



Attenuation of Some Metabolic Deterioration Induced by Diabetes Mellitus Using Different *Jatropha curcas* Extracts

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ABSTRACT

The present research focuses on pharmacological effects of *Jatropha curcas* extracts on specific biochemical parameters in streptozotocin (STZ)-induced diabetic rats as compared to glibenclamide antidiabetic drug. Diabetes mellitus (DM) was induced using STZ (45 mg/kg b.w). *J. curcas* extracts were orally administered at a dose of 250 mg/kg/day and glibenclamide at a dose of 10 mg/kg/day for 30 days. Creatinine, urea, inflammatory biomarkers; C-reactive protein (CRP), tumor necrosis factor alpha (TNF- α) and interleukin-10 (IL-10) levels were measured in rats blood serum. Creatinine, urea, CRP and TNF- α levels were significantly increased in diabetic rats with percentages of 100, 53.33, 136.45 and 78.45%, respectively. However, IL-10 level showed significant decrease with percentage 39.36%. The results showed that all *J. curcas* extracts have a positive effect against creatinine, urea, CRP and TNF- α high level besides, relieving kidney disorders associated with DM. *J. curcas* could be applied effectively to reduce renal complications paralleling to DM.

Keywords: Diabetes mellitus, Glibenclamide, *J. curcas*, STZ.

INTRODUCTION

Diabetes mellitus (DM), a metabolic disorder is characterized by chronic hyperglycemia, damage of pancreatic β -cell, carbohydrate complication, metabolism of fat and protein occurred by abnormal secretion of insulin, defects in insulin action or both.¹ DM is a grave health problem being the third greatest cause of death all over the world, and if not treated, it is responsible for many complications affecting various organs in the body.² DM leads to chronic kidney disease (CKD) in developed countries and developing countries as a consequence of the wide increase in type II diabetes and obesity.³ CKD is a world-wide health problem that affects on more than 50 million people, and more than 1 million of them are receiving renal replacement therapy and its management of CKD is costly.^{4,5} Persons suffering from diabetes and CKD fall under the high risk to lose kidney function. Kidney is the organ responsible for elimination of waste products, toxins and drugs from the body. However, it has many other functions including; water and electrolyte homeostasis, maintenance of plasma osmolarity, acid-base balance, and the production and secretion of hormones, e.g., renin, erythropoietin, 1, 25-dihydroxyvitamin D₃.^{6,7}

Inflammation may play a critical intermediary role in the pathogenesis of type II diabetes.⁸ It has been demonstrated that, various inflammatory cytokines, such as TNF- α , interferon (IFN)- γ and IL-1 β , produced during hepatic injury are involved in promoting tissue damage.⁹ The inflammatory cytokines such as IL-6, TNF- α and CRP to type II diabetes are attributed to insulin resistance due to cytokines inhibit the transcriptional activity and

protein expression of several molecules may be related to insulin signaling and action, such as glucose transport protein (GLUT-4).¹⁰ Moreover, there is an independent risk of CRP and TNF- α for chronic kidney disease in patients with type II diabetes.¹¹ However, IL-10 can acts as β -cell stimulatory factor that could be contributing to the β -cell hyperactivity.¹²

Medicinal plants used for cure hyperglycemia are important for ethno-botanical community due to their content of valuable medicinal activities in their different parts. *J. curcas* (family, Euphorbiaceae) has plentiful biological properties. Different parts of the plant including the leaves, fruits, latex and bark contain bioactive compounds such as glycosides, tannins, phytosterol, flavonoids and steroidal sapogenins with several medicinal properties.¹³⁻¹⁵ Stems of young leaves have been used to successfully treat urinary infections.¹⁶ The ethanolic, methanolic and aqueous extracts of *J. curcas* stem bark had a potential antioxidant activity.¹⁷ Also, the latex of *J. curcas* contains alkaloids including Jatrophine, Jatropham and curcain with anti-cancer activities.¹⁸ Moreover, the ethanolic extract of *J. curcas* areal parts possessed the highest antidiabetic activity may be due to it contained flavonoidal glycosides which may be the responsible compounds for the antidiabetic activity.¹⁹

So, the present study is design to demonstrate the hypoglycemic efficiency of petroleum ether, ethyl acetate, successive and crude methanolic extracts of *J. curcas* as compared to antidiabetic glibenclamide (reference drug) in STZ-induced DM in rats. Creatinine, urea levels and inflammatory biomarkers including CRP,



TNF- α and IL-10 were measured. Histopathological investigation of kidney architectures was also under investigation.

MATERIALS AND METHODS

Chemicals

All kits are the products of Biosystems (Alcobendas, Madrid, Spain), Sigma Chemical Company (St. Louis, MO, USA) and Biodiagnostic Company (Cairo, Egypt). All other chemicals in the present study are of analytical grade, products of Sigma, Merck and Aldrich

Collection of Plant Material and Sample Preparation

J. curcas fresh leaves were collected from the Aromatic and Medicinal Plant Department farm, Agriculture Research Centre, Egypt during July 2013. The plant was authenticated by Agricultural engineering Therese Labib, El Orman Botanical Garden, Egypt (<http://wikimapia.org/9432/Orman-Botanical-Gardens-Giza>). The leaves were washed with tap water then with distilled water to remove dust and dirt. Leaves were air dried under shade condition then grinded and homogenized to coarse powder finally stored in opaque screw tight jars until use.

Successive and Crude Extracts Preparation

Successive Extracts Preparation

Powdered leaves of *J. curcas* were extracted by soaking using successive three solvents with different polarities.²⁰ Solvents used were: petroleum ether, ethyl acetate and methanol with percentage of extraction 1:3 w/v. Briefly, 2.5 kg of *J. curcas* powdered leaves were soaked in 7.5 liter of petroleum ether and shaken on shaker (Heidolph UNIMAX 2010) for 48 hrs. at 150 rpm. The extract was filtered using a Buchner funnel and Whatman No. 4 filter paper and the plant residue was re-extracted with the addition of fresh petroleum ether for another two times. Combined filtrates were concentrated using Rotary evaporator (Heidolph-Germany) at 40 °C under vacuum. The remaining plant residue was dried and soaked in ethyl acetate and methanol successively as described earlier. Finally, all resulting dry extracts were kept at 4 °C for further analysis.

Crude Methanolic Extract Preparation

About 300 g of *J. curcas* powdered leaves were extracted using 900 ml methanol by soaking and shaken on shaker at 150 rpm for 48 hrs. The extract was filtered using a Buchner funnel and Whatman No. 4 filter paper. The filtrate was concentrated using Rotary evaporator at 40 °C under vacuum. The resulting dry extract was kept at 4 °C for further analysis.

Experimental Animals

Female Wister rats (130-150 g) were used for the evaluation of anti-diabetic effects of *J. curcas* petroleum ether, ethyl acetate, successive and crude methanolic extracts. Rats were provided by the Animal House of the

National Research Centre (NRC) and housed in a temperature-controlled environment (26-29 °C) with a fixed light/dark cycle for one week as an adaptation period to acclimatize under normal combination with free access to water and food.

The present study is approved by the Ethical Committee of the National Research Centre (NRC), Egypt, provided that the animals will not suffer at any stage of the experiment.

Experimental Design

Rats selected for this study were divided into eleven groups of ten rats each as follows:

Group 1: Normal healthy control rats, Groups 2-5: Normal rats treated orally with 250 mg/kg body weight of petroleum ether, ethyl acetate, successive and crude methanolic extracts of *J. curcas* leaves for 30 days.²¹ Group 6: Is considered as diabetic groups; where type 2 diabetes was induced by STZ.

Each rat was injected intraperitoneally with a single dose of STZ (45 mg/kg body weight dissolved in 0.01 M citrate buffer immediately before use.^{22,23} After injection, animals had free access for food and water and were given 5% glucose solution to drink overnight to encounter hypoglycaemic shock.

Animals were checked daily for the presence of glycosuria.²⁴ Animals were considered to be diabetic if glycosuria was present for 3 consecutive days. After 3 days of STZ injection fasting blood samples were obtained and fasting blood sugar was determined (>300 mg/dl). Hyperglycemic rats were used for the experiment and classified as follows:

Group 7-10: Diabetic rats orally administered 250 mg/kg body weight petroleum ether, ethyl acetate, successive and crude extracts of *J. Curcas* for 30 days respectively, Group 11: Diabetic rats orally administered antidiabetic glibenclamide reference drug 10 mg/kg body weight daily for 30 days.²⁵

Sample Preparations

After 30 days of treatments, rats were fasted overnight (12-14 hours), anesthetized by diethyl ether and blood collected by puncture of the sublingual vein in clean and dry test tube, left 10 minutes to clot and centrifuged at 3000 rpm for serum separation.

The separated serum was used for biochemical analysis of creatinine and urea. After blood collection, rats of each group were sacrificed, the kidney was removed immediately (a part was fixed in 10% formalin for histopathological examination).

Biochemical Examination

Serum creatinine concentration was measured using colorimetric kit.²⁶ Total urea level was estimated using colorimetric kit.²⁷ Estimation of serum inflammatory markers; CRP, TNF- α as well as IL-10 was performed by ELISA; a sandwich enzyme immunoassay.



Calculation:

$$\% \text{ change} = \frac{\text{Mean of control} - \text{mean of treated}}{\text{Mean of control}} \times 100$$

$$\% \text{ of improvement} = \frac{\text{Mean of treated} - \text{mean of disease}}{\text{Mean of control}} \times 100$$

Histopathological Analysis

Kidney slices were fixed instantaneously in buffer neutral formalin (10%) for 24 hours for fixation then processed in automatic processors, embedded in paraffin wax (melting point 55-60 °C) and paraffin blocks were obtained. Sections of 6 µm thicknesses were prepared and stained with Haematoxylin and Eosin (H & E) stain.²⁸

The cytoplasm stained shades of pink and red and the nuclei gave blue colour. The slides were examined and photographed under a light microscope at a magnification power of x400.

Statistical Analysis

Data presented as mean ± S.D, n=10. Statistical analysis was carried out by using one way analysis of variance (ANOVA) SPSS (version 7) computer program and Co-state computer program, where unshared letter is significant at $P \leq 0.05$.

RESULTS**Creatinine and Total Urea Levels**

Table (1) indicated that, creatinine level was insignificantly affected with different extracts-treated normal rats as compared to untreated control one. Normal treated groups with petroleum ether, ethyl acetate and successive and crude methanolic extracts showed insignificant change in total urea levels as compared to untreated one.

With respect to the present results, diabetic rats showed significant increase in both creatinine and total urea levels with percentage increase reached to 100 and 53.33%, respectively.

Creatinine levels were returned to normal value, showed insignificant change in diabetic-treated groups with petroleum ether, ethyl acetate, successive methanolic, crude methanolic extracts as well as glibenclamide antidiabetic reference drug as compared to normal control group.

On the other hand, diabetic-treated groups with petroleum ether, ethyl acetate, successive and crude methanolic showed insignificant decrease in total urea levels (Table 1). However, crude methanolic extract as well as Glibenclamide supplemented to diabetic rats showed percentages of improvement in total urea level reached to 43.33 and 56.66%, respectively (Table 1).

Table 1: Comparative effects of different extracts of *J. curcas* supplementation on kidney function (creatinine and total urea), in different therapeutic groups

Groups	Parameters	Creatinine (mg/dl)	Urea (mg/dl)
Negative control	Mean± S.D.	0.20±0.02 ^b	30.00±2.25 ^b
Negative petroleum ether extract	Mean ±S.D	0.21±0.01 ^b	31.00±3.10 ^b
	% Change to control	-5	-3.30
Negative ethyl acetate extract	Mean ±S.D	0.24±0.03 ^b	28.00±1.52 ^{bc}
	% Change to control	-20	6.60
Negative successive methanolic extract	Mean ±S.D.	0.14±0.01 ^b	29.00±1.91 ^{bc}
	% Change to control	30	3.33
Negative crude methanolic extract	Mean ±S.D.	0.15 ±0.01 ^b	27.00±1.60 ^{bc}
	% Change to control	25	10.00
Diabetic rats	Mean ±S.D.	0.40±0.03 ^a	46.00±9.98 ^a
	% Change to control	-100	53.33
Diabetic petroleum ether extract	Mean ±S.D.	0.24±0.02 ^b	35.00±3.21 ^b
	% Change to control	-20	-16.66
	% Of improvement	-80	-36.66
Diabetic ethyl acetate extract	Mean ±S.D.	0.22±0.04 ^b	38.00±3.80 ^b
	% Change to control	-10	-23.33
	% Of improvement	-90	-26.66
Diabetic successive methanolic extract	Mean ±S.D.	0.15±0.04 ^b	37.00±3.75 ^b
	% Change to control	25	-16.91
	% Of improvement	-125	-30.00
Diabetic crude methanolic extract	Mean ±S.D.	0.21±0.025 ^b	33.00±3.20 ^{bc}
	% Change to control	-5	-10.00
	% Of improvement	-95	-43.33
Diabetic-antidiabetic drug	Mean ±S.D.	0.21±0.03 ^b	29.00±2.00 ^{bc}
	% Change to control	-5	3.33
	% Of improvement	-95	-56.66

Creatinine and total urea levels are expressed in mg/dl. Data presented as mean ± SD, n=10. Statistical analysis is carried out using Co-state and SPSS computer programs (version 7), where unshared letter is significant at $P \leq 0.05$.

Inflammatory Cytokines; CRP, TNF-α and IL-10 levels

It is noticeable that there is no significant difference in CRP, TNF-α and IL-10 levels in treated normal rats with petroleum ether, ethyl acetate, successive methanolic and crude methanolic extracts as compared to untreated control one. Significant increase in inflammatory markers; CRP and TNF-α was noticed in diabetic rats with percentages 136.45 and 78.45%, respectively however, IL-10 showed significant decrease with percentage reached to 39.36%. Treatment of diabetic rats with crude methanolic extract and glibenclamide drug demonstrated insignificant change in CRP level as compared to control rats. While, CRP level recorded significant increase with petroleum ether, ethyl acetate and successive methanolic extracts with percentages of improvement reached to

93.56, 111.11 and 123.97 %, respectively. TNF- α level showed significant increase in diabetic-treated groups with petroleum ether, ethyl acetate, successive methanolic, crude methanolic extracts as well as glibenclamide standard drug with percentages of improvement 33.39, 41.88, 40.27, 56.95 and 59.12%, respectively. Considering IL-10, it exhibited insignificant change in diabetic-treated groups as compared to normal control one (Table 2).

Histopathological Examination of Kidney

Figures (1a-1l) showed the kidney histopathological examination of normal, diabetic and diabetic - treated rats. Kidney of diabetic rats (Figures 1b, 1c and 1d) demonstrated vacuolation of endothelial lining

glomerular tufts, perivascular oedema associated with inflammatory cells infiltration, vacuolation of epithelial lining renal tubules and atrophy of glomerular tuft.

Treatment of diabetic rats with petroleum ether extract of *J. curcas* (Figures 1e and 1f) showed perivascular oedema and no other histological change. However, treatment with ethyl acetate and successive methanolic extracts declared amelioration in kidney architecture that apparent normal (Figures 1g and 1h). Administration of crude methanolic extract (Figures 1i and 1j) showed focal renal hemorrhage with no other histopathological change. Treatment of diabetic rats with glibenclamide (Figures 1k and 1l) showed vacuolation of epithelial lining renal tubules with no other change.

Table 2: Comparative effects of different extracts of *J. curcas* supplementation on the inflammatory biomarkers; CRP, TNF- α and IL-10 levels in different therapeutic groups.

Groups	Parameters	CRP (ng/ml)	TNF- α (pg/ml)	IL-10 (pg/ml)
Negative control	Mean \pm S.D.	5.13 \pm 9.22 ^e	105.91 \pm 0.33 ^e	65.65 \pm 1.03 ^{ab}
	Mean \pm S.D	5.32 \pm 0.21 ^{de}	108.33 \pm 1.86 ^e	63.52 \pm 2.22 ^{ab}
Negative petroleum ether extract	% Change to control	-3.70	-2.28	3.24
	Mean \pm S.D	5.37 \pm 0.20 ^{de}	105.80 \pm 1.38 ^e	64.91 \pm 2.20 ^{ab}
Negative ethyl acetate extract	% Change to control	-4.67	0.10	1.12
	Mean \pm S.D.	5.61 \pm 0.33 ^{de}	106.68 \pm 1.11 ^e	63.22 \pm 0.92 ^{ab}
Negative successive methanolic extract	% Change to control	-9.35	-0.72	3.70
	Mean \pm S.D.	5.32 \pm 9.61 ^{de}	105.61 \pm 2.40 ^e	65.74 \pm 1.03 ^{ab}
Negative crude methanolic extract	% Change to control	-3.70	0.28	-0.13
	Mean \pm S.D.	12.13 \pm 0.27 ^a	189 \pm 4.97 ^a	39.81 \pm 2.20 ^c
Diabetic rats	% Change to control	-136.45	-78.45	39.36
	Mean \pm S.D.	7.33 \pm 0.42 ^b	153.63 \pm 2.97 ^b	55.95 \pm 0.32 ^b
Diabetic petroleum ether extract	% Change to control	-42.88	-45.05	14.77
	% of improvement	-93.56	-33.39	24.58
	Mean \pm S.D.	6.43 \pm 0.38 ^c	144.64 \pm 1.83 ^c	57.51 \pm 1.10 ^{ab}
Diabetic ethyl acetate extract	% Change to control	-25.34	-36.56	12.39
	% of improvement	-111.11	-41.88	26.96
	Mean \pm S.D.	5.77 \pm 0.19 ^d	146.34 \pm 1.95 ^c	58.69 \pm 1.36 ^{ab}
Diabetic successive methanolic extract	% Change to control	-12.47	-38.17	10.60
	% of improvement	-123.97	-40.27	28.75
	Mean \pm S.D.	5.54 \pm 0.34 ^{de}	128.68 \pm 4.87 ^d	59.25 \pm 0.96 ^{ab}
Diabetic crude methanolic extract	% Change to control	-7.99	-21.49	9.74
	% of improvement	-128.46	-56.95	29.61
	Mean \pm S.D.	5.37 \pm 9.54 ^{de}	126.38 \pm 1.81 ^d	69.08 \pm 17.34 ^a
Diabetic anti-diabetic Drug	% Change to control	-4.67	-19.32	-5.22
	% of improvement	-131.77	-59.13	44.58

CRP is expressed in ng/ml, TNF- α and IL-10 are expressed in pg/ml, Data presented as mean \pm SD, n=10. Statistical analysis is carried out using Co-state and SPSS computer programs (version 7), where unshared letter is significant at P \leq 0.05.

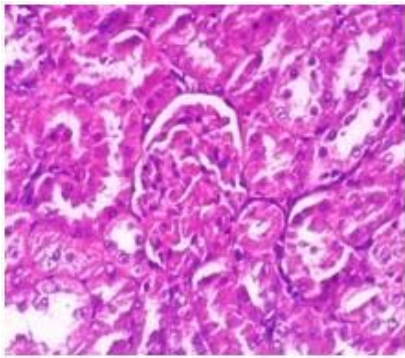


Figure 1a: Kidney of normal control rats showing the normal histological structure of renal parenchyma.

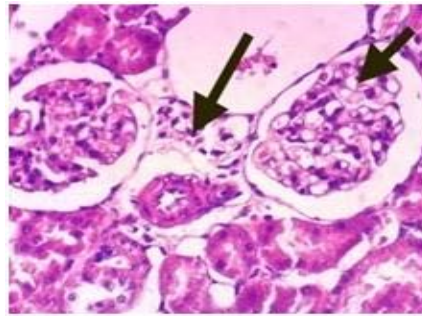


Figure 1b: Kidney of diabetic rats showing vacuolation of endothelial lining glomerular tufts, perivascular oedema associated with inflammatory cells infiltration.

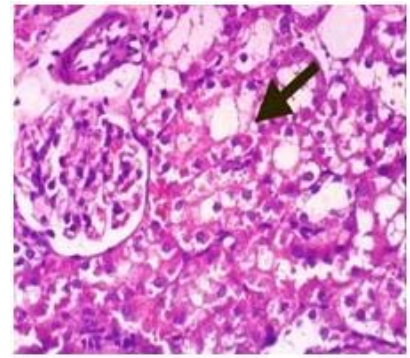


Figure 1c: Kidney of diabetic rats showing vacuolation of epithelial lining renal tubules.

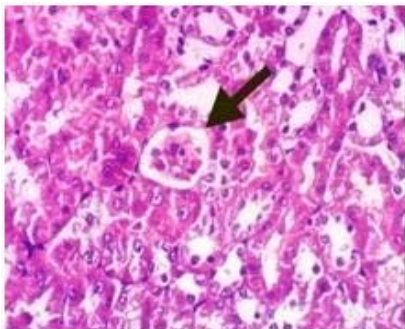


Figure 1d: Kidney of diabetic rats showing atrophy of glomerular tuft.

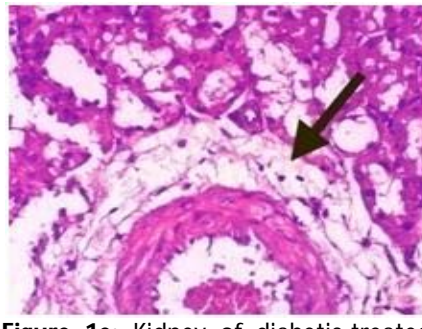


Figure 1e: Kidney of diabetic-treated rats with petroleum ether extract showing perivascular oedema. E X 400).

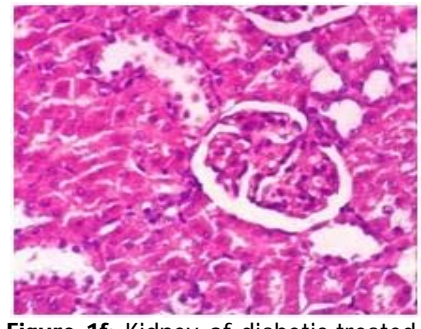


Figure 1f: Kidney of diabetic-treated rats with petroleum ether extract showing no histopathological changes.

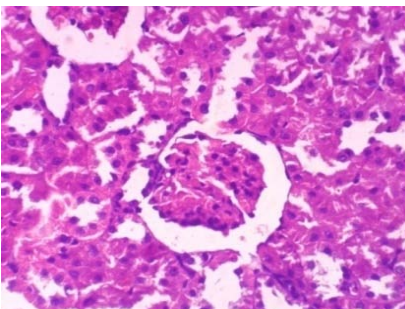


Figure 1g: Kidney of diabetic-treated rats with ethyl acetate extract showing no histopathological changes.

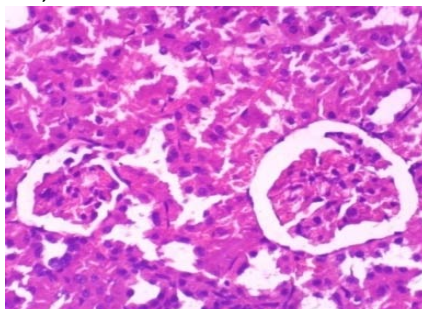


Figure 1h: Kidney of diabetic-treated rats with successive methanolic extract showing no histopathological changes.

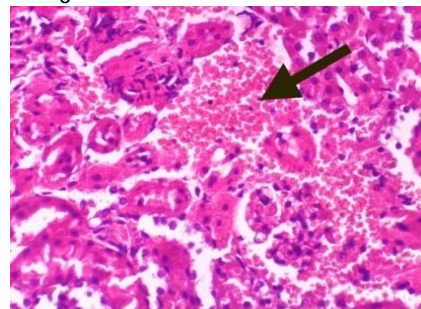


Figure 1i: Kidney of diabetic-treated rats with crude methanolic extract showing focal renal hemorrhage.

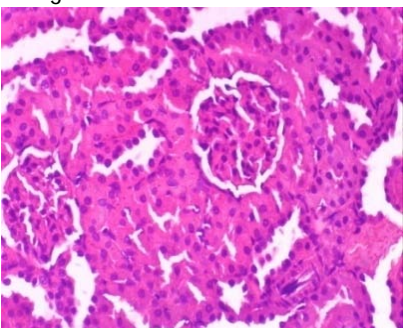


Figure 1j: Kidney of diabetic-treated rats with crude methanolic extract showing no histopathological changes.

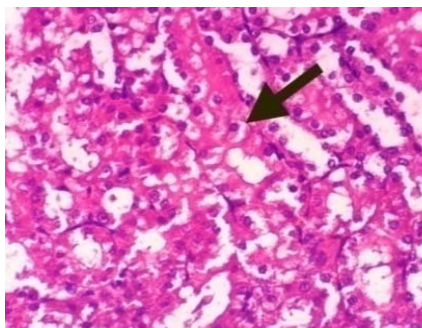


Figure 1k: Kidney of diabetic-treated rats with glibenclamide drug showing vacuolation of epithelial lining renal tubules.

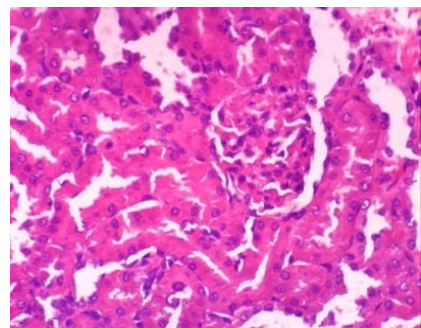


Figure 1l: Kidney of diabetic-treated rats with glibenclamide drug showing no histopathological changes.

Figure 1: Histopathological examination of normal kidney, diabetic and diabetic-treated rats

DISCUSSION

DM is a chronic metabolic disorder that can lead to cardiovascular, renal, neurologic and retinal complications.²⁹ Type II diabetes has a poor metabolic control that is a prevalence of renal damage about 20% is associated with components of the metabolic syndrome.³⁰ Additionally, in diabetic patient, the raised content of plasma creatinine and urea levels may be an indicator on the pre-renal problem such as volume depletion.³¹ Also, high creatinine levels observed in diabetic patients are joined with the impaired function of the nephrons.³² In according to the present results, diabetic rats show significant increase in creatinine and total urea levels with percentages 100% and 53.33% (Table 1), respectively as compared to normal control rats.

All extracts of *J. curcas* as well as glibenclamide in diabetic rats revealed insignificant change in creatinine level as compared to normal control rats. On the other hand, diabetic-treated rats with petroleum ether, ethyl acetate, successive and crude methanolic extracts exhibited insignificant change in total urea level. The high levels of creatinine and urea in diabetes type II were attributed to impaired function of the nephrons and fall in filtrating capacity of the kidney leading to accumulation of waste products.³²

Crude methanolic and ethyl acetate extracts showed the highest ameliorative percentages in creatinine level, respectively while crude methanolic and petroleum ether extracts showed the highest ameliorative percentages in total urea level, respectively. The enhancement of renal biochemical functions with the treatment of *J. curcas* leaves extracts may relies on the explanation of Kissane.³³ The author declared that, the antidiabetic action, resulting in attenuation of altered metabolic status in animals and by the remedial ability of the renal tubules. Hyperglycemia leads to the increased formation of advanced glycation end-products (AGEs), causing inflammation and renal damage.³⁴ Antioxidants phytochemicals such as flavonoids can prevent the accumulation of AGEs.³⁵ The phytochemical screening of *J. curcas* leaves extracts revealed the presence of bioactive compounds including flavonoids, saponins, alkaloids, steroids and tannins.³⁶ Therefore, the positive effect of *J. curcas* extracts on creatinine and total urea levels may be attributed to the presence of these phytochemicals.

Type II diabetes mellitus (T2DM) is considered as a metabolic pro-inflammatory disorder that has severe hyperglycemia and highly levels of circulating cytokines.³⁷ CRP is a sensitive marker of systemic inflammation and is conjugated with type 2 diabetic.³⁸ It is observed that, CRP levels were highly increased in case of diabetic rats. This is may be due to the dysfunction of β -cell in insulin resistance.³⁹ In agreement with the present results, diabetic patients have higher levels of CRP than healthy ones.⁴⁰

Regarding to TNF- α , an adipocytokine, is involved in inflammation and its disturbances metabolism is attributed to insulin resistance.^{41,42} In the present study, TNF- α level is highly increased in diabetic rats. In concern with the present results, elevated levels of TNF- α associated with diabetes were reported.⁴³ With respect to IL-10 cytokines, is identified as an important modulator of inflammatory cytokines production.⁴⁴ The current results are in accordance with obtained by Van Exel et. al.⁴⁵ The authors revealed that IL-10 levels decreased in type 2 diabetic patients (Table 2). Also, high concentrations of glucose lead to high production of intracellular reactive oxygen species (ROS).⁴⁶ Consequently, ROS production can lead to high production of proinflammatory cytokines that can affect β -cells in a paracrine manner.⁴⁷

Administration of *J. curcas* extracts exhibited anti-inflammatory effects however, the crude methanolic extract showed the best anti-inflammatory effects among all extracts. These results may be explained on the basis of Seta and Laga.⁴⁸ The authors mentioned that methanol is a universal solvent that dissolves all types of compounds, polar, semi-polar and non-polar.

Treatments of diabetic rats with *J. curcas* areal parts extracts were shown to improve glucose level that may be in turn, lead to decrease the high levels of inflammatory cytokines.¹⁹ Moreover, *J. curcas* showed the presence of flavonoid compounds such as catechin and quercetin.⁴⁹ In rats, catechins lead to a significant lowering effect in oxidative stress and pro-inflammatory cytokine levels, increasing catalase and superoxide dismutase and decrease NOS, TNF- α , and NF- κ B expression.^{50,51} Also, quercetin inhibits the production of TNF- α and NO and recently it has been shown to prevent insulin resistance and to down-regulate inflammation by attenuating IL-6, IL-1 β , IL-8, and MCP-1 expression.^{52,53} Accordingly, the anti-inflammatory effect of *J. curcas* extracts may be due to the presence of flavonoid such as catechin and quercetin.

Figures (1b, 1c and 1d) of diabetic rat's kidney showed vacuolation of endothelial lining glomerular tufts, perivascular oedema associated with inflammatory cells infiltration, vacuolation of epithelial lining renal tubules and atrophy of glomerular tuft. The present histopathological results of diabetic rats' kidney are agreed with those reported by Zappini et. al.⁵⁴ The authors found decline in glomerular filtration rate in patients with type II diabetes. Treatment of diabetic rats with *J. curcas* extracts showed enhancement in renal architectures as they apparent normal. In this concern, methanolic fraction of *J. curcas* (MFJC) reduced the incidence of liver lesions, lymphocytic infiltrations and hepatic necrosis induced by Aflatoxin B1 (AFB1) in rats suggesting, MFJC could protect liver against AFB1-induced oxidative damage in rats.⁵⁵ Also, rutin (flavonoid compound) has antioxidant and anti-inflammatory effects that lead to reduction of blood glucose level in the STZ-induced diabetic rats besides, functionally and



formatively protection of pancreas, heart, liver, kidney, and retina tissues that attributed to diabetic complications.⁵⁶ The methanolic extract of *J. curcas* leaves showed the presence of flavonoids compounds.⁵⁷ Thus, the protective effect of *J. curcas* leaves may be due to the presence of flavonoid compounds that lead to reducing the oxidative stress resulting normal structures and functions. Hence, administration of *J. curcas* extracts could protect against diabetes disorders.

CONCLUSION

The present results confirmed that different *J. curcas* leaves extracts (successive extracts and crude methanolic extract) had antidiabetic and anti-inflammatory activities through ameliorative the renal dysfunction attributed to diabetes type II. This may be due to the presence of bioactive compounds that may provide promising medication for diabetes.

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