

Urtica Dioica, An Emerald in the Medical Kingdom

Sadegh Fattahi^{1,2}, Monireh Golpour², Haleh Akhavan-Niaki^{1,3*}

1. North Research Center-Pasteur Institute of Iran, Amol, Iran.

2. Cellular and Molecular Biology Research Center, Babol University of Medical Sciences, Babol, Iran.

3. Department of Genetics, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran.

Submitted 23 Jul 2016; Accepted 10 Aug 2016; Published 21 Sep 2016

Urtica dioica is a perennial plant used as herbal medicine due to its many pharmacological and clinical effects. Because of its antioxidant activity, it is widely used in traditional diabetes treatment but is also known as antimicrobial, anti-inflammatory or anti-prostate cancer agent. Extensive studies have been conducted on different parts of this plant and their biological effects. Here we reviewed the effect of different parts of this plant including leave, seed, root and aerial part extracted with various methods in treatment of diseases. Various beneficial effects were reported on animal models without apparent side effects, which led us to consider it as an emerald to be more deeply discovered in the kingdom of health.

Keywords: *Urtica dioica*, diabetes, cancer, antioxidant, anti-inflammatory

In traditional medicine, plants and herbs are widely used in treatment of the disease for their benefits such as having low side effects, being natural sources with low cost. *Urtica dioica* is one of the herbs to be widely used as a medicine due to many pharmacological and clinical effects. *Urtica dioica* or stinging nettle is a member of Urticaceae family, herbaceous perennial plants which have many little hairs and contain histamine, formic acid, acetylcholine, acetic acid, etc... on the leaves and stalks that cause skin irritation after contact. In Iran, it is named gazaneh which means stinging. It is also known as Anonhasquara among native Americans, or Grande ortie among French people (1). Alkaloids, saponins, tannins, flavonoids, steroids and terpenes,

polyphenols and cardiac glycosides are present in the leaves of *Urtica dioica* (2). The investigation of polyphenolic acids in male and female forms of stinging nettle showed that the male has higher polyphenolic acids content than female form and these compounds increase at the stage of full blooming in both forms (3). Regarding a variety of uses of *Urtica dioica* in improving human health, we extensively reviewed the effect of different sections of this plant including leave, seed, root and aerial part extracted with various methods in treatment of diseases.

Root aqueous extract

An anti-prostate cancer effect of the aqueous root extract which is accomplished by inhibition of

*Correspondence: Department of Genetics, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran.
E-mail: halehakhavan@yahoo.com

the binding of 125I-SHBG (human sex hormone binding globulin) to its receptor was reported (4). In fact, pinoselinol, dehydrodiconiferyl alcohol, (-)-secoisolariciresinol, (+)-neoolivil, isolariciresinol, lignans, and 3,4-ivanillyltetrahydrofuran, from the aqueous root extract of *Urtica dioica* bind to SHBG (5). Moreover, this aqueous extract diminishes nocturia in men suffering from prostatic adenoma (6). Wagner et al. showed that aqueous root extract contains a polysaccharide mixture that can be used by some stimulated T lymphocytes and others for influencing the complement system or triggering the secretion of tumor necrosis factor- α (TNF- α) *in vitro*. They also indicated an extended anti-inflammatory activity while performing the rat paw edema assay (7). This extract can induce hypotensive responses due to negative inotropic effect, potassium channels opening and the production of endothelial nitric oxide (8). Patients receiving *Urtica dioica* improved their international prostate symptom score, lower urinary tract symptoms, and the maximum rate of urinary flow with modest decrease in prostate size. Moreover, *Urtica dioica* decreased postvoid residual urine volume (PVR) but did not change serum prostate-specific antigen (PSA) and testosterone levels (9).

Root non-aqueous extract

Antiprostatic effect of GlcN-Ac-(N-acetylglucosamine), a specific lectin from the rhizomes of stinging nettle, also called *Urtica dioica* agglutinin (UDA), exerted by inhibiting the attachment of 125I-EGF (epidermal growth factor) to its receptor (EGF-R) in prostate tissues was demonstrated (10). UDA inhibits the activity of respiratory syncytial virus, cytomegalovirus (CMV), influenza A and human immunodeficiency virus types 1 and 2 (11). It also inhibits the development of the systemic lupus erythematosus-like pathology in Murphy Roths Large (MRL) mice homozygous for the *lpr* (lymphoproliferation) mutation (12). The

combination of *Urtica dioica* root and *Pygeum africanum* bark extracts reduce urine flow as well as residual urine and nocturia in men showing benign prostatic hyperplasia (13). Non-aqueous root extract of *Urtica dioica* inhibits the membrane Na⁺, K⁽⁺⁾-ATPase activity in prostatic tissue showing hyperplasia (14). Petroleum ether and ethanol extracts of *Urtica dioica* have 5 α -reductase inhibitory activity *in vitro*. Moreover b-sitosterol, a molecule used in prostatic hyperplasia therapy, and scopoletin, an anti-inflammatory molecule, are present as major constituents of the extract (15). The combination of extracts of stinging nettle root and *Serenoa repens* fruit showed an efficiency similar to finasteride, an inhibitor of 5 α -reductase. This efficiency was independent of the prostate volume (16). A combination of extracts of roots of stinging nettle and *Sabal serrulata* fruits improves the symptoms observed in lower urinary tracts of elderly men (17).

Root hydroalcoholic extract

The hydroalcoholic extract of stinging nettle root has a cytotoxic activity on human prostatic epithelial cells (18). Aromatase inhibition by the methanolic extract of *Urtica dioica* root was also observed (19).

Leaf aqueous extract

In vivo studies showed that aqueous leaf extract of *Urtica dioica* is helpful in different aspects of diabetes treatment in rats. This extract affects Langerhans islets in diabetic rats and subsequently leads to an increase of insulin secretion and decrease of blood sugar (20). Similarly, simultaneous increase of insulin and decrease of blood glucose after treatment of diabetic rats with *Urtica dioica* accompanied by an increase of the activity of coenzyme acetyl A carboxylase and nucleoside diphosphate kinase in the alloxan induced diabetic rats was reported (21). Antihyperglycemic effect of leaf aqueous extract of

Urtica dioica in the streptozotocin treated hyperglycemic rats as well as significant decrease of the level of lipids, cholesterol but not triglyceride and low density lipoprotein (LDL) was demonstrated (22). Inhibition of, protein tyrosine phosphorylation, Ca²⁺ mobilization and oxidant production which cause platelet hyperaggregability in type 2 diabetes mellitus is caused by *Urtica dioica* extracts (23). The aqueous leaf extract has also an antiplatelet activity *in vitro* (24). Investigation of the effect of aqueous extract in the prostate cancer showed a significant decrease of adenosine deaminase, an important enzyme in nucleotide synthesis (25). *In vitro* studies showed apoptosis induction in MCF-7 breast cancer cell line after exposure to aqueous leave extract of *Urtica dioica* (26). Finally, an antibacterial effect of aqueous extract against pseudomonas and psychrotrophic bacteria present in the ground beef was reported (27).

Leave non-aqueous extract

The non aqueous leave extract of *Urtica dioica* have various clinical effects. The ethanolic leave extract have an anti inflammatory effect on rheumatoid arthritis via inhibition of the proinflammatory transcription factor NF- κ B (28). This extract was also shown to be efficient in allergic rhinitis treatment (29). An antimicrobial effect of extracts on fish and human pathogenic bacteria was demonstrated by disc diffusion method. Considerable antibacterial activity against both Gram negative and positive bacteria was reported (30-32) with hexane extracts showing better antimicrobial activity on Gram negative bacteria (31) and ethyl acetate and hexane extracts exhibiting better antimicrobial activity on Gram-positive bacteria (30). Ethyl acetate extracts were demonstrated to be more efficient than methanol extracts in preventing *in vitro* rat platelet aggregation induction by thrombin (24). The

investigation of ethanolic extract efficiency against four main plant pathogenic fungi, demonstrated that it exert an important antifungal activity. Therefore the ethanolic extract of *Urtica dioica* could be substituted to chemical products routinely used for preventing fungal infections in plants (33). The study of antioxidant, hepatoprotective and anti helminthic activity of methanol extract of leaves of *Urtica dioica in vitro* and *in vivo* showed a significant antioxidant activity comparable to traditional antioxidant compounds such as α -tocopherol, ascorbic acid and butylated hydroxyanisole (BHA). Pretreatment of animals with this extract had a significant increase in superoxide dismutase level and inhibited lipid peroxidation (34). *Urtica dioica* leaf homogenized in 1.15% KCl decreased malonyldialdehyde level therefore preventing oxidative stress induced by tourniquet in rats (35). The methanolic extract also decreased the levels of alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin of serum which indicates its hepatoprotective effect. Antihelminthic activity of the methanolic extract was also reported in *Pheretima posthuma* and mice naturally infected with *Aspicularis etraptera* (36).

Leave hydroalcoholic extract

The hydroalcoholic extract of *Urtica dioica* has an anti allergic rhinitis effect exerted by preventing prostaglandin formation through inhibiting hematopoietic prostaglandin D2 synthase cyclooxygenase-1 and cyclooxygenase-2 which all play essential roles in pro-inflammatory pathways. It also inhibits the activity of mast cell tryptase and histamine-1 receptor (37). The examination of antioxidant activity of hydroalcoholic extract by means of different antioxidant evaluation methods demonstrated an antioxidant effect comparable with traditional antioxidants such as α -tocopherol, butylated hydroxytoluene (BHT) and BHA (38).

Using carrageenan-induced paw edema, formalin test and acetic acid-induced writhing, an anti-inflammatory and antinociceptive effect of the hydroalcoholic leaf extract was demonstrated in Swiss mice and Wistar rats. Therefore, the hydroalcoholic leaf extract may reduce pain and inflammation by suppressing histamine release from mast cells and also suppressing arachidonic acid metabolism (39). *In vivo* evaluation of extract's effect on lactate dehydrogenase, lipid peroxidation and antioxidant enzymes showed a significant increase of superoxide dismutase, glutathione S-transferase, glutathione reductase, NADH-cytochrome b5 reductase, cytochrome b5, DT-diaphorase, glutathione peroxidase, catalase activities in the liver and a decrease of NADPH-cytochrome P450 reductase activities, cytochrome P450, total sulfhydryl groups, as well as a decrease of lactate dehydrogenase, protein bound sulfhydryl groups and nonprotein sulfhydryl groups (40). Injection of this extract before inducing diabetes by streptozotocin in rats, has a hypoglycemic and protective effect on the β -cells of Langerhans islets as well as morphometric features of hepatocytes and seminiferous tubules (41-46). This extract also decreased the number of astrocytes in the dentate gyrus of hyperglycemic rats (47). In fructose-induced insulin resistance rats, treatment with this extract caused a decrease of insulin, LDL, leptin, fasting insulin resistance index (FIRI), serum glucose, LDL/HDL ratio and increase of very low density lipoprotein (VLDL), AST and triglyceride (TG) but no ALP of serum (48). In hypercholesterolemic rats a decrease of the level of total cholesterol, LDL, ALT, AST and weight was shown (49) while a decrease of blood glucose and increase of insulin, acetyl coenzyme A carboxylase and nucleoside diphosphate kinase activities was reported in alloxan induced diabetic rats (21). This extract increased aniline 4-hydroxylase activity,

cofactor requirement (NADH and NADPH) and metal ions (Mg^{2+} and Ca^{2+}) in mice (50). The combination of *Urtica dioica* with *Atriplex halimus*, *Olea europea* and *Juglans regia* decreased glucose levels and improved sugar uptake during glucose tolerance test (51).

Seed non-aqueous extract

The diethyl ether extract of *Urtica dioica* seed decreased serum aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, ceruloplasmin and lipid hydroperoxides levels and increased serum arylesterase, paraoxonase, and catalase levels in rats (52). The diethyl ether seed extract alone or in combination with *Nigella sativa* decreased liver enzyme levels and malonaldehyde in rats and increased their weight as well as the levels of the reduced antioxidants during 60 days treatment (53). The extract showed moderate anti inflammatory effects in tissue inflammation model induced by carrageenan (54). The methanol extract of seeds of *Urtica dioica* was highly effective against *Xanthomonas vesicatoria*, a plant-borne pathogen (55).

Seed hydroalcoholic extract

The hydroalcoholic extract of *Urtica dioica* seeds had a good antioxidant effect compared to traditional antioxidants α -tocopherol, BHT and BHA as demonstrated by different antioxidant evaluation methods such as reducing power, total antioxidant activity, hydrogen peroxide scavenging, superoxide anion radical scavenging, metal chelating activity and free radical scavenging (38).

Aerial aqueous extract

Oral pretreatment of rats with the aqueous extract of aerial part of stinging nettle enabled a decrease of glucose level during oral glucose tolerance test (OGTT) (56). This extract was shown to produce a vasoconstriction of the aorta by activating $\alpha 1$ -adrenergic receptors and caused a

strong bradycardia through non-cholinergic and non-adrenergic pathways (57). Total LDL, cholesterol, LDL/HDL ratio and plasma total AST, lactate dehydrogenase (LDH), ALT and apo B decreased after treatment of rats with aqueous extract of aerial part of stinging nettle (58). This extract affects also arterial blood pressure in rats by increasing diuresis and natriuresis (59).

Antimicrobial, antiulcer, antioxidant and analgesic activities of *Urtica dioica* were investigated by Gülçin et al. who showed that aqueous extract of aerial part of this plant has a remarkable antioxidant activity comparable to standard antioxidants and has antibacterial effect on both Gram-negative and positive bacteria. Nevertheless, pre-treatment of this extract with metamizol and famotidine inhibits the acetic acid-induced writhing and ethanol-induced gastric mucosal injury in rats, respectively (60). The extract increased T lymphocytes proliferation with a moderate increase of CD4+ T cells proportion and due to their scavenging activity inhibited peritoneal macrophages, NO₂ production without affecting cell viability (61). Cytotoxicity and antioxidant effect of this extract was reported on MCF-7 cell line (62).

Aerial non-aqueous extract

Non-aqueous extract exhibited good antibacterial activity on both Gram negative and positive bacteria. Ethyl acetate and hexane extract demonstrated better antimicrobial activity against the Gram-positive bacteria (30). Total LDL, LDL/HDL, cholesterol ratio and plasma total apo B decreased after treating rats with petroleum ether extract of aerial parts of the plant (58).

Aerial hydroalcoholic extract

The hydroalcoholic extract of aerial part of *Urtica dioica* increased HDL, total antioxidant

capacity and superoxidant dismutase and decreased FBS, HBA1C, TG, Log (TG/HDL-c) and systolic blood pressure without any changes in malondialdehyde and glutathione peroxides in type 2 diabetes patients after eight weeks treatment (63, 64). This extract unabled glucose utilization enhance either directly or by increasing the insulin sensitivity *in vitro* (65). Treatment with *Urtica dioica* reduced densities of CA3 hippocampal pyramidal cells in diabetic rats (66).

Conclusion

Various parts of *Urtica dioica* with different modes of extraction have many pharmacological effects. As shown in Table 1, greatest attentions have been conducted on the leaves, roots, seeds and aerial parts of the plant, respectively. The nettle roots, regardless of the extraction method, due to the presence of specific N-acetyl glucosamine have an anti-cancer, especially anti prostate cancer property. The aerial parts and leaves of *Urtica dioica* have anti-diabetic, anti-thrombosis, anti-allergic, anti-microbial, antioxidant properties in addition to anti-cancer. The seed of *Urtica Dioica* which belongs to aerial parts of this plant has antioxidant and anti-microbial properties. Contrary to pharmaceutical drugs which regardless of their side effects have been synthesized for a specific disease, the whole plant of *Urtica Dioica* not only has no side effects, but has many medicinal properties against various diseases. So, this plant perhaps accessible mostly in small traditional drugstores, despite all its benefits, was suggested by authors to be considered as an emerald in the kingdom of health and not as just a simple weed.

Conflict of interest

The authors declared no conflict of interest.

Table 1. Various effects of extracts from different parts of *Urtica dioica*

Part of plant	Extraction method	Diseases or conditions	References
Root	Aqueous	Prostate cancer Anti inflammatory Hypotensive	(3-8)
	Non-aqueous	Prostate cancer Systemic lupus rythematosus	(9-16, 66)
	Hydroalcoholic	Prostate cancer Aromatase inhibitor Breast cancer	(17-18)
Leave	Aqueous	Anti diabetic Thrombosis Atherosclerosis Breast cancer Antimicrobial	(19-24, 26)
	Non-aqueous	Rheumatoid arthritis Allergic rhinitis Antimicrobial Antifungal Antioxidant Antihelminthic Anti diabetic	(23, 27-35)
	Hydroalcoholic	Allergic rhinitis Anti diabetic Antioxidant Anti nociceptive Anti inflammatory	(20, 36-50)
Seed	Non-aqueous	Ischemia/reperfusion injury Sepsis Hepatoprotective Antioxidant Anti-inflammatory Antibacterial	(51-54)
	Hydroalcoholic	Antioxidant	(37)
Aerial part	Aqueous	Anti diabetic Hypotensive Cardiovascular disease Antioxidant Antimicrobial Antiulcer Analgesic T lymphocyte proliferation Antioxidant Breast cancer	(55-61)
	Non-aqueous	Antimicrobial Cardiovascular disease	(29, 57)
	Hydroalcoholic	Anti diabetic	(62-65)

References

1. Moses A G M, Nyarango. Fourier Transformer Infra-Red Spectrophotometer Analysis of *Urtica*

dioica Medicinal Herb Used for the Treatment of Diabetes, Malaria and Pneumonia in Kisii Region, Southwest Kenya. *World App Sc J.* 2013;21:1128-35.

2. Rosłon W, Węglarz Z. Polyphenolic Acids of Female and Male Forms of *Urtica dioica*. *Acta Hort.* 597. 2003;597:101-4.
3. Hryb D J, Khan M S, Romas N A, et al. The effect of extracts of the roots of the stinging nettle (*Urtica dioica*) on the interaction of SHBG with its receptor on human prostatic membranes. *Planta Med.* 1995;61:31-2.
4. Schottner M, Gansser D, Spiteller G. Lignans from the roots of *Urtica dioica* and their metabolites bind to human sex hormone binding globulin (SHBG). *Planta Med.* 1997;63:529-32.
5. Belaiche P, Lievoux O. Clinical studies on the palliative treatment of prostatic adenoma with extract of *Urtica* root. *Phytother Res.* 1991;5:267-9.
6. Wagner H, Willer F, Samtleben R, et al. Search for the antiprostatic principle of stinging nettle (*Urtica dioica*) roots. *Phytomedicine.* 1994;1:213-24.
7. Testai L, Chericoni S, Calderone V, et al. Cardiovascular effects of *Urtica dioica* L. (*Urticaceae*) roots extracts: in vitro and in vivo pharmacological studies. *J Ethnopharmacol.* 2002;81:105-9.
8. Safarinejad M R. *Urtica dioica* for treatment of benign prostatic hyperplasia: a prospective, randomized, double-blind, placebo-controlled, crossover study. *J Herb Pharmacother.* 2005;5:1-11.
9. Wagner H, Geiger W N, Boos G, et al. Studies on the binding of *Urtica dioica* agglutinin (UDA) and other lectins in an in vitro epidermal growth factor receptor test. *Phytomedicine.* 1995 Apr;1:287-90.
10. Balzarini J, Neyts J, Schols D, et al. The mannose-specific plant lectins from *Cymbidium hybrid* and *Epipactis helleborine* and the (N-acetylglucosamine)n-specific plant lectin from *Urtica dioica* are potent and selective inhibitors of human immunodeficiency virus and cytomegalovirus replication in vitro. *Antiviral Res.* 1992;18:191-207.
11. Musette P, Galelli A, Chabre H, et al. *Urtica dioica* agglutinin, a V beta 8.3-specific superantigen, prevents the development of the systemic lupus erythematosus-like pathology of MRL lpr/lpr mice. *Eur J Immunol.* 1996;26:1707-11.
12. Krzeski T, Kazon M, Borkowski A, et al. Combined extracts of *Urtica dioica* and *Pygeum africanum* in the treatment of benign prostatic hyperplasia: double-blind comparison of two doses. *Clin Ther.* 1993;15:1011-20.
13. Hirano T, Homma M, Oka K. Effects of stinging nettle root extracts and their steroidal components on the Na⁺,K⁺-ATPase of the benign prostatic hyperplasia. *Planta Med.* 1994;60:30-3.
14. Nahata A, Dixit V K. Ameliorative effects of stinging nettle (*Urtica dioica*) on testosterone-induced prostatic hyperplasia in rats. *Andrologia.* 2012;44:396-409.
15. Sokeland J. Combined sabal and urtica extract compared with finasteride in men with benign prostatic hyperplasia: analysis of prostate volume and therapeutic outcome. *BJU Int.* 2000;86:439-42.
16. Koch E. Extracts from fruits of saw palmetto (*Sabal serrulata*) and roots of stinging nettle (*Urtica dioica*): viable alternatives in the medical treatment of benign prostatic hyperplasia and associated lower urinary tracts symptoms. *Planta Med.* 2001;67:489-500.
17. Konrad L, Muller H H, Lenz C, et al. Antiproliferative effect on human prostate cancer cells by a stinging nettle root (*Urtica dioica*) extract. *Planta Med.* 2000;66:44-7.
18. Gansser D, Spiteller G. Aromatase inhibitors from *Urtica dioica* roots. *Planta Med.* 1995;61:138-40.
19. Farzami B, Ahmadvand D, Vardasbi S, et al. Induction of insulin secretion by a component of *Urtica dioica* leave extract in perfused Islets of Langerhans and its in vivo effects in normal and

- streptozotocin diabetic rats. *J Ethnopharmacol.* 2003;89:47-53.
20. Qujeq D, Davary S, Moazzi Z, et al. Effect of *Urtica dioica* leaf extract on activities of nucleoside diphosphate kinase and acetyl coenzyme, a carboxylase, in normal and hyperglycemic rats. *Afr J Pharm Pharmacol.* 2011;5:792-6.
21. Das D, Sarma B P, Rokeya B, et al. Antihyperglycemic and antihyperlipidemic activity of *Urtica dioica* on type 2 diabetic model rats. *J of Diabetol.* 2011;2:2:1-6.
22. El Haouari M, Jardin I, Mekhfi H, et al. *Urtica dioica* extract reduces platelet hyperaggregability in type 2 diabetes mellitus by inhibition of oxidant production, Ca²⁺ mobilization and protein tyrosine phosphorylation. *J Appl Biomed.* 2007;5:105-13.
23. El Haouari M, Bnouham M, Bendahou M, et al. Inhibition of rat platelet aggregation by *Urtica dioica* leaves extracts. *Phytother Res.* 2006;20:568-72.
24. Durak I, Biri H, Devrim E, et al. Aqueous extract of *Urtica dioica* makes significant inhibition on adenosine deaminase activity in prostate tissue from patients with prostate cancer. *Cancer Biol Ther.* 2004;3:855-7.
25. Fatthi S, Motevalizadeh Ardakani A, Zabihi E, et al. Antioxidant and apoptotic effects of aqueous extract of *Urtica dioica* on MCF-7 human breast cancer cell line. *Asian Pacific of Cancer Prevention.* APJCP. 2013;14:5317-23
26. Alp E, Aksu M I. Effects of water extract of *Urtica dioica* L. and modified atmosphere packaging on the shelf life of ground beef. *Meat Sci.* 2010;86:468-73.
27. Riehemann K, Behnke B, Schulze-Osthoff K. Plant extracts from stinging nettle (*Urtica dioica*), an antirheumatic remedy, inhibit the proinflammatory transcription factor NF-kappaB. *FEBS Lett.* 1999;442:89-94.
28. Mittman P. Randomized, double-blind study of freeze-dried *Urtica dioica* in the treatment of allergic rhinitis. *Planta Med.* 1990;56:44-7.
29. Modarresi-Chahardehi A, Ibrahim D, Fariza Sulaiman S, et al. Screening antimicrobial activity of various extracts of *Urtica dioica*. *Rev Biol Trop.* 2012;60:1567-76.
30. Singh R, Dar S A, Sharma P. Antibacterial activity and toxicological evaluation of semi purified hexane extract of *urtica dioica* leaves. *Res J Med plant.* 2012;6:123-35.
31. Sabzar Ahmad Dar1, Farooq Ahmad Ganai, Abdul Rehman Yousuf, et al. Bioactive potential of leaf extracts from *Urtica dioica* L. against fish and human pathogenic bacteria. *Afr Microbiol J Res.* 2012;6:6893-9.
32. Hadizadeh I, Peivastegan B, Kolahi M. Antifungal activity of nettle (*Urtica dioica* L.), colocynth (*Citrullus colocynthis* L. Schrad), oleander (*Nerium oleander* L.) and konar (*Ziziphus spina-christi* L.) extracts on plants pathogenic fungi. *Pak J Biol Sci.* 2009;12:58-63.
33. Katak M S, Murugamani V, Rajkumari A, et al. Antioxidant, Hepatoprotective, and Anthelmintic Activities of Methanol Extract of *Urtica dioica* L. Leaves. *Pharmaceutical Crops.* 2012;3:38-46.
34. Cetinus E, Kilinc M, Inanc F, et al. The role of *urtica dioica* (urticaceae) in the prevention of oxidative stress caused by tourniquet application in rats. *Tohoku J Exp Med.* 2005;205:215-21.
35. Turel D, Oto G, Ayaz E, et al. anthelmintic activity of *urtica dioica* l. in mice naturally infected with *Aspiculuris tetraptera*. *J anim vet adv* 2008;8:1628-30.
36. Roschek B, Jr., Fink R C, McMichael M, et al. Nettle extract (*Urtica dioica*) affects key receptors and enzymes associated with allergic rhinitis. *Phytother Res.* 2009;23:920-6.
37. Güder A, Korkmaz H. Evaluation of in-vitro Antioxidant Properties of Hydroalcoholic Solution Extracts *Urtica dioica* L., *Malva neglecta* Wallr and Their Mixture. *Iran J Pharm Res.* 2012;11:913-23.

38. Hajhashemi V, Klooshani V. Antinociceptive and anti-inflammatory effects of *Urtica dioica* leaf extract in animal models. *Avicenna J Phytomed.* 2013;3:193-200.
39. Ozen T, Korkmaz H. Modulatory effect of *Urtica dioica* L. (Urticaceae) leaf extract on biotransformation enzyme systems, antioxidant enzymes, lactate dehydrogenase and lipid peroxidation in mice. *Phytomedicine.* 2003;10:405-15.
40. Gotalipour M J, Ghafari S, Afshar M. Protective role of *Urtica dioica* L. (Urticaceae) extract on hepatocytes morphometric changes in STZ diabetic Wistar rats. *Turk J Gastroenterol.* 2010;21:262-9.
41. Gotalipour M J, Khori V. The protective activity of *Urtica Dioica* Leaves on blood glucose concentration and B-cells in streptozotocin-Diabetic rats. *Pak J Biol Sci.* 2007;10:1200-4.
42. Gotalipour M J, Khori V, Ghafari S, et al. Chronic effect of the hydroalcoholic extract of *urtica dioica* leaves on regeneration of B-cells of hyperglycemic rats. *Pak J Biol Sci.* 2006;9:1482-5.
43. Gotalipour M J, Kabiri Balajadeh B, Ghafari S, et al. Protective Effect of *Urtica dioica* L. (Urticaceae) on Morphometric and Morphologic Alterations of Seminiferous Tubules in STZ Diabetic Rats. *Iran J Basic Med Sci.* 2011;14:472-7.
44. Gotalipour M J, Ghafari S, Kouri V, et al. Proliferation of the B-Cells of Pancreas in Diabetic Rats Treated with *Urtica Dioica*. *Int J Morpho* 2010;28:399-404.
45. Gotalipour M J, Ghafari S, Farsi M M. Effect of *Urtica dioica* L Extract on Quantitative Morphometric Alterations of Liver Parenchymal Cells in STZ Diabetic Rats. *Int J Morphol.* 2009;27:1339-44.
46. Jahanshahi M, Gotalipour M J, Afshar M. The effect of *Urtica dioica* extract on the number of astrocytes in the dentate gyrus of diabetic rats. *Folia Morphol (Warsz).* 2009;68:93-7.
47. Ahangarpour A, Mohammadian M, Dianat M. Antidiabetic Effect of Hydroalcoholic *Urtica dioica* Leaf Extract in Male Rats with Fructose-Induced Insulin Resistance. *Iran J Med Sci.* 2012;37:181-6.
48. Nassiri-Asl M, Zamansoltani F, Abbasi E, et al. Effects of *Urtica dioica* extract on lipid profile in hypercholesterolemic rats. *Zhong Xi Yi Jie He Xue Bao.* 2009;7:428-33.
49. Ozen T, Korkmaz H. The effects of *Urtica dioica* L. leaf extract on aniline 4-hydroxylase in mice. *Acta Pol Pharm.* 2009;66:305-9.
50. Said O, Fulder S, Khalil K, et al. Maintaining a physiological blood glucose level with 'glucoselevel', a combination of four anti-diabetes plants used in the traditional arab herbal medicine. *Evid Based Complement Alternat Med.* 2008;5:421-8.
51. Kandis H, Karapolat S, Yildirim U, et al. Effects of *Urtica dioica* on hepatic ischemia-reperfusion injury in rats. *Clinics (Sao Paulo).* 2010;65:1357-61.
52. Kanter M, Coskun O, Budancamanak M. Hepatoprotective effects of *Nigella sativa* L and *Urtica dioica* L on lipid peroxidation, antioxidant enzyme systems and liver enzymes in carbon tetrachloride-treated rats. *World J Gastroenterol.* 2005;11:6684-8.
53. Tekin M, Özbek H, Him A. Investigation of Acute Toxicity, Anti-inflammatory, and Analgesic Effect of *Urtica dioica* L. *Pharmacologyonline.* 2009;1:1210-5.
54. Korpe D A, Iseri O D, Sahin F I, et al. High-antibacterial activity of *Urtica* spp. seed extracts on food and plant pathogenic bacteria. *Int J Food Sci Nutr.* 2013;64:355-62.
55. Bnouham M, Merhfouf F Z, Ziyat A, et al. Antihyperglycemic activity of the aqueous extract of *Urtica dioica*. *Fitoterapia.* 2003;74:677-81.
56. Legssyer A, Ziyat A, Mekhfi H, et al. Cardiovascular effects of *Urtica dioica* L. in isolated rat heart and aorta. *Phytother Res.* 2002;16:503-7.
57. Daher C F, Baroody K G, Baroody G M. Effect

of *Urtica dioica* extract intake upon blood lipid profile in the rats. *Fitoterapia*. 2006;77:183-8.

58. Tahri A, Yamani S, Legssyer A, et al. Acute diuretic, natriuretic and hypotensive effects of a continuous perfusion of aqueous extract of *Urtica dioica* in the rat. *J Ethnopharmacol*. 2000;73:95-100.

59. Gulcin I, Kufrevioglu O I, Oktay M, et al. Antioxidant, antimicrobial, antiulcer and analgesic activities of nettle (*Urtica dioica* L.). *J Ethnopharmacol*. 2004;90:205-15.

60. Harput U S, Saracoglu I, Ogihara Y. Stimulation of lymphocyte proliferation and inhibition of nitric oxide production by aqueous *Urtica dioica* extract. *Phytother Res*. 2005;19:346-8.

61. GÜLER E R. Investigation of Chemopreventif Properties of *Urtica Dioica* L., in MCF-7 and MDA 231 Breast Cancer Cell Lines. *The new journal of medicine*. 2013;30:50-3.

62. Namazi N, Esfanjani A T, Asghari M, et al. effect of hydroalcoholic nettle (*urtica dioica*) extract

on some cardiovascular risk factor in patients with type 2 diabetes. *J Med Sci*. 2011;11:138-44.

63. Namazi N, Tarighat A, Bahrami A. The effect of Hydro Alcoholic Nettle (*Urtica Dioica*) extract on oxidative stress in patients with type 2 diabetes: A randomized double-blind clinical trial. *Pak J Biol Sci*. 2012;15:98-102.

64. Mobaseri M, Aliasgarzadeh A, Bahrami A, et al. Efficacy of the Total Extract of *Urtica Dioica* on the glucose utilization by the Human Muscle Cells. *Journal of Clinical and Diagnostic Research*. 2012;6:437-40.

65. Fazeli S A, Gharravi A M, Ghafari S, et al. Effects of *Urtica dioica* extract on CA3 hippocampal pyramidal cell loss in young diabetic rats. *Neural Regen Res*. 2010;5:901-5.

66. Galelli A, Truffa-Bachi P. *Urtica dioica* agglutinin. A superantigenic lectin from stinging nettle rhizome. *J Immunol*. 1993;151:1821-31.