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تحية طيبة وبعد،،،

يسر **معامل التأثير والاستشهادات المرجعية للمجلات العلمية العربية (ارسيف – ARCIF)**، أحد مبادرات قاعدة بيانات **"معرفة"** للإنتاج والمحتوى العلمي، إعلامكم بأنه قد **أطلق التقرير السنوي التاسع للمجلات للعام 2024**.

ويسرنا تهنئتكم وإعلامكم بأن **المجلة المصرية للدراسات المتخصصة** الصادرة عن **جامعة عين شمس، كلية التربية النوعية، القاهرة، مصر، قد نجحت في تحقيق معايير اعتماد معامل "ارسيف Arcif"** المتوافقة مع المعايير العالمية، والتي يبلغ عددها **(32) معياراً**، وللاطلاع على هذه المعايير يمكنكم الدخول إلى الرابط التالي: http://e-marefa.net/arcif/criteria/

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Effect of Nettle Leaves (Urtica dioica L.) On Oxidative Stress Status of Induced Diabetic Nephropathy Rats

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Effect of Nettle Leaves (Urtica dioica L.) On Oxidative Stress Status of Induced Diabetic Nephropathy Rats

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Abstract

Oxidative stress plays an important role in the development of diabetic complications. Urtica dioica L. has been traditionally used as an herbal remedy for hypoglycemic. The aim of the present study was to evaluate the effect of stinging Nettle Leaves powder (NLP) and its aqueous extract (NLAE) on oxidative stress status of rats with diabetic nephropathy, The results at the end of biological experiment for diabetic rats fed on basal diet supplemented with NLP or NLAE may be helping to maintain an ideal body weight and feed efficiency ratio

This study recommended that Urtica dioica L. is suitable for diabetic patients with nephropathy.

Keywords: Stinging nettle, Hyperglycemia, Antioxidants Enzymes, Type2 diabetes, Liver Function, Rats.

ملخص:

العنوان : تـأثير أوراق نبـات القـراص (Urtica dioica L.) علـى حالـة الإجهـاد التأكسـدي للفئـران المصابة باعتلال الكلي السكري المحدث

المؤلفون : احمد على أمين ، هانى جابر المصرى ، روان سلطان سدوح الحازمي

يلعب الإجهاد التأكسدي دورًا مهمًا في تطور مضاعفات مرض السكري وعادة ما يتم استخدام اوراق نبات القراص كعلاج عشبي تقليديًا لإنقاص مستوى السكر فـي الـدم. وهـدفت هـذه الدراسـة هـو تقيـيم تأثير مسحوق أوراق نبـات القـراص ومستخلصـه المـائي فـي حالـة الإجهـاد التأكسـدي لـدى الفئـران المصابة باعتلال الكلي السكر ، اظهرت النتائج في نهاية التجربة البيولوجية للفئران المصابة بالسكر والتي تم تغذيتها على نظام غذائي أساسي مدعم بأوراق القراص المجففة أو مستخلصه المائي دورهـا في الحفاظ على وزن الجسم المثالي ونسبة كفاءة الغذاء

أوصت هذه الدراسة بأن اوراق نبات القراص مناسب لمرضى السكري المصابين باعتلال الكلى.

الكلمات الدالة : نبات القراص، ارتفاع سكر الدم، إنزيمات مضادات الأكسدة، مرض السكري من النوع الثاني، وظائف الكبد، الفئران.

Introduction

Diabetes mellitus (DM) is a chronic and progressive metabolic disease which is described with hyperglycemia ensuing impaired insulin secretion and insulin resistance that leads to hyperglycemia **(Végh *et al*., 2023)**. The prevalence of type 2 diabetes is rapidly growing with various complications. One of the most important difficulties of this metabolic disease is diabetic nephropathy, which is believed to be the main cause of end-stage renal failure **(Alhaider *et al*., 2011)**. It is shown that oxidative stress is involved in the progression of Type 2 diabetes **(Ece *et al*., 2012)**. Also, impairment in antioxidant protection systems creates a condition known as oxidative stress **(Nocella *et al*., 2019)**.

Oxidative stress is the result of disequilibrium between increased production and decreased antioxidant capacity of cell **(Elmarakby and Sullivan, 2012)**. Oxidative stress not only takes part in the cluster of procedures that eventually leads to impaired glucose metabolism, insulin resistance and diabetes, but also is important in the development of diabetes-related complications. Oxidative stress plays an important role in both micro and macro vascular complications of diabetes **(Shokrzadeh *et al*., 2017)**.

Hyperglycemia is believed to boost ROS production directly through generation of high amounts of OH free radicals resulting from glucose autoxidation **(Vafaeipour *et al*., 2015)**. With regard to the role of OS in diabetes, many studies focused on antioxidants, especially in herbal medicine to reduce the complications. Plants have different compounds with various biological effects that make it possible to search for natural anti-hyperglycemic agents with minor side effects **(Balekari and Veeresham, 2013)**.

Urtica dioica L., commonly known as stinging nettle, is a perineal herbaceous plant belonging to the family *Urticaceae* **(Jan *et al*., 2017)**. Recently, this plant is gaining attention as a highly nutritious food, where fresh leaves are dried and used as

powder or in other forms. The leaves are rich in many bioactive compounds, such as flavonoids, phenolic acids, and amino acids **(Grauso *et al*., 2020)**. Furthermore, **Bhusal *et al*., (2022) and Taheri *et al*., (2022)** demonstrated that the leaves of *Urtica dioica* are rich in chlorophylls, carbohydrates, carotenoids, fats, vitamins and minerals. In folk medicine, nettle has been used to treat iron deficiency anemia due to its high content of iron. The leaves of the nettle were used as laxative, diuretic and diabetic **(Mikaeili *et al*., 2013)**. Stinging nettle has been reported to have various pharmacological activities such as anti-inflammatory, antioxidant **(Farzaei *et al*., 2018)**, hypocholesterolemic, hypoglycemic, cardiovascular, and hepatoprotective effects **(Zangeneh *et al*., 2020)**. Most animal studies have shown the beneficial effects of *Urtica dioica* in diabetes management **(Rashidi *et al*., 2013)**. Therefore, the present study was conducted to evaluate the effect of stinging Nettle Leaves (*Urtica dioica* L.) powder and its aqueous extract in oxidative stress status of rats with diabetic nephropathy.

Materials and Methods

Materials:

Plant: Dried nettle leaves will be purchased from Agriculture Research Center, Giza, Egypt.

Chemicals: Casein, cellulose, sucrose, choline chloride D-L methionine, vitamins and minerals constituents and streptozotocin were purchased from El-Gomhouria Pharmaceutical Company, Cairo, Egypt.

Animals: Forty-eight adult male rats **(**Sprague Dawley strain), weighing about 150±10g b.wt. were obtained from the Laboratory Animal Colony, Helwan, Egypt.

Methods:

Preparation of Nettle Leaves Powder (NLP) and its Aqueous Extract (NLAE):

a- Nettle Leaves Powder (NLP): Dried nettle leaves were grinded using a coffee grinder into a fine powder till used for chemical composition, isolation phenolic compounds and for preparation of aqueous extract and supplemented diet with powder.

b- Aqueous Extract (NLAE): About 100 g of the obtained powder was extracted with 1000 mL distilled water for 2 h at 40°C by continuous shaking. The extract will be left for 24 h at room temperature; then filtered **(Zangeneh *et al*., 2020)**.

Preparation of Basal Diet:

The basal diet was consisted of protein (14%), corn oil (5%), mineral mixture (3.5%), vitamin mixture (1%), fiber (5%), sucrose (10%), choline chloride (0.25%) and the remainder will be Corn starch up to 100%. These constituents were thoroughly mixed together and formulated according to **Reeves *et al*., (1993)**.

Experimental Design:

The experiment was carried out at the Post Graduated Lab of Home Economics Faculty, Helwan University. Animals were housed in well aerated cages under hygienic conditions and feed on basal diet for one week for adaptation. After the adaptation period, rats were divided into two main groups, as follows:

• **First group:** Negative control group, rats (n=6) were fed on basal diet only during the experimental period.

• **Second group:** Rats (n=42), were injected with a single dose of intraperitoneal injection of streptozotocin (200 mg/kg b.wt) diluted in citrate buffer (pH= 4.6) **(Shokrzadeh *et al*., 2017)**. Fasting blood glucose levels were assessed everyday by glucometer strips. After three days, the rats with plasma glucose level > 250 mg/dL were considered diabetic **(Zangeneh *et al*., 2018)**.

Induction of nephropathy of rats: Rats were giving intramuscular injections of 50% glycerol (10 ml/kg B.wt.) in their hind limbs. Random blood samples were obtained to measure the

kidney functions to ensure the induction of acute renal failure **(Midhun *et al*., 2012)**, then the animals were divided as follows:

Subgroup (1): Rats (served as positive control group) were fed on basal diet only.

Subgroup (2): Rats were fed on basal diet supplemented with the 2.5% NLP per kg of basal diet.

Subgroup (3): Rats were fed on basal diet supplemented with the 5% NLP per kg of basal diet.

Subgroup (4): Rats were fed on basal diet supplemented with the 10% NLP per kg of basal diet.

Subgroup (5): Rats were orally administrated with 1mL of NLAE as one injection gavage.

Subgroup (6): Rats were orally administrated with 2 mL of NLAE as two injection gavages.

Subgroup (7): Rats were orally administrated with 3mL of NLAE as three injection gavages.

Biological Evaluation:

Feed intake was recorded daily and animals were weighed at the beginning and twice a week throughout the experimental period. Body weight gain and feed efficiency ratio were calculated at the end of the experiment according to the method of **Chapman *et al*., (1959),** using the following equations:

$$\text{BWG\%} = \frac{\text{Final body weight} - \text{Initial body weight}}{\text{Initial body weight}} \times 100$$

FER= Body weight gain (g) / Feed intake (g)

Blood Collection and Serum Separation:

At the end of the experimental period 42 days, rats were fasted overnight before scarifying and blood samples were collected from each rat and were centrifuged at 3000 rpm for 15 min to obtain the serum for biochemical analysis.

Biochemical analysis:

Glucose was determined according to **Trinder, (1959)** and Insulin was determined according to **Matthews, *et al*., (1985)**

Liver functions: Serum Aspartate amino transferase (AST) and alanine amino transferase (ALT) were determined according to **Bergmeyer *et al*., (1978)**, Alkaline phosphates (ALP) was determined according to **Belfield and Goldberg (1971)**

Kidney function: Serum urea **(Kaplan, 1984)**, uric acid **(Patton and Crouch, 1977)** and creatinine were measured according to **(Murray, 1984)**.

Lipid profile: Serum total cholesterol (TC) **(Richmond, 1973)**, triglycerides (TG) **(Wahlefeld, 1974)**, High density lipoprotein (HDL) **(Albers *et al*., 1983)** were determined. Meanwhile, low density lipoprotein (LDL) and very low-density lipoprotein (VLDL) were calculated according to **Fridewald *et al*., (1972)**.

LDL-c = TC-[HDL-c + (TG/5)] VLDL-c = TG/5

Antioxidant Enzymes: The plasma level of malondialdehyde (MDA) was calculated to measure lipid peroxidation was determined according to **Draper and Hadley (1990)**. Superoxide dismutase (SOD) activity was evaluated by **Spitz and Oberley, (1989)**. Catalase (CAT) and Glutathione peroxidase (GP_X) were measured methods by **Aebi, (1984), Moin, (1986),** respectively.

Statistical analysis:

All data obtained were analyzed using Statistical Package for the Social Sciences (SPSS) for Windows, version 20 (SPSS Inc., Chicago, IL, USA). Collected data were presented as mean ± standard deviation (SD). Analysis of Variance (ANOVA) test was used for determining the significances among different groups according to **(Armitage and Berry, 1987)**. All differences were considered significant if P-values were ($P< 0.05$).

Results and Discussion

The Effect of Nettle leaves powder and extract on rats with induced diabetic nephropathy

The results in Table (1) show the effect of Nettle leaves powder and extract on body weight of rats with induced diabetic nephropathy. The current investigation has demonstrated that experimentally induced diabetes through STZ administration results in a notable reduction in BWG when compared to the control group. However, the administration of a treated NLP and NLAE to diabetic rats' group may have led to a BWG gain that was comparable to that of healthy animals by the end of the experimental period. There is significant difference ($P<0.05$) in BWG, and BWG% among the treated groups that were fed on basal diet and given different levels of Nettle leaves powder and extract. In addition, there were no significant changes in FER between the groups fed either 5% NLP or 3 ml of NLAE. The mean value of BWG, BWG% and FER were significantly increased ($P<0.05$) for the tested levels as compared to the +ve control group. The highest increased in FBW were recorded at the group given orally NLAE (3 ml/rats). The lowest FI was recorded at the +ve control group. Moreover, feed intake was numerically increased due to supplementation with NLP and NLAE among the tested groups as compared to the control positive group.

Diabetes mellitus (DM), commonly called diabetes, is a group of metabolic disorders characterized by a high blood sugar level through a prolonged period of time. Accordingly, this metabolic disease has several complications and sequels, the treatment and management of which are included as the most important and key issues that should be considered **(Nagib *et al*., 2019)**. A high blood sugar level (glucose) can injure nerves in all parts of the body **(Turton *et al*., 2018)**. These results agree with **Omar and Mohammed, (2024)** found 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 ($P < 0.05$). Similar, **Eldamaty, (2018)** showed that diabetic rats fed on

basal diet supplemented with 5% and 10% nettle showed that nettle leaves powder may help to maintain an ideal body weight and feed efficiency ratio.

Table (1): Effect of Nettle Leaves powder and extract on mean values of body weight gain (BWG), feed intake (FI) and feed efficiency ratio (FER) of rats with induced diabetic nephropathy

Parameters / Groups	FI (g/d/rat)	BWG G	BWG%	FER
Control (-Ve)	21	25.00±0.31^{a}	20.25±0.53^{a}	0.0428±0.001^{a}
Control (+Ve)	10	5.20±0.37^{e}	4.10±0.33^{f}	0.0184±0.001^{d}
(2.5% NLP)	16	12.40±0.67^{d}	9.73±0.51^{e}	0.0276±0.001^{c}
(5% NLP)	18.5	13.20±0.96^{d}	10.32±0.80^{de}	0.0254±0.001^{c}
(10% NLP)	20	14.00±0.31^{cd}	10.90±0.30^{de}	0.0250±0.002^{c}
(1 mL NLAE)	17	16.60±0.40^{bc}	12.75±0.33^{cd}	0.0352±0.001^{b}
(2 mL NLAE)	18.5	19.40±0.50^{b}	14.97±0.41^{bc}	0.0378±0.002^{ab}
(3 mL NLAE)	19	22.80±0.37^{a}	17.34±-.31^{b}	0.0426±0.001^{a}

*Data are expressed as mean ± SE.

*Means with different superscript letters in the column are significantly differences at ($P < 0.05$).

The Effect of Nettle leaves powder and extract on blood glucose and insulin concentrations of rats with induced diabetic nephropathy

The results in table (2) show the effect of Nettle leaves powder and extract on blood glucose and insulin concentrations in rats with induce diabetic nephropathy. Rats injected with STZ had significant ($P \leq 0.05$) higher glucose level but had significant ($P \leq 0.05$) lower insulin concentration, compared to the control negative group. The results of the current study indicate that STZ causes an increase in blood glucose levels and a reduction in insulin levels when compared to the control group. Accordingly, this is consistent with previous studies, demonstrating that the STZ-induced diabetes in the rodent is known as the standard model of diabetes induction **(Ma *et al*., 2015 and Negm, 2020)**. Diabetes significantly affects both lipid and glucose metabolic pathway **(Parhofer, 2015)**. In contrast, in the present study, the administration of NLP and NLAE at different levels significant

change (p>0.05) in serum glucose among the groups. The administration of different NLP and NLAE significantly (P<0.05) decreased the mean value of glucose as compared to the +ve control group. The highest reduction in glucose level was recorded at the group fed on basal diet and given NLAE at 3 ml/rat.

Regarding to insulin concentration, the treatment with NLP and NLAE at the different levels significantly (P < 0.05) increased the level of insulin compared to the positive control group. There is significant change (p>0.05) in serum insulin among the groups that given NLP and oral NLAE. The highest increase in insulin level was recorded at the groups that fed basal diet and NLAE (3 ml/rats). These results agree with **Javadi *et al*., (2022)** indicate that Nettle aqueous extract (50, 100, and 200 mg/kg, i.p.) decreases in serum levels of glucose while increased insulin level in diabetic rats. **Chehri *et al*., (2023)** observed that nettle resulted in significant decreases in fasting blood sugar. Similar, **Omar and Mohammed, (2024)** showed that 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 **(Jahromi *et al*., 2022)**. Furthermore, **Omar and Mohammed, (2023)** showed 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 **(Gushiken *et al*., 2016)**. It is likely that hyperglycaemia was reduced in diabetic rats' group in this study through this mechanism.

Table (2): Effect of Nettle leaves powder and extract on glucose and insulin concentrations of rats with induced diabetic nephropathy

Parameters / Groups	Glucose (mg/dl)	Glucose reduction (%)	Insulin (uIU/ml)	Insulin Increment (%)
Control (-Ve)	90.42±0.40e	-	1.69±0.10a	-
Control (+Ve)	216.42±1.39a	-	0.51±0.02d	-
(2.5% NLP)	190.41±0.41b	12.01	0.37±0.01d	30.71
(5% NLP)	161.40±0.38c	25.41	1.03±0.03c	50.49
(10% NLP)	114.22±0.59d	47.22	1.33±0.01b	61.65
(1 mL NLAE)	181.62±0.84b	16.08	0.56±0.02d	22.26
(2 mL NLAE)	156.40±1.08c	27.72	1.35±0.03b	62.22
(3 mL NLAE)	110.22±1.01d	29.07	1.49±0.04ab	65.77

*Data are expressed as mean ± SE.

*Means with different superscript letters in the column are significantly differences at ($P < 0.05$).

Effect of Nettle leaves powder and extract on liver functions:

Liver function of rats with induced acute diabetic nephropathy and treated with NLP and NLAE are indicated in Table (3). The results show that liver functions (AST, ALT and ALP) are significantly ($P<0.05$) increased at the positive control group as compared to negative control group. These results agreement **Negm, (2020)** observed that the activities of serum AST and ALT were significantly increased ($P\leq0.05$) in the diabetic control group injected with STZ, compared with the corresponding value of normal control group. While, the supplementation with the tested materials at the different levels significantly decreased ($P < 0.05$) the level of liver functions (AST, ALT and ALP) compared to positive control group. There are significant differences in serum liver functions between the groups that given NLP at 2.5 and 5% or NLAE the group given 3 ml/rat. Moreover, there is no significant changes in serum AST, ALT and ALP between the group given (NLP 10% or NLAE 3ml/rat) , (NLP 5% or NLAE 2ml/rat) and (NLP 5% or NLAE

1ml/rat). The highest improvements in liver function are observed at the group that given orally NLAE at (3 ml/rats).

Elevated levels of AST, ALT and ALP 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.*, (2006)**. In line with this research, the serum concentrations of AST, ALT and ALP 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 **Gushiken *et al*., (2016) and Salmani *et al*., (2015)** conducted that *U. dioica* L. extract significantly decreased serum levels of these hepatic enzymes in diabetic rats. These results are consistent with **Eldamaty, (2018)** showed that the diabetics rat fed on 5 and 10% *Urtica dioica* leaves in basal diet were decreased in AST, ALT and ALP were compared with control positive. Oral intake of an aqueous extract of *U. dioica* L. evolved in a significant return of serum AST and ALT levels to normal **(Omar and Mohammed, 2024)**.

Table (3): Effect of Nettle leaves powder and extract on liver function of rats with induced diabetic nephropathy

Parameters / Groups	AST (µ /L)	ALT (µ /L)	ALP mg/dL
Control (-Ve)	18.98±0.25e	38.53±0.50e	114.38±1.41f
Control (+Ve)	48.38±0.31a	97.13±1.07a	174.98±1.09a
(2.5% NLP)	40.39±0.74b	81.93±0.51b	164.18±1.31b
(5% NLP)	32.37±0.17cd	70.95±0.45c	160.34±1.13bc
(10% NLP)	23.35±0.69e	55.33±0.90d	144.57±1.83d
(1 mL NLAE)	38.77±0.39bc	79.39±0.75b	154.88±1.14c
(2 mL NLAE)	30.23±0.08d	64.37±0.99c	144.99±1.09d
(3 mL NLAE)	21.88±0.75e	43.94±0.93e	135.32±1.87e

*Data are expressed as mean ± SE.

*Means with different superscript letters in the column are significantly differences at ($P < 0.05$).

Effect of Nettle leaves powder and extract on kidney functions:

The effects of NLP and NLAE on kidney functions in rats with induced diabetic nephropathy are illustrated in Table (4). Serum urea, creatinine and uric acid are significantly (P<0.05) increased at the control positive group compared to the control negative group. These results agreement **Negm, (2020)** observed that injection with STZ significantly increase (P≤0.05) the level of urea and creatinine, compared to the control negative group. Diabetic hyperglycemia has been found to increase serum urea and serum creatinine; both are crucial indicators of renal damage **(Ma *et al*., 2022)**. 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).

On the other hand, Administration with different levels of NLP and NLAE significantly decreased (P <0.05) serum urea, creatinine and uric acid on the diabetic rats that fed on NLP of (2.5%, 5%and 10%) and NLAE (1, 2 and 3ml/ rat) as compared to positive group. There are significant differences in serum urea and creatinine among the groups fed on basal diet and given NLP and NLAE. Moreover, there is no significant changes in serum uric acid among all treatment groups except NLP at 2.5%. The highest improvement of kidney functions are observed at the group that was given orally NLAE (3 ml/rat).

These results are consistent with **Javadi *et al*., (2022)** indicate that 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 **(Haghshenas *et al*., 2023 and Omar and Mohammed, 2024)**.

These findings are in line with outcomes by **Chehri *et al*., (2023)** observed that nettle resulted in significant decreases in urea, creatinine, liver function tests, insulin, and levels. According to the same findings the water extract of nettle leaves may have had a protective impact against renal damage as well as hyperglycemia, hyperlipidemia, and liver damage.

Table (4): Effect of Nettle leaves powder and extract on kidney function of rats with induced diabetic nephropathy

Parameters / Groups	Urea (mg/dl)	Creatinine (mg/dl)	Uric Acid (gm/dl)
Control (-Ve)	24.12±0.40e	0.70±0.01f	2.65±0.07d
Control (+Ve)	49.53±0.66a	1.68±0.02a	5.92±0.19a
(2.5% NLP)	42.52±0.78b	1.48±0.03b	4.79±0.25b
(5% NLP)	34.64±0.64c	1.30±0.01cd	3.50±0.17c
(10% NLP)	28.21±0.55d	0.94±0.04e	2.93±0.01cd
(1 mL NLAE)	39.48±0.59b	1.40±0.02bc	3.50±0.03c
(2 mL NLAE)	33.97±0.89c	1.20±0.03d	3.08±0.17cd
(3 mL NLAE)	26.91±0.51de	0.83±0.03ef	1.86±0.03cd

*Data are expressed as mean ± SE.

*Means with different superscript letters in the column are significantly differences at ($P < 0.05$).

Effect of Nettle leaves powder and extract on lipid profile:

The lipid profile (TC, TG, HDL-C, VLDL-C, LDL-C) of rats with induced acute diabetic nephropathy and that treated with NLP and NLAE are displayed at Table (5). Rats with acute diabetic nephropathy had significant increase ($P < 0.05$) in lipid profile as compared to normal rats while HDL levels decreased. Hypertriglyceridemia is a prevalent issue frequently diagnosed in diabetic patients. The current investigation has shown that STZ administration resulted in an elevation of lipid profile. These results agree with **Negm, (2020)** observed that injection with STZ significantly increases ($P \leq 0.05$) the level of lipid profile compared to the control negative group.

In contrast, the mean value of TG and VLDL-C is significantly (P<0.05) lowered at the group fed on basal diet and given NLP or NLAE at different levels as compared with the positive control group. Regarding to serum TC and LDL-C, there are significant different (P<0.05) in serum TC and LDL-C among the treated groups. The same trend was observed among the treated groups for the other lipid parameters. On the other hand, it was clear that NLP and NLAE administration significantly (P<0.05) increased the mean value of serum HDL C as compared to the +ve control group. The highest improvement in lipid profile are recorded at the group fed on basal diet and NLP at 10%. The present study showed that there were higher levels of cholesterol, triglycerides, LDL-C and VLDL-C accompanied by low level of HDL-C in STZ induced-diabetic rats. These results are consistent with the study conducted by **Abedi *et al*., (2015)** found that diabetic rats treated with nettle extract showed significantly reduced serum cholesterol and LDL levels compared with non-diabetic mice treated. Similarly, **Jahromi *et al*., (2022)** demonstrated that the aqueous extract of stinging nettle significantly reduced total cholesterol, LDL and VLDL levels, while increasing HDL levels. **Chehri *et al*., (2023)** observed that nettle resulted in significant decreases in lipid profile indicators. This result is in line with **Omar and Mohammed, (2024)** observed that the extract had significantly decreased serum TC and LDL in comparison to diabetic rats' group.

Table (5): Effect of Nettle leaves powder and extract on lipid profile of rats with induced diabetic nephropathy

Parameters / Groups	TC mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl	VLDL mg/dl
Control (-Ve)	125.87±1.21f	83.53±0.52e	60.49±1.17a	48.66±0.94e	16.70±0.10e
Control (+Ve)	187.87±2.20a	143.59±1.59a	26.49±1.45e	132.66±0.65a	28.72±0.31a
(2.5% NLP)	160.69±1.32cd	138.59±0.42ab	33.69±1.37d	99.27±1.17c	27.70±0.08ab
(5% NLP)	153.49±2.40cde	123.58±1.58c	46.51±1.53c	82.26±1.00d	24.71±0.31c
(10% NLP)	148.87±1.87de	107.57±1.77d	53.09±0.88b	74.26±1.12d	21.52±0.55d
(1 mL NLAE)	173.40±1.59b	140.19±0.35ab	31.09±0.73de	114.27±1.12b	28.04±0.07ab
(2 mL NLAE)	162.67±2.49bc	133.56±1.55b	43.49±0.59c	92.46±1.81c	26.73±0.33b
(3 mL NLAE)	148.53±1.82e	111.79±0.56d	47.91±1.17bc	78.25±1.07d	22.36±0.11d

*Data are expressed as mean ± SE.

*Means with different superscript letters in the column are significantly differences at (P < 0.05).

Effect of Nettle leaves powder and extract on Antioxidants Enzymes:

The outcome of NLP and NLAE on antioxidants enzymes was shown in Table (6). The current study indicated that the level of oxidative stress parameters such as MDA increased in diabetic rats and some antioxidant parameters such as CAT, GPx and SOD, decreased when compared to the control group. In this regard, the oxidative stress-induced complications of diabetes may include stroke, neuropathy, retinopathy, and nephropathy. In many studies, Oxidative stress has been demonstrated to participate in the progression of diabetes, which plays an important role in diabetes, including impairment of insulin action and the increased complication incidence rate **(Asmat *et al*., 2016)**.

In contrast, in the present study, the administration of NLP and NLAE at the tested levels appreciably ($P<0.05$) increased the antioxidants enzymes (CAT, GPx and SOD) and significantly reduced MDA in comparison to the +ve control group. There are no substantial SOD changes among all treated groups except at the group that given orally NLAE (3 ml/rat). The most remarkable improvement of antioxidants enzymes was recorded at the group that given orally NLAE (3 ml/rat). Antioxidants have been already shown to be prospective in the treatment of both diabetes type 1 and type 2. Thus, oxidative stress seems to be more worrying about metabolic disorders, especially diabetes **(Ceriello *et al*., 2016)**. These results are consistent with the study conducted by **Javadi *et al*., (2022)** found that nettle (*Urtica dioica*) aqueous extract significantly decreased the levels of MDA increased the antioxidant parameters levels such as SOD, GPx, CAT, and GSH. Moreover, a previous study demonstrated the antioxidant role of *Urtica dioica* in multiple diseases, but its exact roles in the modulation of oxidative stress during diabetes by STZ-induced diabetes neuropathy. It was demonstrated that some parts of this herbal agent have antioxidant properties in some parts of body organs like liver **(Shokrzadeh *et al*., 2018)**.

Table (6): Effect of Nettle leaves powder and extract on antioxidants enzymes of rats with induced diabetic nephropathy

Parameters / Groups	CAT pg/ml	MDA ng/ml	GPx U/ml	SOD U/ml
Control (-Ve)	23.17±0.38a	123.58±0.57f	136.62±0.70a	2.83±0.15a
Control (+Ve)	4.20±0.05f	420.05±1.97a	83.23±0.40d	0.81±0.17c
(2.5% NLP)	8.16±0.27e	404.03±1.61b	94.76±0.35c	1.07±0.11c
(5% NLP)	13.75±0.29c	382.41±1.55c	100.91±0.52c	1.23±0.33bc
(10% NLP)	18.36±0.33b	299.34±1.40d	115.34±0.54b	1.76±0.16abc
(1 mL NLAE)	11.24±0.35d	391.14±1.48bc	98.81±0.37c	1.43±0.22bc
(2 mL NLAE)	18.25±0.42b	302.19±1.74d	121.18±0.63b	1.91±0.14abc
(3 mL NLAE)	21.35±0.44a	200.33±1.16e	129.98±0.47a	2.38±0.36ab

*Data are expressed as mean ± SE.

*Means with different superscript letters in the column are significantly differences at ($P < 0.05$).

Conclusions

Stinging nettle (*Urtica dioica*) is a common herb has a great medicinal value such as relieve of lowering glucose in blood, lowering lipid profile and improvement of body weight, liver and kidney functions. Our data indicated that the administration of nettle (*Urtica dioica*) powder and aqueous extract significantly act as a potent nephropathy protective agent against STZ-induced diabetes and its sequels. Of note, it seems that this effect was mediated via the modulation of oxidative stress.

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