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***Urtica dioica* Improves Glucose Control in Diabetes on the Basis of Animal Studies**

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A comprehensive review on the *Urtica dioica* (common nettle) was recently published (Mehri *et al.*, 2011) that revealed a lot of information about its efficacy and safety for management of type 2 diabetes and its complications. *Urtica dioica* has a long use tradition as an expectorant, antidiarrheal and for treatment of menstrual, hemorrhage, diabetes, rheumatism, eczema and anemia. Although at present, nettle root has a prominent position for treatment of Benign Prostatic Hyperplasia (BPH) (Akbay *et al.*, 2003), several beneficial medical properties are currently attributed to this plant, such as antidiabetic, anti rheumatoid arthritis or osteoarthritis and diuretic (Chrubasik *et al.*, 2007).

On the basis of Mehri *et al.* (2011) review, the most animal studies are in favor of benefits of *U. dioica* in diabetes, but only one human study showed efficacy of this herb when used in combination in the form of Glucoselevel tablets. Moreover, one case study has been reported about hypoglycemia after taking herbal remedy for benign prostatic hypertrophy (Edgcumbe and McAuley, 2008). Nevertheless, latest researches on the pharmacological effects of isolated compounds from *U. dioica* support these findings (Chrubasik *et al.*, 2007). In the recent year, dietary polyphenolic phytochemicals have received considerable recent attention as alternative candidates for treatment of diabetes (Rahimi *et al.*, 2005; Momtaz and Abdollahi, 2010) and evidences confirm that *U. dioica* is a rich source of polyphenolic compounds (Chrubasik *et al.*, 2007). One of the main bioactive isolated phenolic Compounds, Chlorogenic Acid (CGA), from this plant has been found as a potent hypoglycemic (Karthikesan *et al.*, 2010) agent and antioxidant (Kahkonen *et al.*, 2001). CGA can decrease the blood glucose levels and inhibit glucose-6-phosphatase (G-6-Pase), the key enzyme that catalyzes the final step of glycogenesis (release of glucose from the liver) (Hoseini *et al.*, 2006) and gluconeogenesis (promotes the uptake of glucose by liver cells) and regulate overproduction of both glucose by inhibiting G-6-pase; thereby it controls glycemic status in type 2 diabetes (Karthikesan *et al.*, 2010). Moreover, some flavonol glycosides have been found in this plant such as rutin that may potentially play a positive role in carbohydrate metabolism and protection of the functional β -cells to increase secretion of insulin from islets in diabetes (Prince and Kamalakkannan, 2006). Furthermore, compounds that structurally related cyclical peptides have shown to facilitate glucose uptake by forming unique glucose permeable pores (Domola *et al.*, 2010).

Consideration all these findings, as well as data in the review by Mehri *et al.* (2011), it is apparent that *U. dioica* can decrease blood glucose by several mechanisms including pancreatic and extra pancreatic mechanisms especially antioxidant potentials (Hasani-Ranjbar *et al.*, 2009). Despite its protective functions, few accessible research data showed that *U. dioica* causes some side effects in the kidney and liver (Mehri *et al.*, 2011). Probably some compounds in *U. dioica* can cause kidney and other internal organs damage. For instance, one investigation on Chinese herbal medicine indicated that CGA induces liver and kidney injury in dogs (Li *et al.*, 2010). However,

Setarud (IMOD)TM that is a combination of *Urtica* and two other extracts has shown antidiabetic activity (Mohseni-Salehi-Monfared *et al.*, 2010) without any serious side effects (Khairandish *et al.*, 2009) or genotoxic adverse effects (Khorram Khorshid *et al.*, 2008).

Although, there is no evidence that *U. dioica* directly produces renal or hepatic toxicity in human, but it should be standardized on the basis of active compounds and for more information on toxic doses and mechanisms. Therefore, high-profile animal and clinical studies should be planned. As combined herbal formulation containing nettle has been shown to be effective and safe for control of hyperglycemia (Said *et al.*, 2008), type 2 diabetic patients can receive them as a supplement and regularly renal and hepatic function can be monitored in these patients.

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