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The Effect of Extract of U. Pilulifera on Some Kidney Parameters of Diabetic Rats

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ABSTRACT
Diabetes is associated with health impacts and several organs are negatively affected by diabetes including kidneys. Various herbal remedies have been used to treat diabetes. U. pilulifera is one of herbal treatments for diabetes. The main objective of the present study isto investigate the therapeutic potential of U. pilulifera in offering kidney protection through assessment of urea, uric acid and creatinine. Methodology included collection of U. piluliferaand preparation of its extracts, induction of diabetic model and biochemical evaluation of urea, uric acid and creatinine tests. Study findings showed that levels of urea, uric acid and creatinine were significantly increased in diabetic group (P <0.05). Therapeutic options using the extract of U. pilulifera were able to significantly decrease the levels of urea, uric acid, andcreatine (P <0.05).
Taken together, experimental diabetic model showed negative impacts on kidney function tests urea, uric acid and creatinine. Using the extract of U. pilulifera showed significant restoring ability to restore kidney function tests to levels approximate to reference range. Taken together, the extract of U. pilulifera has a potential therapeutic option to be used in diabetic patients with renal impacts.

KEYWORDS: diabetes, kidney function test, urea, uric acid, creatinine, *U. pilulifera*

I. INTRODUCTION

Diabetes mellitus is viewed as chronic metabolic disorders with various impacts onhuman health from physical, psychological and social points of view. Furthermore, it is characterized by several metabolic disturbances including hyperglycemia, altered metabolism of lipids, carbohydrates and proteins[11]. According to study of Chauhan et al (2010), diabetes mellitus is considered the third "killer" of the health of human besides cancer, cardiovascular and cerebrovascular diseases. Epidemiological studies showed that there are more than 240 million diabetics worldwide of whom about 40% develop severediabetic nephropathy. [2]
Several studies have revealed that diabeticexperimental models including STZ models increased the levels of serum blood urea nitrogen (BUN) and serum uric acid. [1,12] It has also been reported that STZ displays nephrotoxic and hepatotoxic activity as well asnecrosis of kidney tubules.[8]

Diabetic nephropathy (DN) leads to what is called asymptomatic kidney failure which may cause narrow and clogged glomerulus. Accordingly, waste products are not likely to be excreted which may lead to cytotoxicity.[7] Jonasson et al (1984) showed that diabetes leads to decreased nerve sensitivity manifested by

response to a filled bladder and the resultingpressure can cause deterioration to kidneys. Because of high sugar concentration, urinary tract infections are likely to occur.

Diabetic patients who developed kidney failureusually have bad choices including painful dialysis or kidney transplantation, both are costly and harmful.[10] Researchers have attempted to develop medications hoping to decline the progression of diabetic kidney damage with less side effects, but no significant outcome are reached.[7] According tothis context, there has been a need to explore more therapeutic options in complementary and alternative medicine that may have potent antidiabetic as well as nephroprotectiveactivity with fewer side effects.[7]

Several studies across literature have emphasized that diabetes is associated or lead to increased measures of urea, uric acid, and creatinine. These studies also pointed to thepower of some herbal remedies known to have antidiabetic activities to ameliorate the impactsof diabetes through restoring the values of urea, uric acid, and creatinine to levels approximate to reference range. [5,7,14]

Momordica dioica was investigated for itseffects as antidiabetic agent by Gupta et al (2011). Researchers reported nephroprotective effects of *Momordica dioica* in addition to restoring levels of urea, uric acid and creatinine. Similar findings have been obtainedusing *Olea europaea L* and *Gymnemamontanum* . [5,14] Another study by Basha et al (2011) pointed to protective effects Annona squamosa extract against diabetic STZ model.

In the present study, *Urtica pilulifera* was chosen to investigate the effects of its extract as an antidiabetic agent. The rational beyond selection of *U. pilulifera* is due to its involvement in folk medicine, and there is a need to investigate some of its chemical and pharmaceutical properties.

II. STUDY OBJECTIVES

The main objective of the present study is to investigate the therapeutic potential of *U. pilulifera* in offering kidney protection throughassessment of urea, uric acid and creatinine

III. STUDY HYPOTHESIS

There is a body of existing literature pointing to the therapeutic potential of herbal treatmentsto decrease impacts of diabetes on kidneys through restoring kidney function tests (urea, uric acid and kidney) to levels approximate to reference ranges.
According to this context, it is hypothesized that *U. pilulifera*, a herbal treatment used by people to treat diabetes, will offer nephrotectic protection and lower the kidney function tests significantly as compared with control group.

IV. METHODOLOGY

Methodology included collection of *U.pilulifera* and preparation of its extracts, induction of diabetic model and biochemical evaluation of urea, uric acid and creatinine tests.

Collection of *U. pilulifera* and preparation of its extraction

U. pilulifera leaves were collected fromappropriate areas at Jordan, air-dried in shadewell-ventilated area and then ground into finepowder. About 350 g of powder was put in aSoxhlet cold extractor using absolutemethanol as solvent and remained for threeconsecutive days (Sadki et al., 2001). Theextract was concentrated to dryness in rotaryevaporator under reduced pressure andcontrolled temperature (45°C) to yield an11.4% viscous greenish-colored extract. Theextract was kept at 4°C in a glass containeruntil use. Wister rats were used in this study, inwhich their average weight was 170 g. Theanimals were carefully checked and monitoredevery day for any changes. After determinationof lethal dose (LD50), two doses wereselected 1.25 g/kg and 1.88 g/kg of bodyweight. Doses were prepared throughdissolving required amount of the viscousextract in 10 mL Tween-20: 0.9% NaCl (1:9,V/V).

Diabetic model

Diabetes was induced employing alloxan so that rats were injected by alloxan monohydrate"B.O.H chemical LTD England" intraperitoneally at a dose of 150 ml/kg body weight (dissolved in fresh normal saline) to 18 hr fasted rat. Rats were monitored for blood glucose and rats with blood glucose level over 200 mg/ml, were considered diabetic and employed in the study. Animals were assigned into the following groups:

Group I: control group; Group II: diabetic group; Group III: diabetic treated with 1.25mg/kg of body weight; Group IV: diabetic treated with 1.88 mg/kg of body weight.

Statistical analysis

Data analysis was carried out using SPSS 20. Data were presented as mean and standard deviation. T test was used to investigate the difference between kidney function tests in study groups. Significance level was considered at alpha level ≤ 0.05.

V. RESULTS

The concentration of urea in study groups

As shown in table 1, the mean concentration of urea in control group was 26.92 $\pm$ 1.83 mg/dl. The concentration of urea increased significantly (P <0.05) in diabetic group 39.62 $\pm$ 3.16 mg/dl. Diabetic group that was treated with the extract of *U. pilulifera* (1.25 mg /kg) had significant decreased concentration of ureacompared with diabetic group (25.52$\pm$ 1.62 mg/dl; P <0.05). Treatment using higher dose of the extract of *U. pilulifera* also decreased the concentration of urea significantly compared with diabetic group (28.32 $\pm$ 2.41 mg/dl; P < 0.05).

The concentration of uric acid in study groups

As shown in table 1, the mean concentration ofuric acid in control group was 1.61 $\pm$ 0.22 mg/dl. The concentration of urea increased significantly (P <0.05) in diabetic group 2.34 $\pm$ 0.16 mg/dl. Diabetic group that was treated with the extract of *U. pilulifera* (1.25 mg /kg) had significant decreased concentration of uric acid compared with diabetic group (1.42$\pm$ 0.06 mg/dl; P <0.05). Treatment using a higher doseof the extract of *U. pilulifera* also decreased the concentration of uric acid significantly compared with diabetic group (1.62 $\pm$ 0.12 mg/dl; P < 0.05).

The concentration of creatinine in study groups

As shown in table 1, the mean concentration of cratinine in control group was 0.98 $\pm$ 0.08 mg/dl. The concentration of cratinine increasedsignificantly (P <0.05) in diabetic group 2.16 $\pm$ 0.12 mg/dl. Diabetic group that was treated with the extract of *U. pilulifera* (1.25 mg /kg) had significant decreased concentration ofcratinine compared with diabetic group (1.39$\pm$ mg/dl; P <0.05). Treatment using higher dose of the extract of *U. pilulifera* alsodecreased the concentration of cratininesignificantly compared with diabetic group (1.26 $\pm$0.14 mg/dl; P < 0.05).

Table 1: Concentration of Urea, Uric acid and Creatinine in study groups

Gr	Treatment	Urea (M$\pm$ SD) (mg/dl)	Uric acid (M$\pm$ SD) (mg/dl)	Creatinine (M$\pm$ SD) (mg/dl)
I	Control	26.92 $\pm$ 1.83	1.61$\pm$ 0.22	0.98 $\pm$ 0.08
II	Diabetic (alloxan)	39.62 $\pm$ 3.16*	2.34 $\pm$ 0.16*	2.16$\pm$ 0.12*
III	Treated group (1.25 mg/kg)	25.52$\pm$ 1.62**	1.42 $\pm$ 0.06**	1.39 $\pm$ 0.06**
IV	Treated group (1.88 mg/kg)	28.32 $\pm$ 2.41**	1.62 $\pm$ 0.12**	1.26 $\pm$ 0.14**

VI. DISCUSSION

We conducted the present study to investigate the effects of the extract of *U. pilulifera* on reducing the impacts of diabetesin kidneys. We depended on experimental diabetic model.

The data of the present study showed that all kidney function tests under study, urea, uric acid and creatinine were significantly ($P<0.05$)increased in diabetic group compared with control group. These findings are within the context of other studies in which it has been demonstrated that diabetic models were accompanied with increased levels of serumblood urea nitrogen (BUN) and serum uric acid(Piyachaturawat, Poprasit, Glinsukon, 1991; Asayama et al., 1994). It has also beenreported that STZ displays nephrotoxic and necrosis of kidney tubules (Hasan et al., 1999).

The data of the present study demonstrated thattreatment using the extract of *U. pilulifera* for one month was able to reverse the impacts of diabetes on kidneys of diabetic rats. Using either dose of *U. pilulifera* was able to restore all kidney function tests under study urea, uric acid and creatinine to levels approximate tonormal levels. These variations among treated groups and diabetic groups were statistically significant ($P <0.05$). These findings are consistent with other studies in which various herbal treatments were used to treat diabetes and resulted in positive outcomes in improvingkidney function tests. Gupta et al (2011) reported positive outcomes of kidney function tests by using *Momordica dioica*. Other researchers reported similar findings using *Olea europaea L*, *Gymnema montanum*, and *Annona squamosa* (Eidi et al., 2009; Ramkumar et al., 2009; Basha et al., 2011).

VII. CONCLUSION

Experimental diabetic model showed negative impacts on kidney function tests urea, uric acidand creatinine. Using the extract of *U. pilulifera* showed significant restoring ability to restore kidney function tests to levels approximate to reference range. Taken together, the extract of *U. pilulifera* has a potential therapeutic option to be used in diabetic patients with renal impacts.

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