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Antihyperglycemic Effect of Aqueous Extract of *Urtica dioica* L. Leaves Growing in Kurdistan Region-Iraq

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THE primary aim of this investigation is to assess the effect on diabetes of *U. dioica* L. in rats with diabetes induced by alloxan. Male albino rats were assigned randomly to 3 groups: normal control rats; diabetic rats administered 500 mg/kg BW of *U. dioica* aqueous extract for 30 days, and diabetic rats induced by intraperitoneal alloxan injection (110 mg/ kg b. w). Serum fasting blood glucose level, lipid profile, liver and kidney parameters as well as body weight (BW) and relative weight of kidney, heart and liver were determined.

The findings of this research conducted that when a diabetic group received 500 mg/kg BW of *U. dioica* leaves water extract., their BW and relative kidney to BW both increased significantly ($P < 0.05$), while their serum fasting glucose level (FBG) decreased significantly ($p < 0.0001$). Moreover, the extract had no statistically significant effects on triglycerides (TG), very low-density lipoprotein (VLDL), or high-density lipoprotein (HDL) at ($P > 0.05$) in comparison to diabetic rats' group, but significantly decreased serum cholesterol (TC) and low-density lipoprotein (LDL) at ($P < 0.05$). Concentrations of S.GOT, S.GPT, and S. urea rose before returning to normal. Our results showed that water extract of *U. dioica* L. made improvements to hyperglycemia, hyperlipidemia, liver enzymes, and renal function.

Keywords: Alloxan, Blood glucose, Lipid profile, Liver function, Diabetes mellitus, *Urtica dioica* L.

Introduction

The most prevalent chronic disease in the world, diabetes (known as hyperglycemia), is characterized by either insulin insufficiency, insulin resistance, or both [1] . Hyperglycemia, which affects several organs and interferes with the metabolic pathway of proteins, lipids, and carbohydrates, is the primary indicator of diabetes [2]. According to the World Health Organization (WHO), there will be over 300 million diabetics globally by 2025. Even though this topic has received a lot of research, new approaches for diabetes early diagnosis, treatment, and prevention against complications are urgently required to enhance public health, minimize healthcare costs, and lower death rates [3].

According to researcher, diabetes is distinguished by high TG and LDL, and low HDL levels, hyperglycaemia, and a poor lipid metabolism [4]. Abdullah *et al.,* (2018) provided suggestions that hyperglycaemia and hyperlipidaemia should only affect oxidative stress, which damage cells in several organs; liver, pancreas, and kidneys [5]. In diabetic rats, it had been shown that the levels of serum liver enzymes; S-GPT, S-GOT, and ALP are elevated,

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indicating greater release from damaged hepatocytes as a result of peroxidation brought on by diabetes [6,7]. One of the primary consequences of metabolic syndrome is diabetic nephropathy, which is widely believed to be the principal contributor to end-stage of renal failure [8].

In recent years, a number of researchers have been captivated by the revelation and application of botanical extracts as substitutes for synthetic compounds, with the aim of discovering safer and more efficacious antihyperglycemic medications. The utilization of plants in the treatment of diabetes and its associated complications has already been explored [9]. Consequently, numerous investigations have effectively demonstrated the anti-hyperglycaemic activity of *U. dioica* L.

Urtica dioica L., sometimes known as the stinging nettle, is a perennial herbaceous flowering plant that is indigenous to Europe and Asia. Plant parts from the *U. dioica* L. species have been utilized to treat different diseases, including haemorrhage, arthritis, eczema, seasonal allergies, iron deficiency, and diarrhoea [10,11]. The *U. dioica* L. plant yields a wide range of important therapeutic chemical substances, including amino acids, chlorophylls, carbohydrates, carotenoids, essential fats, flavonoids, polyphenols, proteins, phytosterols, saponins, tannins, and rich in minerals, provitamin A, and vitamin C.

The major objective of this investigation is to find out whether a water extract of *U. dioica* L. leaves may prevent diabetes, lower cholesterol levels, and improve hepatic and renal function in normal and alloxan-induced diabetic rats.

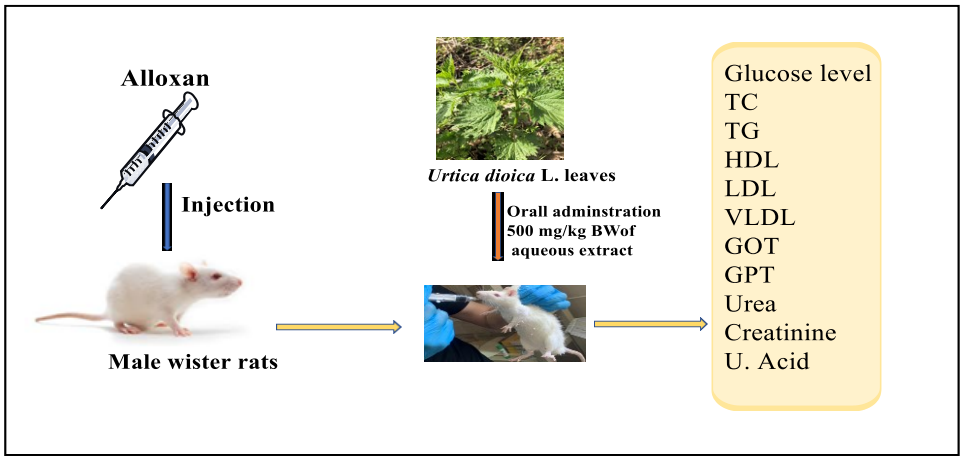

Fig. 1. The Experimental steps for administration of water extract of U. dioica L. in diabetic rats.

Material and Methods

Collection of Plant

Leaves of the *U. dioica* L. plant are collected in Zakho City, Kurdistan Region of Iraq, during April - May of 2021. After being cleaned with tap water, distilled water was used to rinse the leaves of *U. dioica* L. before they were left to air dry for 10 to 15 days in a dark place. After that, the leaves were grinded into a powder and stored in a deep freezer in dark containers until the day of usage. The highest purity reagents were used and they were all obtained from the Sigma Aldrich Company.

Fig. 2. Stinging nettle (*Urtica dioica* L.)

Methods

The process of preparing water extract of *U. dioica* L. leaves. Ten gram of leaves powder were put in a thimble, soaked in Soxhlet overnight, after that extraction is achieved by using 100 ml of distilled water for 10 h at 90 °C. By using a rotary evaporator, the extract was collected into conical flasks separately and concentrated at low temperature and lowered pressure. The dried extract is stored in the freezer until use [12].

Experimental animals

In the present study, a total of 18 males' albino rats (180-250 g) were recruited at the animal house of the faculty of science at Zakho University. Rats are kept under standardized conditions (temperature; 22 ± 3 °C and 12 h cycles of light and darkness), and they provided a standard diet [13]. The Research Ethics and Evaluation Committee of the Faculty of Science, Chemistry Department, Zakho University, approved the use of research animals.

Induction of experimental diabetes

The rats underwent a process of weighing and fasting blood glucose level measurement following an overnight fast that lasted between 12 and 16 h. To induce diabetes in the rats, a single intraperitoneal injection of alloxan monohydrate was administered at a dosage of 110 mg/kg BW. The procedure, as outlined by Šoltésová and Herichová [14] involved the fresh dissolution of alloxan in 0.5 ml of citrate buffer (0.1 M, pH 4.5) for each rat, in accordance with its weight prior to injection. After the administration of the medication, water and food were made available, and for 2 days, the animals were given a 5% glucose solution to counteract the hypoglycemic effects of the drug, as per Shaban et al., study [15]. Figure 2 depicts the experimental design, showcasing the effects of the water extract of *U. dioica* L. leaves on rats with alloxan-induced diabetes.

The initial diagnosis of diabetic rats was conducted through the observation of 2 symptoms, namely polydipsia and polyuria. Subsequently, a glucometer was utilized to measure their fasting blood sugar levels after a period of 72 h. To confirm the diabetic status of the rats, their fasting blood sugar levels were measured once more after duration of 7 days. Rats with fasting blood sugar concentration higher than 200 mg/dl were selected for the experiment.

Design of Experiments:

In the present investigation, a total of 18 rats were employed. The rats were randomly chosen for 3 groups, each consisting of 6 rats, as outlined below:

Group I: Normal rats (control) were subjected to standard conditions.

Group II: Diabetic control rats were subjected to intraperitoneal injections of alloxan monohydrate (110 mg/kg BW) and subjected to standard conditions.

Group III: Diabetic rats were orally administered *U. dioica* L. water extract (500 mg/kg b. w) on a daily basis for duration of one month [16].

The administration of the plant extract and collection of blood samples were carried out. The plant extract was prepared and dissolved in water, leaving no residue. The fully dissolved sample was then administered orally to the rats through an intra-gastric tube continuously for a period of 1 month. After that, blood samples were collected from the rat's tail vein on a weekly basis until the end of the experiments. The estimation of fasting blood glucose levels was conducted using an electronic glucometer on the 1st, 7th, 14th, 21st, and 30th days of the research. On the 30th day of the experiment, the overnight fasted rats were sacrificed under slight chloroform anesthesia. Blood was collected from the heart and placed in a serum-separating tube, which was left to clot for approximately 2 h. The clotted blood was then centrifuged at 3000 rpm for 15 min, and the resulting serum was stored in a freezer at -20 °C until the measuring of biochemical parameters.

The administration of the plant extract and the collection of blood samples were carried out in a methodical manner. The plant extract was prepared and dissolved in distilled water, ensuring that no residue was left behind. The dissolved sample is then orally administered to the rats using an intra-gastric tube continuously for a period of 30 days. Subsequently, blood samples were collected from the rat's tail vein on a weekly basis until the experiment is finished. The measuring of fasting blood sugar is conducted using an electronic glucometer on the 1, 7th, 14th, 21st, and 30th days of the experiment. On the 30th day of the experiment, the overnight fasted rats were sacrificed under slight chloroform anaesthesia. Blood was collected from the heart and placed in a serum-separating tube, which was left to clot for approximately 2 h. The clotted blood was then centrifuged at 3000 rpm for 15 minutes, then the resulting serum was stored in a freezer at -20 °C for measuring of biochemical parameters.

The quantification of animal BW and organ weight was carried out utilizing an electronic balance. The initial measurement of each rat's BW was taken at the onset of the experiment, and subsequently at the end of each week. Upon dissection of the animals and the collection of blood samples for biochemical assays, the liver, heart and kidney are extracted and weighed. The calculation of the relative organ weight is then determined utilizing a prescribed formula [17].

% Relative organ weight

$$= \frac{\text{absolute organ weight (gm)}}{\text{rat's BW on the sacrifice day (gm)}} \times 100$$

Determination of biochemical parameters

The biochemical parameters were assessed using Biolis 24i Premium automatic analysers (Tokyo Boeki) to determine the levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), glutamic pyruvic transaminase (GPT), urea, creatinine, and uric acid. All biochemical tests were conducted using viable kits and enzymatic methods.

Data analysis

Using SPSS software version 26, the data of fasting blood sugar, BW, relative organ weight to BW, and biochemical parameters are examined. The information was shown as Mean ± SE. One-way ANOVA is used for group-by-group comparisons, then by Tukey's post hoc test analysis. Statistical significance is determined at the $p < 0.05$ level, with a highly significant threshold of $p < 0.0001$.

Results

The impact of the aqueous extract derived from U. dioica L. *leaves on the fasting blood glucose levels of alloxan-induced diabetic rats:*

Rats were given a dosage of 110 mg/kg alloxan to start the diabetes induction process. Blood sugar levels were checked before taking alloxan and 1 week afterwards. Table 1 demonstrates how the treatment of alloxan caused a rise in fasting blood glucose that was around 3 times greater than in healthy rats. At the end of the study, the diabetic control rats' fasting blood glucose levels rose from 476.33 ± 39.01 mg/dl in the 1st week to 491.0 ± 32.62 mg/dl in the 5th. After receiving a daily oral dose of 500 mg/kg BW of *U. dioica* L. leaves an aqueous extract for 30 days as part of diabetes treatment, the group's blood sugar levels dropped from 361.03 33.61 mg/dl to 111.33 ± 5.04 mg/dl.

According to statistical analysis, the variance in blood sugar levels between the groups was significant at $p < 0.0001$. Throughout the experiment, the diabetic group's fasting blood glucose levels were significantly higher than those of the control group ($p < 0.0001$), whereas the treated diabetic group's fasting blood glucose levels were significantly lower than those of the untreated diabetic control group ($P < 0.0001$). On the 0 and 7th days, there was a significant difference in fasting blood glucose levels between the control groups and the treated diabetic groups, but on the 14th, 21st, and 30th days, there was no significant difference between the 2 groups ($P > 0.05$).

TABLE 1. The impact of orally administered aqueous extract of *U. dioica* L. leaves on the blood glucose level in alloxan-induced diabetic rats.

Groups	Concentration of fasting blood sugar (mg/dl)				
	Day 0	Day 7	Day 14	Day 21	Day 30
Control	104.50±2.60	91.83±4.95	97.16±4.62	98.16±5.84	100.66±2.60
Diabetic rats	476.33±39.01**	512.16±30.35**	478.33±34.82**	487.33±32.66**	491.00±34.62**
Diabetic +aqueous extract	361.0±33.61**,†	228.16± 35.67*††	158.83±9.30††	130.00±6.60††	111.33±5.04††
***P* value among three groups**	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001

The outcomes are exhibited as M ± SE for 6 rats in each group. Statistical significance was observed with *$P < 0.05$ in comparison to control group, ** $P < 0.0001$ in comparison to control group, † $P < 0.05$ in comparison to diabetic group, and †† $P < 0.0001$ in comparison to diabetic rats. The data is analyzed using ANOVA, following by Tukey's post hoc test.

The impact of the aqueous extract of U. dioica L. *on the BW of rats with alloxan-induced diabetes*

Each group's BW was assessed on days 0, 7, 14, 21, and 30. The BWs of the 3 groups displayed significant differences at a level of significance of $P < 0.05$, as indicated in Table 2. When compared to the control group on day 30, the untreated diabetic rats' BW did not significantly decrease ($P > 0.05$). Contrary to the untreated diabetic control rats, administration of the aqueous extract of *U. dioica* L. effectively prevented the loss of BW in the diabetic rats. As a result, at a level of significance of $P < 0.05$, a comparison between the healthy group and the treated diabetic group revealed a notable rise.

At a level of significance of $P > 0.05$, a comparison of the BWs of the diabetic and control rats revealed a substantial difference on days 0 and 7, but no noticeable change on days 14 and 21. On days 0 and 21, the treated diabetic group's BW significantly increased when compared to the diabetic control group, however on days 7 and 14, no significant change was seen at a level of significance of p $P > 0.05$.

TABLE 2. The effect of an oral aqueous extract of *U. dioica* L. leaves on BW in diabetic rats' group.

Groups	BW (g)					
	Day 0	Day 7	Day 14	Day 21	Day 30	Weight loss/gain
Control	180.16±0.16	186.83±0.83	198.0±4.21	194.50±3.66	210.0±1.84	29.83±1.81
Diabetic rat	252.33±2.02*	234.33±4.81**	227.0±5.81	215.0±5.92	203.33±9.03	-49±8.10
Diabetic rats+ aqueous extract	236.83±1.40*,†	241.0±7.85**	255.5±13.91*	274.5±17.08**,†	261.5±21.29*,†	26.16±18.91
***P* value among three groups**	$P < 0.0001$	$P < 0.0001$	$P < 0.007$	$P < 0.003$	$P < 0.03$	

The outcomes are exhibited as Mean ± SE for six rats in each group. Statistical significance was observed with * $P < 0.05$ in comparison to control group, ** $P < 0.0001$ in comparison to control group, † $P < 0.05$ in comparison to diabetic group, and †† $P < 0.0001$ in comparison to diabetic rats. The data is analyzed using ANOVA, following by Tukey's post hoc test.

The impact of the aqueous extract of U. dioica L. *on the relative weight of organs in rats induced with alloxan*

Based on the findings presented in Table 3, the impact of plant extracts on the relative weight of organs in alloxan-induced diabetic rats was assessed. According to the investigation's findings, there was no statistically significant difference between the research groups in terms of the relative weight of the heart ($P > 0.05$). Additionally, as compared to the normal control group and the treated diabetic group, the untreated diabetic group did not show a statistically significant decrease in the relative weight of the liver ($P > 0.05$). However, diabetic rats showed a considerable rise in the kidney's relative weight.

TABLE 3. The impact of the orally administered aqueous extract of *U. dioica* L. leaves on organ weight in rats with alloxan-induced diabetes.

Groups	% of relative organs to BW (%)		
	Heart	Liver	Kidney
Control (healthy rats)	0.33± 0.01	3.28 ± 0.15	0.40 ± 0.009
Diabetic rats	0.30 ± 0.02	2.99± 0.19	0.57 ± 0.03 *
Diabetic rats + aqueous extract	0.33 ± 0.01	3.21 ± 0.22	0.37 ± 0.01 *,†
P value among three groups	$P > 0.47$	$P < 0.53$	$P < 0.001$

The outcomes are exhibited as M± SE for 6 rats in each group. The statistical significance of the results was determined by comparing them to the control rats, denoted by *$P < 0.05$, and to the diabetic rats, denoted by †$P < 0.05$. The data was analyzed using ANOVA, following by Tukey's post hoc test.

The impact of the aqueous extract of U. dioica L. *on the lipid profile of rats induced with alloxan*

After a duration of 4 weeks, it was observed that diabetes-induced alloxan resulted in a significant increase in the levels of TC, TG, LDL, and VLDL, while the level of HDL was significantly reduced ($P < 0.05$), as demonstrated in Table 4. However, after a period of 30 days, a significant decrease in the levels of TC, TG, LDL, and VLDL was observed in treated diabetic rats, along with an increase in HDL, following a daily dosage of 500mg/kg BW of leaves *U. dioica* L. water extract ($P<0.05$). The change in serum TC levels in diabetic rats was notably higher than that of control rats ($P < 0.05$), and the level of serum TC in the treated-diabetic group was significantly reduced compared to the diabetic control group ($P < 0.0001$). There were no statistically significant variations in blood TC levels between the diabetes group treated with plant extract and the healthy control group when comparing the two groups ($P > 0.05$).

Furthermore, it was observed that the serum triglyceride (TG) levels in both diabetic and treated diabetic groups were substantially higher than control group ($P < 0.05$). When compared to the diabetic rats, the blood TG levels in the treated plant extract group did not vary significantly ($P > 0.05$). Additionally, as compared to control rats, diabetic rats had a significantly lower level of serum (HDL) and a higher amount of (VLDL) ($P < 0.05$). In contrast, while there were no statistically significant variations in serum HDL and VLDL levels between the diabetic group treated with the *U. dioica* extract and the diabetic control group, the VLDL level was considerably higher when compared to healthy rats ($P > 0.05$). In comparison to the control group, diabetic rats had a substantially larger relative change in blood (LDL) levels ($P < 0.05$). In contrast to diabetic control rats, the treated-diabetic group showed a substantial decline in blood LDL levels ($P < 0.05$). Between the treated diabetic rats and the control rats, there was no discernible change ($P > 0.05$).

TABLE 4. The impact of orally administered aqueous extract of *U. dioica* L. leaves on the lipid profile of alloxan-induced diabetic rats.

Groups	Lipid profile mg/dl				
	TC	TG	HDL-c	LDL-c	VLDL-C
Control (healthy rats)	51.33±2.13	19.00±3.92	32.08±1.18	15.78±1.39	3.80±0.78
Diabetic rats	70.33±5.11*	51.66±6.54*	23.40±3.09*	36.60±7.09*	10.33±1.30*
Diabetic rats + aqueous extract	43.50±1.56††	42.33±2.81*	25.20±1.45*	10.03±0.90†	8.26±0.64*
P value among three groups	P < 0.001	P < 0.001	P < 0.02	P < 0.001	P < 0.05

The outcomes are exhibited as M ± SE for six rats in each group. Statistical significance was determined by * $P < 0.05$ in comparison to control rats, ** $P < 0.0001$ in comparison to control rats, † $P < 0.05$ in comparison to diabetic rats, and †† $P < 0.0001$ in comparison to diabetic rats. The data was analyzed using ANOVA, followed by Tukey's post hoc test.

The impact of the aqueous extract of U. dioica L. *on the hepatic and renal functions of rats with alloxan-induced diabetes*

The concentrations of both S.GOT and S.GPT in diabetic and treated diabetic groups on the 30th day were found to be statistically significant ($P < 0.05$) in comparison to the normal group. The present study revealed that after 1month, diabetic rats exhibited a considerable higher concentration of both S.GOT and S.GPT activity than the control group. When compared to diabetic rats that were not treated, the administration of U. dioica L. water extract significantly decreased the levels of S.GOT and S.GPT over the 30days treatment period ($P < 0.05$) (0.0001), respectively. As demonstrated in Table 5, there was no significant difference between treated diabetic rats and control rats ($P > 0.05$).

Table 5 presents the results of the analyzed biochemical markers in the kidney. Alloxan-induced toxicity significantly increased the level of urea in diabetic rats ($P < 0.0001$) when compared to normal rats. Conversely, the concentration of urea significantly decreased in treated diabetic rats when compared to diabetic control rats ($P < 0.0001$). No significant difference was observed between treated diabetic rats and the normal group ($P > 0.05$). The level of creatinine and uric acid were reduced in treated diabetic rats as compared with the diabetic group, but the difference was not significant at $P > 0.05$. The levels of uric acid and creatinine between the treated plant extract, diabetic group, and normal group in this study were not significantly different ($P > 0.05$).

The findings of kidney biochemical markers are shown in Table 5. Comparing diabetic group to control group, induction of diabetes by alloxan is considerably raised the concentration of urea ($P < 0.0001$). Comparing diabetic group to treated diabetic rats, the concentration of urea considerably decreased ($P < 0.0001$) in the treated diabetic rats. Diabetes-treated rats and the normal group did not vary significantly from one another ($P > 0.05$). When compared to the diabetic group, treated diabetic rats had lower levels of uric acid and creatinine, but the difference was not statistically significant $P > 0.05$).

The findings are exhibited as Mean ± SE for 6 rats in each group. Statistical significance was observed with * $P < 0.05$ in comparison to control rats, ** $P < 0.0001$ in comparison to control rats, † $P < 0.05$ in comparison to diabetic rats, and †† $P < 0.0001$ in comparison to diabetic rats. The data was analyzed using ANOVA, followed by Tukey's post hoc test. The abbreviations GOT and GPT refer to glutamic oxaloacetic transaminase and glutamic pyruvic transaminase, respectively.

Discussion

Based on the results of this research, the oral administration of water extracts derived from *U. dioica* L. leaves at a dosage of 500 mg/kg BW led to a significant reduction in fasting blood glucose concentration in the group of diabetic rats after a period of 30 days. These outcomes are in line with previous findings conducted by various groups, which have demonstrated the hypoglycaemic effect of *U. dioica* L. on alloxan-induced diabetic rats [18-21]. However, the findings of Ozkol *et al.,* contradict these outcomes, as they demonstrated that *U. dioica* L. had no anti-hyperglycaemic effect on the group studied [22].

It is widely accepted that *U. dioica* L. extract possesses antidiabetic properties that operate through a variety of molecular mechanisms. These mechanisms include an increase in pancreatic insulin secretion [23,24], the formation of individual carbohydrate permeable pores to ease glucose uptake [25], a decrease in insulin resistance [26], an elevation in the enzymatic activity of acetyl- COA carboxylase which acts as a glucose sensor to aid insulin secretion, and NDP- kinase, which is implicated in cellular respiration energy [27].

TABLE 5. Effect of an oral administration water extract of *U. dioica* L. leaves on liver and kidney functions in alloxan diabetic rats.

Groups	Analyte levels				
	GOT (U/L)	GPT(U/L)	Urea (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
Control (healthy rats)	157.16±16.52	40.66±2.20	39.66±0.91	0.523±0.02	1.60±0.44
Diabetic rats	301.50±68.78*	152.166±24.79**	152.33±15.86**	0.58±0.03	1.81±0.30
Diabetic rats + aqueous extract	99.16±6.39†	45.16±2.94††	61.33±7.89††	0.58±0.02	1.53±0.43
***P* value among the three groups**	$P < 0.03$	$P < 0.004$	$P < 0.0001$	$P > 0.27$	$P > 0.87$

Alkaloids, tannins, phenols, flavonoids, and saponins have all been identified by phytochemical analysis of *U. dioica* L. extract [28]. It has been shown that terpenes and flavonoids isolated from various medicinal plants with hypoglycaemic qualities promote secretion or have actions similar to those of insulin. In streptozocin (STZ)-induced diabetic rats, ferulic acid and quercetin flavonoids have been demonstrated to affect pancreatic β-cells, boosting β-cell proliferation and resulting in an increase in insulin secretion [29]. It is likely that hyperglycaemia was reduced in diabetic rats' group in this study through this mechanism.

The current investigation has demonstrated that experimentally induced diabetes through alloxan administration results in a notable reduction in BW when compared to the control group. However, the administration of a treated plant extract to diabetic rats' group may have led to a BW gain that was comparable to that of healthy animals by the end of the experimental period. Additionally, this plant extract has been observed to safeguard the organs weight in diabetic rats' group. These findings are consistent with those of prior studies conducted by Shokrzadeh *et al.,* and Zangeneh *et al.,* [30,31].

Diabetes significantly affects both lipid and glucose metabolic pathway [32] . According to Havsteen (2002), greater blood insulin levels in the postprandial state encourage fuel storage in the form of triglycerides and increase lipoprotein lipase enzyme activity in adipose tissue [33]. On the other hand, as seen by Koski (2006), insulin insufficiency decreases lipoprotein lipase activity, leading to aberrant lipid metabolism during diabetes [34]. The lipoprotein metabolism of the diabetic albino rats' group in the current study significantly changed, and their blood cholesterol levels significantly rose. Alloxan most likely boosts fatty acid-oxidation, which raises acetyl CoA levels. Alternatively, as reported by Yakubu and Afolayan [35], it may increase the amount of substrate that is available through cholesterol production.

The results of this study indicated that diabetic rats had significantly increased serum total cholesterol, LDL and VLDL cholesterol levels, while HDL levels decreased. However, when diabetic rats took *U. dioica* L. leaf extract, there was a decrease in serum cholesterol, LDL and VLDL levels, as well as an increase in HDL levels. These results are consistent with the study conducted byJahromi et al., (2022) which demonstrated that the aqueous extract of stinging nettle significantly reduced total cholesterol, LDL and VLDL levels, while increasing HDL levels [20]. Similarly, Abedi Gaballu *et al*., found that diabetic rats treated with nettle extract showed significantly reduced serum cholesterol and LDL levels compared with non-diabetic mice treated [36]. Others also reported the reductions in LDL and cholesterol levels in rats fed a hypercholesterolemic diet. These results suggest that these herbs may be beneficial in preventing diabetes and its complications and enhancing lipid metabolism by minimizing blood total and LDL cholesterol levels and increasing HDL levels [37,38].

Hypertriglyceridemia is a prevalent issue frequently diagnosed in diabetic patients. The current investigation has shown that alloxan administration resulted in an elevation of serum (TG) levels. Although, treatment with water extract of *U. dioica* L. resulted in a considerable reduction in serum TG levels in diabetic rats. This result is in line with those of other investigations which demonstrated that *U. dioica* L. treatment resulted in a significant reduction in serum TG concentrations in diabetic rats [36,19,20,39]. Contrary to our research, it was found that diabetic rats treated with nettle hydroalcoholic extract had considerably greater levels of TG [26]. The significant reduction in serum TG levels observed in our study following treatment with the water extract of *U. dioica* L. leaves suggests that *U. dioica* L. plant may have potential in preventing diabetes [40].

Elevated levels of S.GOT and S.GPT enzymes are considered to be indicative of liver damage. Moreover, an elevation in liver enzymatic activities

has been linked with fatty liver disorder and a decrease in hepatic insulin responsiveness in type II diabetes, as reported by Schindhelm *et al.,* [41]. In line with this research, the serum concentrations of GOT and GPT were shown to be significantly increased in diabetic rats. However, treatment with *U. dioica* L. water extract led to a remarkable reduction in these levels. This finding is consistent with the results reported by Kanter (2005), who found that nettle plant significantly decreased liver enzymatic activities in rats treated with CCl_4 [42]. Similarly, other research groups have conducted that *U. dioica* L. extract significantly decreased serum levels of these hepatic enzymes in diabetic rats [29,43]. Oral intake of an aqueous extract of *U. dioica* L. evolved in a significant return of serum GOT and GPT levels to normal. However, these findings are in disagreement with the outcomes of another researchers, as they found that *U. dioica* L. had no protective impact on hepatic enzymes [26,36,44].

Diabetic hyperglycemia has been found to increase serum urea and serum creatinine; both are crucial indicators of renal damage [45]. The present study revealed that serum urea concentrations in diabetic rats' group significantly increased ($P < 0.05$), along with an increase in serum creatinine and uric acid concentrations, although the latter is not statistically significant ($P > 0.05$). However, treatment with aqueous extract of *U. dioica* L. leaves significantly reduced serum urea levels ($P < 0.05$) in diabetic rats 'group, compared to the mean value of the diabetic group. Similarly, administration of nettle extract has decreased the raising of uric acid concentrations caused by hyperglycemia, in comparison to diabetic group (untreated). Previous studies have demonstrated that treated *U. dioica* L. leaves can reduce serum urea and creatinine concentrations in diabetic rats [46,30,31] although this finding contradicts that of Gunesh *et al.*, who reported that treatment with water extract of nettle plant had no protective impact against nephrotoxicity [44].

The current study has shown that *U. dioica* L. did not cause any notable changes in the serum creatine levels of the diabetic rat's group. These findings are in line with outcomes by Kianbakht et al. (2013), as they found that *U. dioica* L. had no impact on the serum creatine concentrations of diabetic group. According to the same findings the water extract of nettle leaves may had a protective impact against renal damage as well as hyperglycemia, hyperlipidemia, and liver damage) [47].

Conclusion

The species *U. dioica* L. is cultivated in our region (Kurdistan) and is utilized by our population as a folk medicinal remedy for a variety of diseases. The findings of the current investigation indicate that the oral administration of 500 mg/kg BW of aqueous extract derived from *U. dioica* L. leaves has a noteworthy hypoglycaemic and hypocholesterolaemia impact on diabetic rats. Additionally, it exhibits a safeguarding impact on BW, relative organs, enhancement of liver enzymes, and amelioration of renal damage.

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Conflicts of interest:

"The authors declare no conflict of interest."

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التأثير الخافض لنسبة السكر في الدم للمستخلص المائي لأوراق القراص *Urtica dioica* L. النامية في إقليم كوردستان العراق

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الهدف الرئيسي من هذا البحث هودراسة التأثير الوقائي لهذا النبات في الجرذان المصابة بداء السكري التي يسببها الألوكسان. تم تقسيم ذكور الجرذان البيضاء بشكل عشوائي إلى ثلاث مجموعات: الجرذان العادية، والجرذان المصابة بداء السكري المحرض عن طريق الحقن داخل الصفاق من الألوكسان (110 مجم / كجم من وزن الجسم)، والجرذان المصابة بداء السكري المعاملة ب 500 مجم / كجم من وزن الجسم. من لأوراق القراص مائي لمدة 30 يومًا. تم قياس وزن الجسم والوزن النسبي لبعض الاعضاء، مستوى الجلوكوز في الدم، مستوى الدهون، الكبد والكلى.

أشارت نتائجنا إلى أن المستخلص المائي عند (500 مغم / كغم من وزن الجسم) حماية سلامة ملف الدهون والكلى والكبد الكيميائي الحيوي. علاوة على ذلك، لم يكن هناك تغير معنوي في مستوى جلوكوز الدم الصائم ووزن الجسم والكبد النسبي والقلب لوزن الجسم بينما سُجلت معنوية في الكلية النسبية لوزن الجسم مقارنة بين الجرذان الطبيعية المعالجة وفئران المقارنة. كما أظهرت نتيجة هذه الدراسة أن مجموعة مرضى السكر عولجت عن طريق الفم (500 مغم / كغم من وزن الجسم) تسببت خلاصة ماء أوراق النبات القراص (*Urtica dioica* L.) في انخفاض معنوي $P < 0.0001$ في مستوى الجلوكوز الصائم في الدم وزيادة معنوية عند $P < 0.05$ في وزن الجسم مقارنة بمجموعة التحكم في مرض السكري. القلب والكبد النسبي لوزن الجسم لم يتغير معنوي (P >0.05) بينما انخفض الوزن النسبي للكلى / الجسم بشكل كبير($P < 0.05$) . بالإضافة إلى ذلك ،و بالمقارنة مع الجرذان المصابة بمرض السكري ، قلل المستخلص بشكل ملحوظ من كوليسترول الدم و LDL-C عند ($P < 0.05$) بينما قلل من TG و VLDL وزيادة HDL-C ليس بشكل ملحوظ ($P > 0.05$). 500 مغم / كغم من وزن الجسم جرعة مستخلص الماء في الفئران المصابة بداء السكري، وهذا أدى بشكل كبير إلى نقصان مستويات S.GOT و S.GPT و اليوريا وعاد إلى طبيعته. من ناحية أخرى، لم يتم تغيير كرياتينين المصل وحمض البوليك ($P > 0.05$).
بينت النتائج التي توصلنا إليها أن المستخلص المائي أوراق النبات القراص يخفف من ارتفاع السكر في الدم وفرط شحميات الدم والإنزيمات الكبدية ووظائف الكلى .