

Case Report

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The Use of *Urtica dioica* (Stinging Nettle) as a Blood Sugar Lowering Herb: A Case Report and a Review of the Literature

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ABSTRACT

Introduction: Medicinal plants have been used in traditional medicine to manage blood sugar levels in patients with diabetes, but only a few of them have received scientific investigation. Many patients tend to self-medicate with herbal supplements, based on information they obtain from various sources.

Case Summary: A 57 year-old African-American male with diabetes had been prescribed metformin. He started on his own taking Stinging Nettle concurrently with metformin, which led to hypoglycemia. He then stopped taking metformin and continued with the herb. His morning fasting blood sugar stayed at less than 120 mg/dL. Because of accessibility, several months later he then discontinued taking Stinging Nettle, at which time his blood glucose level climbed up to 140-160 mg/dL. At this point, he saw his healthcare provider who put him back on metformin, and his blood glucose was well managed after that.

Conclusion: A systematic literature evaluation on Stinging Nettle showed some evidence of the blood sugar lowering effect of the plant. The patient in this case may have benefited from this property of the plant. Considering poor regulation and the possible variation of herbal supplement products in the market, routine use of Stinging Nettle should not be encouraged. However, there is some evidence on the blood lowering property of Stinging Nettle.

KEYWORDS: *Urtica dioica*; Stinging nettle; Diabetes.

ABBREVIATIONS: PPAR: Peroxisome Proliferator-Activated Receptor; TZDs: Thiazolidinediones; SGOT: Serum Glutamic Oxaloacetic Transaminase; HbA1c: Glycated hemoglobin; IL-6: Interleukin 6; TNF-alpha: Tumor Necrosis Factor-alpha; hs-CRP: High Sensitive C-Reactive protein.

INTRODUCTION

Diabetes mellitus affects over 250 million people worldwide and is expected to affect some 380 million by 2025.¹ Each year another 7 million people develop diabetes. The first line treatment for type 2 diabetes is diet, weight control and physical activity. If blood glucose level remains high despite a trial of these lifestyle measures, then medications are usually advised. Although, there are many effective drugs available on the market, the majority of persons with type 2 diabetes eventually fail to respond to a commonly used first-line oral medication (e.g. metformin). There are several categories of drugs for type 2 diabetes, including sulfonylureas, biguanides, thiazolidinediones, meglitinides, dipeptidyl peptidase IV, insulin, etc. Finding an effective alternative oral treatment to avoid administration of exogenous insulin and/or other therapies by daily needle injection would be desirable. Some persons with diabetes continue to self-medicate with alternative products such as herbs and other supplements.

The blood glucose lowering effect of Stinging Nettle has been noted in old writings.

Recently, some investigations have reported on the hypoglycemic effect of *Urtica dioica*, but so far, the mechanism of this effect has not been deduced. Some studies show that it may work as a secretagogue, or as a Peroxisome Proliferator-Activated Receptor (PPAR) agonist. PPAR agonists are drugs that lower blood glucose level by enhancing insulin secretion by Langerhans Islets.

CASE REPORT

A 57 year-old African-American contacted our drug information center regarding the use of Stinging Nettle in lowering his blood sugar. The caller admitted to having a history of diabetes mellitus and had been on metformin 500 mg twice daily for a few years prior. His other medications included aspirin 81 mg daily, metoprolol 50 mg twice daily, and atorvastatin 40 mg once daily. He started using Stinging Nettle about a year or so ago previously. He prepared a tea by boiling the fresh leaves in hot water and straining out the leaves. He consumed the hot tea once daily in the morning. After experiencing a few hypoglycemic episodes, he stopped taking metformin, but continued taking the herb. His follow up self-reported average morning fasting blood glucose was less than 120 mg/dL. After about 9 months, he moved to another city and stopped taking the herb because he was not able to get the fresh leaves anymore. Within 2 months, his blood glucose level started to rise to a range of 140-160 mg/dL. At the time of his call to our center, he was put back on metformin. The patient stated that his current metformin dosage regimen at the time he contacted us was 500 mg three times daily, which resulted in good blood sugar control. In a follow up call in preparation for this publication, the patient also admitted that after he moved to the new city, he has not been exercising as much. No other lab data or medical record was available for review. We now provide a critical review of the published literature to assess the potential therapeutic value of Stinging Nettle as a natural product with blood glucose lowering properties.

DISCUSSION

Urtica dioica L. (Family: Urticaceae)²

Stinging Nettle is a small plant that has fine hairs on the leaves and stems. The scientific name for the plant is *Urtica dioica*. The genus name *Urtica* comes from the Latin verb *urere* that means, "to burn" because of these stinging hairs. The species name *dioica* means "two houses" because the plant usually contains either male or female flowers. 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, serotonin, and choline that produce a stinging sensation when they come into contact with humans and other animals.³ The plant has been used for hundreds of years as a diuretic and to treat painful muscles and joints, eczema, and arthritis. Today, many people use Stinging Nettle to treat benign prostatic hyperplasia. Stinging nettle prod-

ucts are usually made from the leaves and stems, and sometimes from the roots. (Figure 1)



Figure 1: *Urtica dioica* (stinging nettle).

LITERATURE REVIEW

Medicinal plants have been a repository of a wide variety of biologically active compounds for many centuries but are still largely unexplored.⁴ More than 400 traditional plants have been recorded with antidiabetic effects, but very few of these traditional plants have received proper scientific or medical investigation.⁵ It is estimated that today, plant materials are present in, or have provided models for development of about half of the Western drugs.⁶ Because of their perceived effectiveness, minimal side effects in clinical experience and relatively low cost herbal drugs are prescribed widely even when their biologically active compounds are unknown.⁷

Several studies suggest that the Stinging nettle works as a PPAR gamma agonistic and alpha-glucosidase inhibitory agent.^{8,9} The two most common receptor targets for a number of PPAR agonist marketed drugs are PPAR-alpha and PPAR-gamma receptors. PPAR-alpha receptors are the main target for fibrate drugs used in reducing triglycerides, while PPAR-gamma receptors are the main target of the drug class of Thiazolidinediones (TZDs) used for blood glucose lowering in persons with diabetes mellitus.

Pancreatic α -amylase and intestinal α -glucosidase are enzymes that play major roles in the digestive system in catalyzing starch by hydrolyzing the α -1,4-glucoside linkages. The inhibition of these enzymes significantly decreases the digestion and uptake of carbohydrates, thereby decreasing the postprandial blood glucose level in persons with non-insulin dependent diabetes mellitus.⁸ Drugs such as acarbose, miglitol and voglibose are currently used as α -glucosidase and α -amylase inhibitors. The main drawback of these drugs is that their hypoglycemic effect is lower than that of other oral antidiabetic agents, including sulfonylureas. They are therefore recommended as add-on therapy only. Another drawback of these agents is their side effects such as abdominal distention, bloating, flatulence and possibly diarrhea if not titrated up slowly.¹⁰ It has been suggested that the gastrointestinal effects might be caused by the excessive inhibition of the pancreatic α -amylase, leading to the abnormal bacterial fermentation of undigested carbohydrates in the colon.¹¹ It has been postulated that natural products such as Stinging Nettle that have been shown to possess a low inhibitory effect against α -amylase and high inhibitory activity against

α -glucosidase can be used as an effective means to reduce postprandial hyperglycaemia with minimal adverse effects.¹²

One of the most recent studies published in the use of Stinging Nettle in lowering blood sugar was done by Kianbakht, et al.⁹ The authors conducted a randomized double-blind placebo-controlled clinical trial to evaluate the effects of taking Stinging Nettle leaf extract (one 500 mg capsule every 8 hours for 3 months) combined with the conventional oral anti-hyperglycemic drugs.⁹ The authors evaluated the effect of the extracts on the blood levels of fasting glucose, postprandial glucose, Glycated hemoglobin (HbA1c), creatinine, Serum Glutamic Oxaloacetic Transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and systolic and diastolic blood pressures. The clinical trial included 46 patients in the treatment arm and 46 patients in the placebo group. The results demonstrated that the extract significantly lowered the blood levels of fasting glucose. It was also shown that it decreases the 2-hour postprandial glucose level and HbA1c. However, there was no significant effect on the other parameters compared with placebo. The authors concluded that these results demonstrated that Stinging Nettle is safe and may have a beneficial effect on glycemic control in patients with advanced type 2 diabetes mellitus that typically require insulin therapy.

Another recent study in Iran on Stinging Nettle leaves has shown evidence that the plant may have potential in anti-diabetic therapy.¹³ In this study, the Stinging Nettle consisted of freeze-dried extract from 100 g of powdered dried leaves in 100 ml of water. The results showed time- and concentration-dependent inhibition of α -amylase. According to the authors, the Stinging Nettle extracts showed the same inhibitory pattern as that of acarbose, a known α -glycosidase inhibitor, which is only one among a class of drugs with similar activities. However, drugs in this class also act as strong competitive inhibitors of α -amylase. Acarbose, for example, is a well-known, natural product produced by several species of Actinoplanes. This compound has a pseudosugar ring and the glycosidic nitrogen linkage that mimics the transition state for the enzymatic cleavage of glycosidic bond and hence competitively inhibits α -amylase.¹⁴ In this study, the authors reported that a 0.4 mg/ml of Stinging Nettle leaf extract demonstrated a 60% inhibition of α -amylase activity. The level of inhibition was also time-dependent. The inhibitory effect increased from 40% at 5 minutes to 60% at 30 minutes.

A study in 2011 by Namazi, et al. evaluated the effect of hydroalcoholic extract of Stinging Nettle on insulin sensitivity and some inflammatory indicators on a cohort with type 2 diabetes.¹⁵ Diabetes is a metabolic disorder that is strongly associated with micro-complications, such as retinopathy, nephropathy, and neuropathy and macro-complications including cardiovascular risk. Inflammation is a potential risk factor for diabetic complications particularly cardiovascular disease. These anti-inflammatory indicators were measured in this study along with insulin sensitivity. The study was a randomized double-blind

clinical trial and included 50 men and women with type 2 diabetes. The study was done over 8 weeks. The authors adjusted the study participants for age, sex and duration of diabetes, and then randomly assigned them into two groups, an intervention and a control group. The treatment groups received 100 mg/kg body weight nettle extract or placebo in three portions a day for 8 weeks. The parameters measured included Interleukin 6 (IL-6), Tumor Necrosis Factor-alpha (TNF-alpha), high sensitive C-Reactive protein (hs-CRP), and fasting insulin concentration. The researchers calculated Insulin Sensitivity, at the beginning and the end of the study. After 8 weeks, IL-6 and hs-CRP showed a significant decrease in the intervention group compared to the control group ($p < 0.05$). The findings showed that the hydro-alcoholic extract of Stinging Nettle lowered the inflammatory markers, IL-6 and hs-CRP, in patients with type 2 diabetes after eight weeks intervention.

A study by Ahngarpour, et al. showed the effect of hydro-alcoholic extract of Stinging Nettle on fructose-induced insulin resistance rats.¹⁶ Forty male Wistar rats were randomly divided into five groups: 1) Control; 2) Fructose; 3) Extract 50; 4) Extract 100; and 5) Extract 200. The control group received vehicle. The fructose and extract groups received fructose 10% for eight weeks. The extract groups received single daily injection of 50, 100 or 200 mg/kg/day of extract for the two weeks. The results showed that the extract groups had a significant reduction in serum glucose and insulin levels. The study also showed a reduction in LDL. Leptin and LDL/HDL ratio. The authors concluded that Stinging Nettle extract decreases serum glucose, and thus may be useful for treatment of type 2 diabetes. They also speculated that Stinging Nettle might improve metabolic syndrome by the positive effect shown on lipid profile and also by lowering effect on leptin levels.

SAFETY AND ADVERSE EFFECTS

Stinging Nettle is relatively a safe plant if used appropriately. The major adverse effect that has been documented in animal studies is that it lowers blood pressure and heart rate.¹⁷ Those with heart conditions should seek the advice and supervision of a health practitioner to determine if the herb is suitable for their condition. Nettle has been documented to have diuretic effects. Thus, chronic use of this plant may be contraindicated in various medical conditions where diuretics are not advised. Because of the herb's diuretic effects, it may enhance the effect of blood pressure medications including ACE inhibitors, beta-blockers, or calcium channel blockers. It can also increase the effects of other diuretics, including thiazides and loop diuretics, thus raising the risk of dehydration and electrolyte disturbances.¹⁸

Other occasional side effects include mild stomach upset, fluid retention, sweating, diarrhea, and hives or rash (mainly from topical use). It is important to be careful when handling the nettle plant because touching it can cause an allergic rash. Stinging Nettle should never be applied to an open

wound. Because, Stinging Nettle can alter the menstrual cycle and may contribute to miscarriage, pregnant women should not use Stinging Nettle.

LIMITATIONS

Detailed medical history and complete demographic data of the patient were not collected. The amount of Stinging Nettle leaves used by the patient each time to prepare tea was not obtained. In the literature reviewed in this paper, there are no reported large multi-center and placebo-controlled studies on the benefits of the Stinging Nettle in patients with diabetes. However, based on the studies reviewed, the plant may have some potential benefits in this patient population. Further studies involving a large number of patients are required to confirm the benefits.

BENEFITS

If patients choose to use Stinging Nettle for management of diabetes on their own initiative, they should be encouraged to monitor their blood sugar very closely. In addition, they should also be advised to notify their physician of such use. The herb is also rich in vitamins A and C, iron, potassium, manganese, and calcium. It has a flavor similar to spinach and cucumber when cooked. In its peak season, Stinging Nettle contains up to 25% protein, dry weight, which is high for a leafy green vegetable.¹⁹ Soaking Stinging Nettles in water or cooking removes the stinging chemicals from the plant, which allows them to be handled and eaten without injury.

CONCLUSION

Following a call to our drug information center by a patient regarding the use of Stinging Nettle for treating diabetes, we conducted a review of the literature on medicinal properties of Stinging nettle. Previously published small human clinical trials suggest that the plant may be considered for investigation as a natural product source of a novel as-yet-unidentified active compound with glucose lowering activity.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONSENT

The patient has provided written permission for publication of the case details.

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