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Therapeutic effects of *Urtica dioica L*: A review study

Sepide Miraj

M.D., Gynecologist, Fellowship of Infertility, Assistant Professor, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran

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ABSTRACT

Urticadioicais an herbaceousperennialflowering plant in the family Urticaceae. It is native to Europe, Asia, northern Africa, and western North America, and introduced elsewhere.The aim of this study was to overview therapeutic effects of Urtica dioica L. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and Iran Medex databases .The initial search strategy identified about 115 references. In this study,59studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of Urtica dioica L. and dated mainly from the year 1990 to 2016.The search terms were "Urtica dioica L", "therapeutic properties", "pharmacological effects". It is commonly used for its Antioxidant properties ,Bone formation properties ,Nutrients properties Hypoalgesia , Anti-Liver damage , Testicular tissue treatment effect ,Inflammatory properties ,Protease activity ,Analgesic effect , Anti-Fungal properties ,Modulatory effect , Cardiovascular effects ,Anti-cancer effect ,Herbicidal effects , Adipogenesis effect. Urtica dioica L.is used for the treatment of various diseases. Due to its remarkable power of healing, this plant *has got the place among the top ranked evidence based herbal medicines. This is also revealed that most of the therapeutic properties of this plant are due to the presence of linoleic acid which is major bioactive component of the essential oil. The present review is an effort to provide a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of this plant.*

Keywords: Urtica dioica L, Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative and complementary medicine.

INTRODUCTION

It is proved that herbal medicine is effective in the treatment of many diseases [1-20].Urticadioicais anherbaceousperennial flowering plant in the family Urticaceae. It is native to Europe, Asia, northern Africa, and western North America, and introduced elsewhere [21].

It is the best-known member of the nettle genus Urtica. The species is divided into six subspecies, five of which have many hollow stinging hairs called trichomes on the leaves and stems, which act like hypodermic needles, injecting histamine and other chemicals that produce a stinging sensation when contacted by humans and other animals. The plant has a long history of use as a source of medicine (22), food, and fiber. Urtica dioica from Thomé, Flora von Deutschland, Österreich und der Schweiz 1885Urtica dioica is a dioecious, herbaceous, perennial plant, 1 to 2 m (3 to 7 ft) tall in the summer and dying down to the ground in winter[23].

It has widely spreading rhizomes and stolons, which are bright yellow, as are the roots. The soft, green leaves are 3 to 15 cm (1 to 6 in) long and are borne oppositely on an erect, wiry, green stem. The leaves have a strongly serrated margin, a cordate base, and an acuminate tip with a terminal leaf tooth longer than adjacent laterals. It bears small, greenish or brownish, numerous flowers in dense axillary inflorescences. The leaves and stems are very hairy with nonstinging hairs, and in most subspecies, also bear many stinging hairs (trichomes), whose tips come off when touched, transforming the hair into a needle that can inject several chemicals: acetylcholine, histamine, 5-HT (serotonin), moroidin, leukotrienes, and possibly formic acid[24, 25].

This mixture of chemical compounds causes a painful sting or paresthesia from which the species derives one of its common names, stinging nettle, as well as the colloquial names burn nettle, burn weed, and burn hazel[25].

Antioxidant properties

The antioxidant potential of Urtica dioica L. Was assessed .Release studies indicated that the release rate of NE in 95% ethanol simulant significantly decreased .Moreover, the formation of nanoliposomes decreased the increasing effect of temperature on the release rate as when storage temperature increased from 4□°C to 40□°C [26].

Urtica dioica L. types were examined to determine their mineral, vitamin, phenolic contents and their antioxidant properties. Among the various macronutrients estimated in the plant samples, potassium was present in the highest quantity followed by calcium and phosphate. Kaempferol and resveratrol were not determined in some nettle samples but rutin levels were determined in all samples. The results show that Urtica dioica L. collected from Tunceli in Turkey could be considered as a natural alternative source for food, pharmacology and medicine sectors [27].

Effects of hydro alcoholic extract of Nettle on oxidative stress in type 2 diabetes were evaluated. The findings showed that the hydro alcoholic extract of nettle has increasing effects on TAC and SOD in patients with type 2 diabetes without no changes in Malondialdehyde (MDA) and Glutathione Peroxides (GPX) after eight weeks intervention [28].

The potential role of UD plant for prevention of oxidative stress in muscle tissues generated by tourniquet application in rats was investigated. Basal MDA levels were obtained from tibialis anterior muscles of 8 control rats, which were not exposed to ischemia. MDA levels were lower in the UD-treated rats than those in untreated and KCl-treated rats after either 1 or 2 h of ischemia and 1 h reperfusion. These results indicate that UD has a potential antioxidant effect on ischemic muscle tissues [29].

Sex-related differences in the extent of photo-oxidative stress in male and female individuals of U. dioica was investigated. Results showed that an application of the NPK fertilizer to the soil had a positive effect on drought-stressed plants, reducing the extent of lipid peroxidation in both males and females. P deficiency led to residual photoinhibition, as indicated by significant reductions in the Fv/Fm ratio, and enhanced lipid peroxidation in females, but not in males [30].

The effects of Urtica dioica L. regarding to anti-apoptotic and antioxidative effects was examined. The result indicate a significant reduction in the activity of in situ identification of apoptosis using terminal dUTP nick end labelling. The I/R + UD group showed a decrease in malondialdehyde levels and an increase in the activities of superoxide dismutase, catalase and glutathione peroxidase in comparison with the I/R group. It could be concluded that protective effects of UD on the I/R testicles are via reduction of histological damage, apoptosis, oxidative stress and lipid peroxidation [31].

Bone formation properties

In an animal study, effect on bone formation of U. dioica in response to expansion was assessed .the findings showed that Systemic administration of SN may be effective in accelerating new bone formation and reducing inflammation in the maxillary expansion procedure. It may also be beneficial in preventing relapse after the expansion procedure [32].

Nutrients properties
The effect of cooking on the macronutrient, anti-nutrient and elemental composition of L. peduncularis and U. dioica leaves was investigated. The results showed a decrease in the crude fat, ash, carbohydrate and vitamin C content with cooking, but an increase in the vitamin E content. The anti-nutrient content (cyanides, phytates and saponins) increased slightly with cooking, while the oxalate content has decreased. The result indicated that both positive and negative relationships between nutrients, anti-nutrients and elements were observed in the plant leaves[33].

Aqueous extract of aerial parts of Urtica dioica L. (Urticaceae) was examined. The results demonstrate an acute hypotensive action of U. dioica that indicates a direct effect on the cardiovascular system. Moreover, diuretic and natriuretic effects were also observed, suggesting an action on the renal function. Finally, the plant extract seems to have a toxic effect at the higher dose[34].

Hypoalgesia
The effect of Urtica dioica (UD) extract against memory dysfunction and hypoalgesia was evaluated UD significantly reduced the blood glucose and polydypsia, as well as improved the body weight, insulin level, cognition and insensate neuropathy. Result showed the findings of this plant is comparable to rosiglitazone in reversing the long standing diabetes induced complications such as central and peripheral neuronal dysfunction [35].

Anti-Liver damage
the possible protective effects of Urtica dioica (UD) was evaluated against liver damage in the common bile duct-ligated rats. The change demonstrating the bile duct proliferation and fibrosis in expanded portal tracts includes the extension of proliferated bile ducts into the lobules; inflammatory cell infiltration into the widened portal areas were observed in BDL group. The data indicate that UD attenuates BDL-induced cholestatic liver injury, bile duct proliferation and fibrosis [36]. the effect of Urtica dioica L. (UD), in I/R induced renal injury was investigated. The results suggest that UD treatment has a protective effect against renal damage induced by renal I/R. This protective effect is possibly due to its ability to inhibit I/R induced renal damage, apoptosis and cell proliferation[37].

Polyphenol oxidase of nettle (Urtica dioica L.) was used for its characterization. The most effective was found to be sodium diethyl dithiocarbamate which acted as a competitive inhibitor with a Ki value of 1.79 x 10(-9) M. In addition one isoenzyme of PPO was detected by native polacrylamide slab gel electrophoresis[38].

Testicular tissue treatment effect
This histopathological and morphometrical study was conducted to determine the effects of the hydroalcoholic extract of Urtica dioica leaves on testis of streptozotocin-induced diabetic rats. This study showed that hydroalcoholic extract of Urtica dioica leaves, after induction of diabetes; has no treatment effect on seminiferous tubules alterations in streptozotocin-induced diabetic rats[39].

Inflammatory properties
Hydro alcoholic extract of Nettle (Urtica dioica) on insulin sensitivity and some inflammatory indicators in type 2 diabetic patients were studied. The findings showed that the hydro alcoholic extract of nettle has decreasing effects on IL-6 and hs-CRP in patients with type 2 diabetes after eight weeks intervention [40].

The effects of the hydroalcoholic extract of Urtica dioica leaves on seminiferous tubules of diabetic rats. Hydroalcoholic extract of U. dioica was tested and it showed to has protective role on seminiferous tubules alterations [41].

The effect of Urtica dioica, known as stinging nettle, seed oil (UDO) treatment on colonic tissue and blood parameters of trinitrobenzene sulfonic acid (TNBS)-induced colitis in rats was investigated. It was found that UDO decreased levels of pro-inflammatory cytokines, lactate dehydrogenase, triglyceride, and cholesterol, which were increased in colitis. UDO administration ameliorated the TNBS-induced disturbances in colonic tissue except for MDA. In conclusion, UDO, through its anti-inflammatory and antioxidant actions, merits consideration as a potential agent in ameliorating colonic inflammation [42].

A nettle (Urtica dioica) extract shows in vitro inhibition of several key inflammatory events that cause the symptoms of seasonal allergies. These include the antagonist and negative agonist activity against the Histamine-1 (H(1))

receptor and the inhibition of mast cell tryptase preventing degranulation and release of a host of pro-inflammatory mediators that cause the symptoms of hay fevers[43].

the cellular response of mononuclear cells, polymorphonuclear cells and mast cells was examined in six people 5 min and 12 h after nettle contact. These results suggest that part of the immediate reaction to nettle stings is due to histamine introduced by the nettle. However, the persistence of the stinging sensation might suggest the presence of substances in nettle fluid directly toxic to nerves or capable of secondary release of other mediators[44].

Protease activity
The inhibitory effect of stinging nettle leaf extract on the protease activity of botulinum neurotoxin type A and B light chains was investigated. Results demonstrated that a water-soluble fraction obtained from the nettle leaf infusion inhibited type A, but did not inhibit type B light chain protease activity. The inhibition mode of water soluble fraction against protease activity of type A light chain was analyzed and found to be a non-competitive[45].

Analgesic effect
The antioxidant properties of nettle (Urtica dioica L.) WEN were evaluated Those various antioxidant activities were compared to standard antioxidants such as butylatedhydroxyanisole (BHA), butylated hydroxytoluene (BHT), quercetin, and alpha-tocopherol. In addition, total phenolic compounds in the WEN were determined as pyrocatechol equivalent. WEN also showed antimicrobial activity against nine microorganisms, antiulcer activity against ethanol-induced ulcerogenesis and analgesic effect on acetic acid-induced stretching[46].

Anti-Fungal properties
The plant chitinases Urtica dioica agglutinin (UDA) and Arabidopsis thaliana Chia4 (ATCHIT4) proteins were over-expressed in bacteria and the interaction between these proteins and P. françai surface was analyzed by immunocytochemistry. it showed that UDA and ATCHIT4 proteins can interact with surface-exposed chitin from P. françai[47].

Modulatory effect
The effects of two doses of an ethanol-water (80%-20%) extract of Urtica dioica L. and butylatedhydroxyanisole (BHA) were investigated for antioxidant enzymes. The extract was effective in inducing GST, DTD, SOD and CAT activity in the forestomach and SOD and CAT activity in the lung at both dose levels. BHA-treated Swiss albino mice induced DTD, GST and all antioxidative parameters in the kidney, lung and forestomach[48].

Cardiovascular effects
a possible direct cardiovascular action of the plant was evaluated . The same fraction produced a marked decrease of inotropic activity, in spontaneously beating atria of guinea-pig, and a marked, but transient, hypotensive activity on the blood pressure of anaesthetized rats. It is concluded that U. dioica can produce hypotensive responses, through a vasorelaxing effect mediated by the release of endothelial nitric oxide and the opening of potassium channels, and through a negative inotropic action[49].

The specific cardiac and vascular effects of AEN was assessed .the findings indicate that AEN produces a vasoconstriction of the aorta which is due to activation of alpha1-adrenergic receptors. However, AEN also induces a strong bradycardia through non-cholinergic and non-adrenergic pathways which might compensate for its vascular effect and account for the hypotensive action of Urtica dioica L described in vivo[50].

Anti-cancer effect
the cytotoxic and apoptotic effects of Urtica dioica was examined in MDA-MB-468, human breast adenocarcinoma cells. The result showed that the induction of apoptosis was the main mechanism of cell death that induce by Urtica dioica extract. Besides, it was suggested that urtica dioica dichloromethane extract may contain potential bioactive compound(s) for the treatment of breast adenocarcinoma[51].

Extracts from the roots of the stinging nettle (Urtica dioica) are used in the treatment of benign prostatic hyperplasia. It inhibited the binding of 125I-SHBG to its receptor. The inhibition was dose related, starting at about 0.6 mg/ml and completely inhibited binding at 10 mg/ml[52].

Histological and hypsometrical results showed that dorsal and lateral type 1 and 2 lobes were not changed significantly but the ventral and anterior lobes have changed significantly. Over all, the nettle root could prevent from some of prostatic hyperplasia effects, so that percentage of folded alveoli in ventral lobe reduced insignificantly[53].

The effects of stinging nettle (Urtica dioica L.) (UD) on benign prostatic hyperplasia (BPH) induced by testosterone investigated. Measurement of prostate/body weight ratio, weekly urine output and serum testosterone levels, prostate-specific antigen levels (on day 28) and histological examinations carried out on prostates from each group led us to conclude that UD can be used as an effective drug for the management of BPH[54].

ADA inhibition by Urtica dioica extract might be one of the mechanisms in the observed beneficial effect of Urtica dioica in prostate cancer[55].

The activity of a 20% methanolic extract of stinging nettle roots (Urtica dioica L., Urticaceae) on the proliferative activity of human prostatic epithelial (LNCaP) and stromal (hPCPs) cells was evaluated. The antiproliferative effect of ME-20 of stinging nettle roots observed both in an in vivo model and in an in vitro system clearly indicates a biologically relevant effect of compounds present in the extract[56].

Cytotoxic effects of Urtica dioica extract were assessed. the herbal extract was shown to be able to induce apoptosis in prostate cancer cells. findings also demonstrated that the plant extract substantially increases the caspase 3 and 9 mRNA expression, while decreases Bcl-2. Cell cycle arrest was occurred in G2 stage, due to the results of flow cytometry. These results indicate that dichloromethanolic extract of Urtica dioica can successfully induce apoptosis in PC3 cells. Therefore, it could be used as a novel therapeutic candidate for prostate tumor treatment[57].

Herbicidal effects

The effect of four pyrazine derivatives on the content of phenolic compounds in Urtica dioica L. and rutin in FagopyrumesculentumMoench was studied. A slight weight reduction of above ground biomass was shown only after application of Si and S2. Dark necrosis on the edges and center of the leaves was observed in all treated plants after pyrazine application. The results suggest that all the pyrazine derivatives possess herbicidal effects[58].

Adipogenesis effect

The effects of Urtica dioica L. (UT) was examined on adipocytes. In adipocytes, the ability of UT to antagonize the negative effects of FFA by modulating ceramidase activity and ceramide accumulation is dependent on the presence of adiponectin. However, the ability of UT to enhance Akt phosphorylation is independent of adiponectin expression. These studies demonstrate direct effects of UT on adipocytes and suggest this botanical extract is metabolically beneficial[59].

CONCLUSION

Urtica dioica L.is used for the treatment of various diseases. Due to its remarkable power of healing, this plant has got the place among the top ranked evidence based herbal medicines. This is also revealed that most of the therapeutic properties of this plant are due to the presence of linoleic acid which is major bioactive component of the essential oil. The present review is an effort to provide a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of this plant.

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