BIOCHEMICAL EFFECT OF CITRULLUS COLOCYNTHIS IN EXPERIMENTAL DIABETES MELLITUS IN RATS

Omayma,A.R. Abou Zaid.[a], **Khalid, M. Fararh.**[b] **and Aliaa, H.Ali.**[a]

[a] *Departments of Biochemistery, Faculty of Veterinary Medicine, Benha University,* [b] *Departments of Clinical pathology, Faculty of Veterinary Medicine, Benha University.*

A B S T R A C T

The aim of the present study was to evaluate the antidiabetic activity of citrullus colocynthis (CT)in sterptozotocin induced diabetic rats on sixty male rats and weighting 200 – 250 gm. were divided into three equal groups of 20 rats. Group 1: control normal group injected with citrate buffer only (CN).Group 2: diabetic group (DN) injected with a single intrapertinoel dose of 60 mg/kg.bw of streptozotocin for diabetic induction. Group 3: diabetic citrullus colocynthis treated group (CCT), where citrullus colocynthis were given orally at dose of (60 mg/kg bw /day).blood samples were collected from all animal groups after 4 , 6 and 8weeks from the onset of treatment and processed directly for determination of serum glucose, urea, creatinine , uric acid , albumin , total cholesterol, triacylglycerols, HDL, LDL concentrations as well as AST, ALT activities in addition to MDA and GSH concentrations and SOD activity in RBCs. The obtained results revealed that, a significant increase in serum glucose , urea, creatinine, uric acid, total cholesterol, triacylglycerol, LDL , MDA levels AST, ALT activities with a marked depletion in GSH content and SOD activity in the blood of diabetic rat when compared with the control. Contrary results were obtained in diabetic group (DN) treated with citrullus colocynthis. From the obtained results, it could be concluded that administration of citrullus colocynthis to diabetic rat, which may improve hyperglycemia, impaired kidney and liver functions, liver enzyme, dyslipidemia, and attenuates the states of antioxidant enzyme and oxidative stress produced by diabetes mellitus

Key Words: Experimental diabetic mellitus; Citrullus colocynthis; Oxidative stress; Lipid profile; Hepatorenal function

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1. INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels [1].

Some medicinal plants have been reported to be useful in diabetes worldwide and have been used empirically as antidiabetic and antihyperlipidemic remedies [2]. Antihyperglycemic effects of these plants were attributed to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes. However, searching for new antidiabetic drugs from natural plants is still attractive because they contain substances which take alternative and safe effect on diabetes mellitus. Most of plants contain glycosides, alkaloids, terpenoids, Flavonoids, cartenoids, etc., that are

frequently implicated as having antidiabetic effect [3]. *Citrullus colocynthis* demonstrates multiple beneficial anti-diabetic mechanisms, including modulation of carbohydrate metabolism, restoration of beta-cell integrity, insulin-releasing activity and improvements in glucose uptake utilization [4]. Moreover, it decreases gluconeogenesis and inhibits release of counter-regulatory hormones. On the other hand, it has been suggested that the mechanism responsible for the serum glucose lowering effect of *Citrullus colocynthis* were attributed to an inhibitory effect of glucose absorption ; an increased incorporation of circulating glucose as hepatic glycogen, or an enhanced secretion of insulin. Furthermore, components of Citrullus colocynthis extract appear to have structural similarities to animal insulin, as measured by electrophoresis and infrared spectrum analysis [5].

Accordingly, this study was performed to investigate the hypoglycemic, antioxidant and hypolipidemic effect of *Citrullus colocynthis on* experimentally induced diabetic rats.

2. MATERIALS AND METHODS

2.1. *Animals:*

Sixty male albinos Wister rats of 6-8 weeks old and weighting 200 – 250 gm were used in this study. Rats were housed in separated metal cages 10-25 per cage and kept under the same constant environmental and nutritional condition through out the period of experiment. Water was supplied ad-libitum.

2.2. *Chemicals:*

sterptozotocin were purchased from Sigma chemical company (USA) for trading chemicals, medicines and medical appliances, Egypt other chemical and kits purchased from Diamond, Vitro (Egypt).

2.3. *Nutraceuticals preparation:*

Preparation of Citrullus colocynthis: The dried pulp of fruits was homogenized with grinder to fine powder before extraction. The pulp powder from individual CCT (250 gm) was extracted three times at room temperature with 100 ml of water/ethanol mixture (80/20) v/v for 6hr each round and given as oral daily dose for each rat in (Group III) for 50 days [6] .

Diabetes induction: Rats were fasted for 18 hours and allowed free access of water. The experimental induction of diabetes in male was induced by intrapertinoel (i.p) injection of 60 mg/kg of sterptozotocin (STZ) (dissolved in citrate buffer 0.1 mol/l, PH 4.2) [7].

2.4. *Experimental design:*

The rats were divided into three equal main groups as following:

GroupI (control normal group): included 20 male rats, injected with citrate buffer only served as control group.

GroupII (Diabetic group): included 20 rats fed with normal diet injected with streptozotocin intrapertinoel dissolved in citrate buffer PH (4.2) at a dose of 60 mg/kg b.w [7].

GroupIII (diabetic citrullus colocynthis treated group CCT): consists of 20 rats fed with normal diet then after 3dayes of STZ injection treated daily with citrullus colocynthis fruit extract at a dose of 50 mg/kg bw for 50 days by oral gavages [8].

2.5. *Blood sampling:*

Blood samples were collected after overnight fasting fasted in glass tubes via occular vein puncture from all animal groups, and each sample was divided in two tubes, heparinized and non– heparinized. The non heparinized blood samples were allowed to coagulate and then centrifugated at 3000 r.p.m. for 10 minutes.

2.6. *Biochemical analysis*

The separated serum used was directly determined for the estimation of serum glucose [9], urea [10], creatinine [11], uric acid [12], albumin concentration [13], AST, ALT activity [14], total cholesterol, triacylglycerols [15], HDL-C [16], LDL-C [17] and (in RBCs) L- MDA [18], GSH [19] concentrations and SOD activity [20].

2.7. *Preparation of erythrocytes:*
Red blood cells were washed as the following method. To 0.2 ml of collected heparinized blood, 2 ml of sodium chloride solution was added, mixed well and centrifugated for 15 minutes at 3000 r.p.m the plasma and buffy coat were discarded by careful suction (this process was repeated 3 times). After centrifugation, aliquots were used for determination of L-Malondialdehyde (L-MDA), Super oxide dismutase (SOD), Glutathione (GSH) determination according to the method described by [21].

2.8. Statistical analysis
Statistical analysis was done using SPSS software version 15. The inter-group variation was measured by one way analysis of variance (ANOVA) followed by Post Hoc LSD test. Results were expressed as mean ± SEM. The mean difference is significant at the $p \leq 0.05$ levels [22].

3. RESULTS

3.1. Effect of citrullus colocynthis administration on some biochemical changes in sterptozotocin induced diabetes mellitus in rats:

The obtained results demonstrated in table (1,2and3) showed significant increase in serum glucose concentration, urea, creatinine, uric acid concentration, Cholesterol, triacylglycerols, LDL and L-MDA concentration AST, ALT activity, in rat injected with sterptozotocin. On the other hands, a significant decreased in albumin, HDL-C concentrations, GSH and SOD activity after 4, 6 and 8 weeks of STZ injection, when compared with control rats. The presented data in tables(1,2&3) revealed that, Citrullus colocynthis administration showed significant decrease in serum glucose, urea, creatinine, triacylglycerols, and L-MDA concentrations and ALT activity in citrullus colocynthis treated diabetic rats after 6 and8 weeks and showed significant decrease in total cholesterol after 4 weeks, also AST and LDL-C decreased after 8weeks of citrullus colocynthis administration . On the other hands, a significant increased in albumin, HDL-C concentrations, GSH and SOD activity after 4, 6 and8 weeks of Citrullus colocynthis administration, when compared with diabetic rats.

Table (1): Effect of four weeks of citrullus colocynthis administration on some biochemical blood parameters of diabetic rats:

	Glucose (mg/dl)	Urea (mg/dl)	Creat. (mg/dl)	Uric acid (mg/dl)	ALT (U/ml)	AST (U/ml)	Albumin (g/dl)	Total Chol. (mg/dl)	Tri. (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	L-MDA (nmol/ml)	GSH (mmol/ gm Hb)	SOD (U/gm Hb)
A	109.00 ± 2.96 b	49.21 ± 21.42 b	0.85 ± 9.36 b	2.18 ± 0.39 b	10.00 ± 0.53 c	10.86 ± 0.67 c	3.96 ± 0.12 a	145.33 ± 4.00 c	58.14 ± 6.93 b	40.56 ± 1.23 a	94.71 ± 7.96 b	76.33 ± 1.88 d	46.10 ± 1.92 b	23.57 ± 1.83 b
B	568.71 ± 37.92 a	81.10 ± 37.92 a b	3.00 ± 4.88 a	9.58 ± 0.41 a	23.86 ± 2.40 b	61.43 ± 6.60 b	1.93 ± 0.17 c	221.71 ± 5.80 b	169.43 ± 4.28 a	22.87 ± 2.60 c	161.63 ± 7.48 a	160.77 ± 2.52 a	16.73 ± 0.41 d	18.33 ± 0.50 c
C	565.43 ± 26.21 a	97.13 ± 10.01 a	2.87 ± 0.12 a	8.97 ± 0.49 a	34.43 ± 1.70 a	89.86 ± 7.83 a	2.10 ± 0.14 b c	242.57 ± 4.05 a	184.29 ± 4.05 a	33.09 ± 1.45 b	173.47 ± 4.04 a	122.90 ± 0.67 b	29.31 ± 0.86 c	28.59 ± 2.097 a

Data are present as Mean± SE, Mean values with different superscripts letters on the same column are significantly different at $p \leq 0.05$. A : control normal group, B: Diabetic group, C: diabetic citrullus colocynthis treated group CCT.

Table (2): Effect of six weeks of citrullus colocynthis administration on some biochemical blood parameters of diabetic rats:

parameters / groups	Glucose (mg/dl)	Urea (mg/dl)	Creat. (mg/dl)	Uric acid (mg/dl)	ALT (U/ml)	AST (U/ml)	Albumin (g/dl)	Total Chol. (mg/dl)	Tri. (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	L-MDA (nmol /ml)	GSH (mmol/ /gm Hb	SOD U/gm Hb
Control group	108.57 ±3.12 c	27.94 ± 2.78 c	1.27 ± 0.33 c	2.73 ± 0.53 b	11.14 ± 0.51 c	7.57 ± 1.02 b	4.27 ± 0.16 a	163.14 ± 8.58 b	57.29 ± 5.85 c	37.00 ± 0.97 a	122.54 ± 10.20 b	78.10 ± 2.04 d	40.33 ± 0.79 b	26.73 ± 1.64 a b
Diabetic group	572.7 ±34.16 a	97.43 ± 5.57 a	3.01 ± 6.66 a	8.46 ± 0.31 a	28.29 ± 2.47 a b	72.29 ± 6.41 a	1.93 ± 0.12 c	217.71 ± 9.11 a	195.71 ± 5.54 a	20.39 ± 1.95 c	165.14 ± 9.02 a	161.84 ± 2.58 a	18.00 ± 0.51 d	14.80 ± 0.99 b
Citrullus - colocynthis diabetic treated group	475.00 ± 26.42 b	73.14 ± 10.44 b	2.31 ± 0.15 b	8.17 ± 0.17 a	25.71 ± 1.27 b	61.29 ± 4.44 a	2.89 ± 0.16 b	229.43 ± 6.42 a	175.43 ± 4.28 b	40.51 ± 1.35 a	166.26 ± 4.70 a	109.89 ± 1.81 c	63.10 ± 0.310 a	42.47 ± 16.97 a

Data are present as Mean± SE., Mean values with different superscripts letters on the same column are significantly different at $p \leq 0.05$.

Table (3): Effect of eight weeks of citrullus colocynthis administration on some biochemical blood parameters of diabetic rats:

Parameters / groups	Glucose (mg/dl)	Urea (mg/dl)	Creat. (mg/dl)	Uric acid (mg/dl)	ALT (U/ml)	AST (U/ml)	Albumin (g/dl)	Total Chol. (mg/dl)	Tri. (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	L-MDA (nmol /ml)	GSH (mmol/ /gm Hb	SOD U/gm Hb
Control group	107.00 ± 3.89 c	25.14 ± 2.48 c	0.96 ± 7.17 c	3.44 ± 0.24 b	9.86 ± 0.59 c	10.00 ± 0.58 c	4.14 ± 0.19 a	170.00 ± 12.12 b	52.29 ± 4.85 c	36.71 ± 1.84 b	145.57 ± 6.54 a b	92.83 ± 13.06 b	44.89 ± 1.24 b	28.04 ± 2.12 b
Diabetic group	728.57 ± 83.78 a	108.01 ± 6.79 a	2.99 ± 5.49 a	7.76 ± 0.23 a	46.00 ± 2.33 a	77.29 ± 6.61 a	1.95 ± 7.80 c	198.00 ± 4.72 a	210.29 ± 11.17 a	19.91 ± 1.89 c	162.81 ± 7.65 a	155.10 ± 7.54 a	19.60 ± 1.09 d	12.90 ± 0.78 c
Citrullus - colocynthis diabetic treated group	370.14 ± 22.37 b	62.86 ± 7.45 b	2.22 ± 0.12 b	7.12 ± 0.14 a	21.00 ± 1.31 b	48.71 ± 3.35 b	3.34 ± 0.13 b	200.14 ± 3.03 a	163.43 ± 6.79 b	47.23 ± 1.23 a	136.04 ± 3.91 b	96.89 ±1.02 b	50.84 ±2.67 a	26.91 ±1.15 b

Data are present as Mean± SE, Mean values with different superscripts letters on the same column are significantly different at $p \leq 0.05$.

4. DISCUSSION

Diabetes mellitus also causes renal damage due to abnormal glucose regulation, including elevated glucose and glycosylated protein tissue levels, hemodynamic changes within the kidney tissue and increased oxidative stress [23]. Diabetic nephropathy (DN) is one of the most serious problems in nephrology, as 40% of the cases of end stage renal disease (ESRD) are due to this entity [24].

Serum glucose concentration in diabetic rats showed significant increase in serum glucose concentrations in experimental diabetic rats all over the periods of the experiments. These results were nearly similar to those reported by [25] who reported that after the STZ had been injected the glucose concentration increase due to the diabetogenic action of STZ due to the direct result of irreversible damage to the pancreatic beta cells resulting in degranulation and loss of capacity to secrete insulin.

Treatment with *Citrullus colocynthis* in diabetic rats showed significant reduction in serum glucose level after 50 days of *Citrullus colocynthis* administration. These results are nearly similar to those reported by [26] who reported that, administration of *Citrullus colocynthis* to diabetic rats showed amelioration in serum glucose concentration. which decrease in serum glucose level may be due to that plant extracts has antihyperglycemic effect by promoting regeneration of beta cells or by protecting the pancreas from destruction, by restricting glucose load as well as by promoting unrestricted endogenous insulin action or its effect beta cells to release insulin and active to the insulin receptors to absorb the blood sugar [26].

Concerning to biomarkers of kidney function tests, there was significant increase in the concentrations of serum urea, creatinine and uric acid in diabetic rats all over the following compared to the control of experiment. This results agree with data reported by [27] who recorded that predominant increase in kidney function was observed in patients with type I diabetes due to impaired glomerular filtration rate .The increased concentration of urea, creatinine and uric acid were attributed to the renal damage caused by abnormal glucose regulation, including elevated glucose and glycosylated protein tissue levels, hemodynamic changes within the kidney tissue, and increased oxidative stress. Also, mild hyperuricemia was further shown to induce renal microvascular disease independent of blood pressure, as consequence of activation of the renin–angiotensin–aldosterone system, [28].

Treatment with *Citrullus colocynthis* in experimental diabetic rats showed significant reduction in serum urea and creatinine and non-significant reduction serum uric acid after 50 days of *Citrullus colocynthis* administration. These results are nearly similar to those reported by [29] who reported that, administration of *Citrullus colocynthis* to diabetic rats. The amelioration in kidney function by *Citrullus colocynthis* extract possesses hypoglycemic effect of this extract acts through an increase in insulin production and the subsequent increase in activity of glycolytic enzyme and decrease in activity of enzymes of gluconeogenesis **[**30].

Concerning to liver enzymes marker, there was significant increase in the activities of AST and ALT in diabetic rats compared to the control ones after 4, 6, 8 weeks, however serum albumin level showed significant decrease. These results agree with those reported by [31]. The increased AST and ALT activities could be attributed to increased protein catabolism accompanying gluconeogenesis and urea formation in diabetic rat. Moreover, loss of insulin effect on the liver leads to glycogenolysis with high hepatic glucose production, which may enhance the increase in AST and ALT [32].

Treatment with *Citrullus colocynthis* in experimental diabetic rats significantly reduced ALT, AST activities and increased albumin concentration after 50 days of administration. These results are nearly similar to those reported by [33]. Who attributed this improvement in AST and ALT activity may be due to *Citrullus colocynthis* demonstrates multiple beneficial anti-diabetic mechanisms, including modulation of carbohydrate metabolism, restoration of beta-cell integrity, insulin releasing activity and improvements in glucose uptake/utilization [34]. It decreases gluconeogenesis and inhibits release of counter regulatory hormones.

Concerning to serum lipid profile, there was significant increase in the concentration of total cholesterol, triacylglycerols and LDL in diabetic rats when compared to the control ones after 4, 6, 8 weeks. Meanwhile HDL showed significant decrease. These results agree with [35] who reported that the increase in impaired Liver function in patients with type I diabetes may be due to this increase to hypercholesterolemia is common in diabetes, contributing to the high prevalence of coronary heart disease [35].

Treatment with *Citrullus colocynthis* in experimental diabetic rats significantly reduced serum total cholesterol, triacylglycerols, LDL-C and increased in HDL concentrations after 50 days of administration. These results are nearly similar to those reported by [36]. Who attributed this improvement to the hypolipidemic effect of *C. colocynthis* extract. Or may be due to depressed hepatic gluconeogenesis. Apositive relationship between gluconeogenesis and lipogenesis is well documented we previously reported that the pulp extract of *Citrullus colocynthis* has a regulatory effect on gluconeogenetic enzymes [36]. Furthermore, the presence of high amounts of saponins in *Citrullus colocynthis* might contribute to the reduction of cholesterol levels by reducing the absorption of cholesterol, increasing the repel of feces estrol, and diarrhea due to increase in peristalsis. Thus, it is reasonable to assume that the effect of *Citrullus colocynthis* on the blood lipid profile in rabbits might also be owing to the presence of these saponins [37].

The obtained results showed that, there was significant decrease in erythrothytes GSH content, and SOD activity in diabetic rats compared to the control ones after 4,6,8 weeks of experiment. While L-MDA concentration showed significant increased. These results agree with [38] who reported that the increase in MDA level were attributed to increased formation of ROS might occur in diabetes. Also, agreement with [39].who reported that this decreased in GSH content was observed in diabetic rats' liver. Decreased GSH levels represent increased utilization due to increased oxidative stress. Also, [40].who attributed this decrease in SOD may be due to the utilization of antioxidant enzymes in the removal of released H_2O_2 released. So that hyperglycemia reduces the synthesis and activities of a number of antioxidant enzymes including SOD presumably by glycation.

Treatment with *Citrullus colocynthis* in experimental diabetic rats significantly reduced L-MDA level and increased GSH content and SOD activity after 50 days of administration. These results are nearly similar to those reported by [41] who investigated that lipid peroxide mediated tissue damage observed in the development of type I and type II DM. Also, *Citrullus colocynthis* extract-induced changes in the antioxidant defense system by estimating TBARS level in serum treated rats. Who observed that significant increases in levels of lipid peroxidation biomarkers was observed in diabetic rats [42]. Reduced glutathione (GSH) is a key antioxidant, which is an important constituent of intracellular protective mechanisms against oxidative stress. In addition, the increase in SOD activity after administration of

Citrullus colocynthis in diabetic rats could be attributed to interfering with their biosynthesis or due to the presence of a free radical scavenging activity of the extract. Thus, the extract could exert a beneficial action against pathological alterations caused by the presence of H2O2, O2 and OH [43]. Flavonoids and phenolic compounds are widely distributed in plants which have been reported to exert multiple biological effects, including antioxidant, free radical scavenging abilities, anti-inflammatory, anticarcinogenic, etc [44].

CONCLUSION: It could be concluded that, *Citrullus colocynthis* plays an important role as antidiabetic activity in experimental diabetic rat, because it shows ameliorating action against its secondary complications due to: hypoglycemic, antioxidant and Hypolipidemic effect.

5. REFERENCES

1. Robertson, R.P. 2004: Chronic oxidative stress: a central mechanism for glucose toxicity in pancreatic islet beta cell in diabetes. *J. Biol. Chem*. 279: 4235-2354.
2. Huang, T.H., Kota, B.P., Razmovski, V., and Roufogalis, B.D. 2005: Herbal or natural medicines as modulators of peroxisome proliferator-activated receptors and related nuclear receptors for therapy of metabolic syndrome. *Basic Clin. Pharmacol. Toxicol*., 96: 3-14.
3. Loew, D., and Kaszkin, M. 2002: Approaching the problem of bioequivalence of herbal medicinal products. *Phytother. Res*., 16: 705-711.
4. Agarwal, V., Sharma, A.k., Upadhyay, A., Singh, G., and Gupta, R. 2012: Hypoglycemic effects of citrullus colocynthis roots .*Acta poloniae pharmaceutica drug research*.; 69(1):75-79.
5. Atef, E., Abd, E.B., and Hatem, K.A. 2011: Effect of citrulus colocynthis ameliorates the oxidative stress and nepharopathy in diabetic experimental. *International Journal of Pharmaceutical Studies and Research*. 2:1-10.
6. Yoshikawa, M., Morikawa, T., Kobayashi, H., Nakamura, A., Matsuhira, K., Nakamura, S., and Matsuda, H. 2007: Bioactive saponins and glycosides. XXVII. Structures of new cucurbitane-type triterpene glycosides and antiallergic constituents from Citrullus colocynthis .*Chem.Pharm.Bull*, 55:428-434.
7. Abdel Wahab, Y.H., O'Harte, F.P., Ratcliff, H., McClenaghan, N.H., Barnett, C.R., and Flatt P.R. 1996: Glycation of insulin in the islets of Langerhans of normal and diabetic animals. *Diabetes*, 45: 1489-1496.
8. Abdel-Hassan, I.A., Abdel-Barry, J.A., and Mohammeda, S.T. 2000: The hypoglycaemic and antihyperglycaemic effect of Citrullus colocynthis fruit aqueous extract in normal and alloxan diabetic rabbits. *J. Ethnopharmacol*., 71: 325-330.
9. Trinder, P.; 1969: Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Ann Clin Biochem*.; 6:24-7.
10. Patton, C. L.; and Crouch, S. R.; 1977: Colorimetric determination of Urea. *Analytical Chemistry*., 49, 464 469.
11. Murray, R. 1984c: Creatinine; in Kaplan et al., (1984): The C.V. Mosby Co. St Louis.Toronto. Princeton: 1261-1266 and 418.
12. Teitz, N. W., Clinical guide to laboratory tests, W.B., 1995: SaundersCo, Philadelphia, PA, 3rd Edn, p. 238.
13. Doumas, B., (1971): Colorimetric determination of albumin. Clinical Chemical Acta.
14. . Reitman, S., and Frankel, S., 1957: Colorimetric determination of GOT and GPT activity. *American Journal of Clinical Pathology* 28, 56.

15. Schettler, G., and Nüssel, E., 1975: Colorimetric determination of Triglycerides and cholesterol. *Arb. Med. Soz. Med. Präv. Med*. 10, 25.
16. Gordon, T., Castell, W. P., Hjortland, M. C., Kannel, W. B., and Dawber, T. R., 1977: High-densitylipoprotein as a protective factor against coronary heart disease. *Am. J. Med*., 62, 707-714.
17. Friedewald, W.T., 1972: *Clin. Chem.*, 18: 49.
18. Esterbauer, H., Cheeseman, K. H., Danzani, M. U., Poli, G.; and Slater, T. F. 1982: Separation and characterization of the aldehyde products of ADP/Fe+2 C stimulated lipid peroxidation in rat liver microsomes. *Biochem. J*; 208: 129-140.
19. Beutler, E., Duron, O., and Kelly, M.B. 1963: Improved method of estimation of blood) yglutathione. Lab. *Clin. Med.*, 61(5): 882.
20. Nishikimi, M., Roa, N.A., and Yogi, K. 1972: *Biochem. Bioph. Res. Common*., 46: 849-854.
21. Kornberg, A., and Horecker, B. L. 1955: Glucose 6 phosphate dehydrogenase. In Methods in Enzymology Vol. 1, edited by S. P. Colowick and N. 0. Kaplan, pp. 323-325. Academic Press, New York.
22. Snedecor, S., and Cochran, A. 1969: Statistical method 6th ed. e Iowa State University., Press, Iowa, USA.
23. Aurell, M., and Bjorck, S. 1992: Determination of progressive renal disease in diabetes mellitus. *Kidney Int*; 41:38-42.
24. Lasaridis, A.N., and Sarefidis, P.A. 2003: Diabetic nephropathy and antihy-pertensive treatment: what are the lessons from clinical trials?. *Am.J. Hypertens*. 16:689-97.
25. Dias, A.S., Porwski, M., Alonso, M., Marroni, N., Collado, P.S., and Gonzalez-Gallego, J. 2005: Quercetin decreases oxidative stress, NF-κB activation, and iNOS overexpression in liver of streptozotocin-induced diabetic rats. *The Journal of Nutrition* 135 (10), 2299–2304.
26. Jadhav, J.K., Masirkar, V.J., and Deshmuck, V.N. 2009: Anti-hyperglycemic effect of diaspyros meloxylon bark against alloxan induced diabetic rats, *International Journal of Pharmtech Research*, 1, pp. 196-200.
27. Rosolowsky, E.T., Ficociello, L.H., and Maselli, N.J. 2008: High-normal serum uric acid is associated with impaired glomerular filtration rate in non proteinuric patients with type 1 diabetes. *Clin J Am Soc Nephrol*; 3: 706–713.
28. Mazzali, M., Kanellis, J., Han, L., Feng, L., Xia, Y.Y., Chen, Q., Kang, D.H., Gordon, K.L., Watanabe, S., Nakagawa, T., Lan, H.Y., and Johnson, R.J. 2002: Hyperuricemia induces a primary renal arteriolopathy in rats by a blood pressure-independent mechanism. *Am J Physiol Renal Physiol*; 282:F991–F997.
29. Falah Hosseini, H., Ardeshir Larijani, Mohammad Bagher, Fakhrzadeh, H., Darvish Zadeh, F., Rahmani, M., Heshmat Ramin Jafariazar, Z., and Shikh Samani, A.H. 2006: The Clinical investigation of Citrullus colocynthis (L.) fruit in free radical scavenging potential of Citrullus colocynthis (L.) Schrad. methanolic fruit extract. *Acta Pharm*., 58(2): 215-20.
30. Mohammad Dallak, Nabil Bashir; Mohammad Abbas; Riyadh Elessa; Mohamed Haidara ; Mohammad Khalil ; Mahmoud A. AL-Khateeb 2009: Concomitant Down Regulation of Olycolytic Enzymes, Upregulation of Gluconeogenic Enzymes and Potential Hepato-Nephro-Protective Effects Following the Chronic Administration of the Hypoglycemic, Insulinotropic Citrullus colocynthis Pulp Extract, *American Journal of Biochemistry and Biotechnology*, 5:(4), 153-161.
31. Jorda, A., Gomez, M., Cabo, J., and Gandrisolia, S. 1982: Effect of

sterptozotocin. *Journal of Immunology* 68: 216-27.
32. Begum, N., and Shanmugasundaram, K.R. 1978: Transaminases in experimental diabetes. *Arogya J Health Sci*; 4:116-22.
33. Rajesh, M. G., and Latha, M. S. 2004: "Preliminary Evaluation of the Antihepatotoxic Activity of Kamilari, a Polyherbal Formulation," *Journal of Ethnopharmacology*, 91: 99-104.
34. Agarwal, V., Sharma, A.K., Upadhyay, A., Singh, G., and Gupta, R. 2012: Hypoglycemic effects of citrullus colocynthis roots .Acta poloniae pharmaceutica drug Research; 69(1):75-79.
35. Gentile, S., Turco, S., and Guarino, G. 2000: Comparative efficacy study of ator-vastatin vs. simvaslatin, provastatin, lovastnlin and placebo in type 2 diabetic patients with hypercholcslerolemia. *Diabetes*, 2: 355-362.
36. Boulange, A., Planche, E., and Gasquet, P. 1981: *Me tab Clin Exp.* 30: 1045-1052.
37. Zamani, M., Rahimi, A.O., Mahdavi, R., Nikbakhsh, M., Jabbari, M.V., and Rezazadeh, H., (2007): Assessment of anti-hyperlipidemic effect of Citrullus colocynthis. *Revista Brasileira de Farmacognosia*; 17(4):492-6.
38. Knoll, K.E., Pietrusz, J.L., and Liang, M. 2005: Tissue-specific transcriptome responses in rats with early streptozotocin-induced diabetes. *Physiol Genomics*, 21:222-9.
39. Dallak, M., in vivo, (2011): hypolipidemic and antioxidant effects of Citrullus colocynthis pulp extract in alloxan-induced diabetic rats. *African Journal of Biotechnology*; 10(48): 9898-903.
40. Yoshida, S.I., Hashimoto, T., Kihara, M., Ima, N., Nomur, K., Hirawa, N., Toya, Y., Kitamura, H., and Umemura, S. 2008: Urinary oxidative stress markers closely reflect the efficacy of Candesartan treatment for diabetic nephropathy. *Nephron Exp Nephrol*, 111:20-30.
41. Feillet Coudray, C., Rock, E., Coudray, C., Grzelkowska, K., Azais Braesco, V., Dardevet, D., and Mazur, A. 1999: Lipid peroxidation and antioxidant status in experimental diabetes. *Clin. Chem. Acta*. 284: 31-43.
42. Ross, D. 1988: Glutathione, Free radicals and chemotherapeutic agents. Mechanisms of free radical induced toxicity and Glutathione dependent protection. *Pharmocol. Ther*, 37: 231-249.
43. Scheen, A.J. 2003: Treatment of type 2 diabetes. *Acta Clinica Belgica*, 58(5): 318 – 324.
44. Miller, A. L. 1996: Antioxidant flavonoids: structure, function and clinical usage. *Alt. Med. Rev*. 110: 3–11.

الدور الكيميائي الحيوي لبعض العوامل المؤثرة على القصور الكلوي لمرض السكرى المحدث تجريبياً وعلاقتها بالجلطة الوريدية

أميمة أحمد رجب أبو زيد[1]، خالد محمد مصطفى فرارة [2]، علياء حسن على البقلى[3]

[3، 1] قسم الكيمياء الحيوية -كلية الطب البيطري-جامعة بنها.
[2] قسم الباثولوجيا الإكلينيكية – كلية الطب البيطري بمشتهر – جامعة بنها

الملخص العربي

يعتبر مرض البول السكري من أكثر الأمراض شيوعاً وهو عبارة عن مجموعة من المتغيرات التي تحدث في الاحتراق والأيض داخل الجسم نتيجة لقلة أو عدم إفراز هرمون الأنسولين من خلايا البنكرياس والارتفاع المزمن في نسبة الجلوكوز في الدم تؤدى إلي تدمير خلايا الكليتين والأعصاب والجهاز الدوري لذلك انتشر فى الآونة الاخيرة استخدام النباتات الطبية في علاج الأمراض المختلفة دون دراسة كافيه لتأثير هذه المواد على الجسم ومنها الحنظل وذلك لفاعليته كمضاد للبكتيريا، مضاد للالتهاب هذا بالإضافة الى معرفة التأثيرات المضادة للأكسدة من المعالجة بالحنظل على التغيرات الكيميائية الحيوية لبعض المؤشرات الحيوية والأنزيمات والتغيرات الحادثة فى الكلى الناتجة من التعرض لمرض البول السكري لفترات طويلة. لقد أجريت هذه الدراسة على عدد (60) ستون من ذكور الفئران البيضاء والتي تتراوح أعمارها بين شهر وشهر ونصف وأوزانها بين 200–250 جرام حيث تم تغذيتها على نفس نوع العليقة دون تمييز قسمت إلى3 مجموعات: 1–المجموعة الأولى: (المجموعة الضابطة) احتوت على عدد 20 من ذكور الفئران البيضاء. 2–المجموعة الثانية: (المجموعة المحدث بها مرض البول السكري): احتوت على 20 من ذكور الفئران البيضاء تم حقنهم بمادة الأستربتوزتوسين في الغشاء البروتوني بجرعة مقدارها 60 ميللي جرام لكل كيلوجرام. 3 –المجموعة الثالثة:) مجموعة مستخلص الحنظل والمحدث بها مرض البول السكري) : احتوت على 20 من ذكور الفئران البيضاء تجريعهم بمستخلص الحنظل لمده 50 يوم عن طريق الفم بجرعة مقدراها 50 مليجرام لكل كيلوجرام من وزن الجسم طوال فترة التجربة وذلك بعد حقنهم بمادة الأستربتوزتوسين.
تم جمع العينات على ثلاث فترات بعد 4 و6 و8 أسابيع من بداية العلاج وقد أوضحت الدراسة ما يلي: حدث نقص معنوي فى كل من الجلوكوز، اليوريا، الكرياتنين، ألانين أمينو ترانس فيراز وأسبرتات أمينو ترانس فيراز، الكولسترول الكلى وثلاثي الجلسريدات، الكوليسترول المنخفض الكثافة، الأكسدة الفوقية للدهون (ال–مالون داى ألدهيد) في حين حدث زيادة معنوية فى الكوليسترول العالي الكثافة، إنزيم الجلوتاثيون، السوبر اوكسيد ديسميوتيز، الألبومين (الزلال) بالمقارنة بمجموعة مرض البول السكرى.

(مجلة بنها للعلوم الطبية البيطرية: عدد 25(1):218–227, سبتمبر 2013)