fiber nettle (*Urtica dioica* L.) and its potential use in the natural textile industry: A review. American Journal of Alternative Agriculture. 2003;18(3):119-128.
22. El-Haouari Mohammed, Juan Rosado A. "Phytochemical, anti-diabetic and cardiovascular properties of *Urtica dioica* L. (Urticaceae): A Review." Mini reviews in medicinal chemistry. 2019;19(1):63-71.
23. Krystofova O, Adam V, Babula P, Zehnalek J, Beklova M, Havel L, *et al*. Effects of various doses of selenite on stinging nettle (*Urtica dioica* L.). International journal of environmental research and public health. 2010;7(10):3804-3815.
24. Riehemann K, Behnke B, Schulze-Osthoff K. Plant extracts from stinging nettle (*Urtica dioica*), an antirheumatic remedy, inhibit the proinflammatory transcription factor NF-κB. FEBS letters. 1999;442(1):89-94.
25. Obertreis B, Giller K, Teucher T, Behnke B, Schmitz H. Anti-inflammatory effect of *Urtica dioica* folia extract in comparison to caffeic malic acid. Arzneimittel-forschung. 1996;46(1):52-56.
26. Krzeski T, Kazón M, Borkowski A, Witeska A, Kuczera J. Combined extracts of *Urtica dioica* and *Pygeum africanum* in the treatment of benign prostatic hyperplasia: double-blind comparison of two doses. Clinical therapeutics. 1993;15(6):1011-1020.
27. Tickner DP, Angold PG, Gurnell AM, Mountford JO. Alien invaders: a case study of competition between *Impatiens glandulifera* and the native *Urtica dioica* in a riparian environment. Aspects of Applied Biology. 2000;(58):213-220.
28. Pollard AJ, Briggs D. Genecological studies of *Urtica dioica* L. III. Stinging hairs and plant-herbivore interactions. New Phytologist. 1984;97(3):507-522.
29. Ghorbanibirgani A, Khalili A, Zamani L. The efficacy of stinging nettle (*Urtica dioica*) in patients with benign prostatic hyperplasia: a randomized double-blind study in 100 patients. Iranian Red Crescent Medical Journal. 2013;15(1):9.
30. Sahin M, Yilmaz H, Gursoy A, Demirel AN, Tutuncu NB, Guvene ND. Gynaecomastia in a man and hyperoestrogenism in a woman due to ingestion of nettle (*Urtica dioica*). The New Zealand Medical Journal (Online). 2007;120:1265.
31. Adel M, Caipang CMA, Dawood MA. Immunological responses and disease resistance of rainbow trout (*Oncorhynchus mykiss*) juveniles following dietary administration of stinging nettle (*Urtica dioica*). Fish & Shellfish Immunology. 2017;71:230-238.
32. Tabrizi R, Sekhavati E, Nowrouzi-Sohrabi P, Rezaei S, Tabari P, Ghoran SH, *et al*. Effects of *Urtica dioica* on Metabolic Profiles in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Clinical Trials. Mini reviews in medicinal chemistry, 2021.
33. Olszewski G, Boryło A, Skwarzec B. A study on possible use of *Urtica dioica* (common nettle) plants as uranium (234U, 238U) contamination bioindicator near phosphogypsum stockpile. Journal of Radioanalytical and Nuclear Chemistry. 2016;308(1):37-46.
34. Randall CF. Treatment of musculoskeletal pain with the sting of the stinging nettle: *Urtica dioica*, 2001.
35. Konrad L, Müller HH, Lenz C, Laubinger H, Aumüller G, Lichius JJ. Antiproliferative effect on human prostate cancer cells by a stinging nettle root (*Urtica dioica*) extract. Plantamedica. 2000;66(01):44-47.
36. Halder S, Sharma A. A review on *Urtica dioica* L. World J Pharm Sci. 2017;6:404-421.
37. Ziaei R, Foshati S, Hadi A, Kermani MAH, Ghavami A, Clark CC, *et al*. The effect of nettle (*Urtica dioica*) supplementation on the glycemic control of patients with type 2 diabetes mellitus: A systematic review and meta-analysis. Phytotherapy Research. 2020;34(2):282-294.
38. Namazi N, Esfanjani AT, Heshmati J, Bahrami A, Nazemiyeh H. A systematic review about effects of aerial portions of *Urtica dioica* (nettle) on some cardiovascular risk factors in diabetes mellitus. International journal of pharmacology. 2012;8(5):306-313.