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Effect of Camel Milk on Oxidative Stresses in Experimentally Induced Diabetic Rabbits

El-Said El-Sherbini El-Said[1*]
Gehad Ramadan El-Sayed[1]
Esraa Tantawy[1]

[1]*Department of Biochemistry and Chemistry of Nutrition, Faculty of Veterinary Medicine, Mansoura University, Mansoura, Egypt*

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Abstract

Camel milk has an importance in the treatment of diabetes. It has been shown that the patients who drink camel milk daily, their need to insulin decrease. Therefore, this study aimed to investigate the effect of camel milk in comparison with insulin treatment in experimentally-induced diabetes. This study was carried out on forty male New Zealand rabbits, divided into four groups with ten rabbits in each. The first group G1 was considered as control non-diabetic group and received only normal saline solution. The other animals were injected intravenously with alloxan for induction of diabetes mellitus and then divided into three groups' ten rabbits each as the follows: G2 considered as control diabetic and left untreated, G3 was considered as diabetic and treated with insulin, and G4 was considered as diabetic and received camel milk. At the end of the experiment (4 weeks), blood (whole blood & serum) and tissue samples (liver, kidney and pancreas) were collected from all the animals for analysis of: enzymatic SOD and catalase, non-enzymatic GSH antioxidant enzyme activities. Serum malondialdeyde, glucose, insulin and lipid profile also were analyzed. The results showed that the camel milk was effective in the treatment of diabetes in comparison to insulin treatment alone. In addition to its hypoglycemic effect, camel milk improved the diabetes-induced oxidative stress. The histopathological evaluations demonstrated that there was a regeneration in β cells and the islets of Langerhans among the pancreatic acini in rabbits receiving camel milk. Our findings suggested that the camel milk administration in case of insulin dependant diabetes mellitus might be recommended as an oral anti-diabetic remedy.

Key Words: Camel milk, Oxidative stress, Diabetes mellitus, Rabbit

***Corresponding author:**
El-Said El-Sharbini El-Said
Department of Biochemistry and Chemistry of Nutrition, Faculty of Veterinary Medicine,Mansoura University, Mansoura, Egypt
E-mail address: sshrbini@mans.edu.eg

Introduction

Diabetes mellitus is a metabolic disorder in which the body does not produce or properly use insulin. It causes disturbances in carbohydrates, protein and lipid metabolism. During diabetes a profound alteration in the concentration and composition of lipids occur.[1] Despite numerous studies in the understanding and management of diabetes, the disease and the disease-related complications are increasing unabated.[2] Glucose is a substrate and an indispensable energy supplier, which supports cellular function. Glucose measurements are used in the diagnosis and monitoring of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia and pancreatic islet carcinoma.[3]

Oxidative stress plays a central role in the onset of diabetes mellitus as well as in the development of vascular and neurologic complications of the disease.[4] The source of oxidative stress is a cascade of reactive oxygen species (ROS) leaking from the mitochondria,[5] and this process has been associated with the onset of type 1 diabetes via the apoptosis of pancreatic β-cells and also the onset of type 2 diabetes via insulin resistance.[6] Onset of diabetes is a complex mechanism because hyperglycemia may be the cause and effect of increased oxidative stress.[7]

The existence of hyperglycemia produces increased oxidative stress (OS) via non-enzymatic glycation, glucose autoxidation, and alterations in polyol pathway activity with subsequent influences on the whole organism .[7] Type I diabetes demonstrated increased oxidative stress (lower SOD and GSH) when compared with the normals.[8] The most prominent indicators of oxidative stress are an increased level of lipid peroxidation products and in particular malondialdehyde.[9]

Camel milk possesses insulin like activities, which decreases the requirement of exogenous insulin in Type 1 diabetic patients .[10] The hypoglycemic effect of camel milk and β -cell functions improvement may be due to: (1) euglycemia possibly reduces β-cell work, leading to β -cell rest, preserving β -cell function, (2) tolerance induction in the body due to high concentration of circulating insulin, (3) camel milk immunoglobulins, of relatively small size and weight, might offer an interplay with host cell protein leading to an induction of regulatory cells and finally leading to a downward regulation of immune system and β -cell salvage and (4) presence of half-cystine, lactoferrin or insulin like factor in camel milk.[11] In addition, patients treated with camel milk needed less insulin to achieve better control than the controlled group, in which there was slight improvement in β -cell function.[12] Moreover, Agrawal *et al*. (2004) have reported the hypoglycemic activity of camel milk in streptozotocin induced diabetic rats.[13]

This study aimed to evaluate the effect of insulin and camel milk administration on diabetic rabbits Type I. Therefore, serum insulin, glucose, malondialdehyde (MDA) and lipid profile in addition to whole blood SOD, catalase and GSH were determined in non-diabetic, untreated diabetic, insulin treated diabetic, camel milk treated diabetic rabbits. Histopathological evaluation on liver, kidneys and pancreatic tissues was also carried out.

Materials and Methods

Housing and feeding of animal: The present study was carried out on forty male New Zealand Male White (NZW) rabbits weighing between 1.8 and 2.0 kg. The animals were obtained from a private farm. These animals were kept for a week feeding on a control diet for acclimatization at the animal house of the Faculty of Veterinary Medicine, Mansoura University, Egypt. Rabbits were transferred and housed and fed on a

formulated ration *ad-libitum* according to NRC (1994).[14] Fresh clean tap water was available at all times from automatic nipple drinkers.

Induction of diabetes in rabbits: A single dose of alloxan monohydrate (90 mg kg^{-1}), dissolved in 5mL of normal saline given intravenously on the marginal ear vein as described by Gomes *et al*. (2007)[15] for induction of experimental diabetes mellitus Type I. Biosynthetic human insulin (HuNil ®U40) was purchased from Elli Lilly chemical Company, Egypt, and it was administrated on daily base (SC) at a dose of 1.5 IU kg^{-1} body weight.[16] Fresh camel milk was obtained from Ismailia desert (Manaief El-Mataiea) weekly, administrated with feeding syringe daily at a dose of 7ml kg^{-1} according to Agrawal *et al*. (2003a).[12]

Grouping of rabbits: Rabbits were fasted for 12 to 14 hr before induction of diabetes by alloxan and divided into four groups; each group contained ten rabbits as follows: Group I (G1) was a control and non-diabetic group received normal saline solution. Groups II-IV(G2-G4) included the other thirty rabbits injected with a single intravenous dose of alloxan (hydrate) $C_4H_2N_2O_4.H_2O$ via the ear vein 90 mg kg^{-1} dissolved in 5mL of normal saline.[15]

Group II (G2) was an untreated diabetic group and left untreated for four weeks. Group III (G3) was a diabetic group was treated with biosynthetic human insulin (HuNil®) daily in a dose rate of 1.5 IU kg^{-1} body weight subcutaneously for four weeks.[16] Group IV (G4) was a diabetic group was given camel milk daily by feeding syringe orally at a dose of 7 ml kg^{-1} body weight for four weeks.[12]

Blood glucose measurement: Blood glucose levels were monitored by one touch Ultra test strips® (Life Scan Johnson & Johnson, Milpitas, CA, USA), in addition to glucose kits. Blood glucose over 200 mg dL^{-1} was considered diabetic.[17]

Blood analysis: At the end of the experiment, the animals were sacrificed by decapitation for collection of blood and tissue samples. The collected blood sample was divided into two parts: the first part as the fresh blood was collected in heparinized tube to prevent blood coagulation and used for determination of superoxide dismutase activity (SOD) ,[18] catalase activity (CA) [19] and reduced glutathione "GSH" level .[20] The second part of the blood sample was collected in a sterile vial without anticoagulant and centrifuged at 3000 r.p.m. for collection of clear serum sample used for analysis of MDA,[21] glucose,[22] insulin,[23] triacylglycerols (TG),[24] total cholesterol (TC),[25] HDL-cholesterol and LDL-cholesterol[26] and phospholipids (PLs).[27]

Tissue samples were collected from the liver, pancreas and kidney and were dissected and separated, kept in formalin 20% for histopathological examination.[28]

Results

MDA content in serum of G2 was significantly ($P \leq 0.05$) higher than to that of G1. MDA content in serum of G3 was significantly ($P \leq 0.05$) lower than that G2, but significantly ($P \leq 0.05$) higher than that of G1 as shown in Table 1. In G4, MDA content in serum was significantly ($P \leq 0.05$) lower than that of G3. These results were supported by histopathological findings in rabbit liver (Fig. 1-B, and 2-B), kidneys (Fig. 3-B) and pancreas (Fig. 4-B). The other histopathological findings about the normal, insulin- and camel milk-treated groups are depicted in Figures 1-4.

SOD activity in G2 showed a significant decrease than that of G1. SOD activity in G3 was not significantly ($P > 0.05$) higher than that of G1 but significantly ($P \leq 0.05$) higher than G2 and injection of insulin in G3 returns the SOD level to G1 (Table 1).

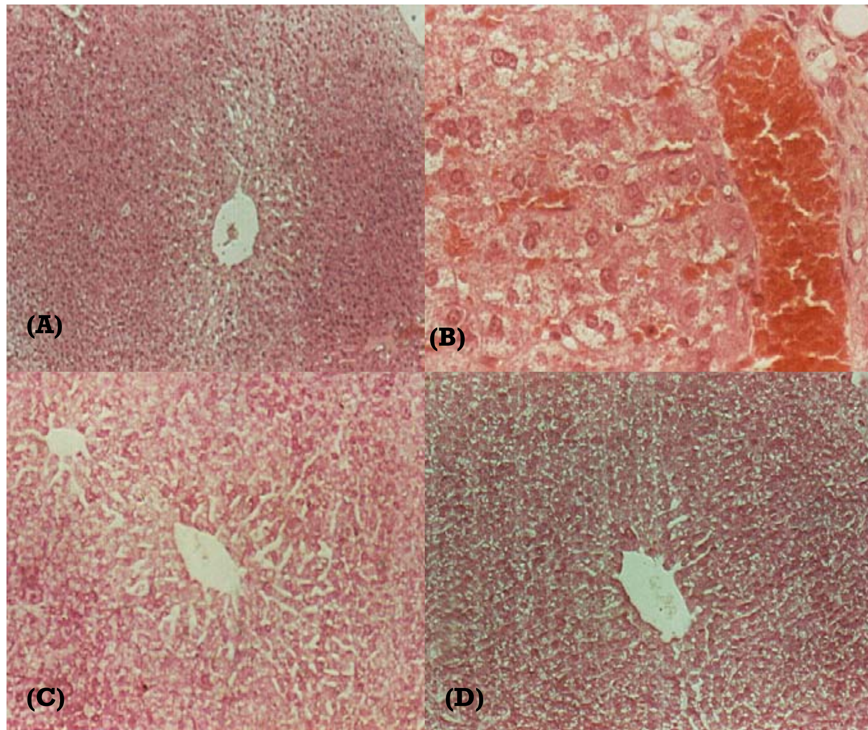

Fig 1. Photomicrographs of haematoxylin and eosin stained sections of rabbit liver; **(A)** group I showed normal hepatic plates, **(B)** Group II represented a severe congestion of the hepatic sinusoids resulted in focal hepatic necrosis, besides telangiectasis, **(C)** Group III indicated a moderate hydropic degeneration and **(D)** Group IV demonstrated a mild vacuolation (H&E, 10×).

At the same time, SOD activity in G4 was not significantly higher than ($P > 0.05$) than that of G1, but significantly lower ($P \leq 0.05$) than the G3 (Table 1).

GSH content in G2 was significantly ($P \leq 0.05$) lower than that of G1. The mean value of whole blood GSH content G2 was significantly lower ($P \leq 0.05$) than that of G1. GSH content in rabbits G4 was neither significantly ($P > 0.05$) higher than G2 nor the G3, but significantly ($P \leq 0.05$) lower than that of G1 (Table 1).

Catalase activity in G2 was not significantly ($P > 0.05$) lower G1. Blood catalase activity in G2 was significantly ($P \leq 0.05$) lower than that G3 (Table 1). Catalase activity in G4 was not significantly higher ($P > 0.05$) than that of G3, but remarkably ($P \leq 0.05$) higher than that of G2.

Glucose level of serum in G4 was not significantly ($P > 0.05$) different from that of G1, but significantly lower ($P \leq 0.05$) than that G3 (Table 1). These results supported by histopathological examination of liver (Fig.2-B, 2-C, and 2-D) showed severe glycogen infiltration in liver cells due to experimental diabetes.

Serum insulin of G3 was significantly higher ($P > 0.05$) than that of G2. The histopathological examinations in pancreas (Fig. 4-A, 4-B and 4-C) indicated the necrosis in the pancreas "endocrine portion" of diabetic rabbits, then the restoration of islets of Langerhans among the pancreatic acini in insulin treated diabetic rabbits. The pancreas of rabbits receiving camel milk showed the high restoration number of islets of Langerhans among the pancreatic acini (Fig. 4-D).

Table 1. Effect of the insulin and camel milk on some biochemical parameters in experimentally-induced diabetic rabbits

groups	MDA(nmol ml^{-1})	SOD (U ml^{-1})	CA (U L^{-1})	GSH (mg dL^{-1})	Glucose (mg dL^{-1})	Insulin(μIU ml^{-1})
G1	6.5±0.3[c]	222.1±18.6[ab]	237.9±15.4[c]	16.9±1.9[a]	135.0±9.2[cd]	4.8 ±0.2[c]
G2	8.7±0.2[a]	161.0±12.5[cd]	204.7±17.9[cd]	8.6±0.6[d]	528.4±28.2[a]	2.4 ±0.1[d]
G3	7.9±0.1[b]	224.3±9.0[a]	374.6±15.7[ab]	9.8±1.5[cd]	205.7±15.[b]	5.6 ±0.4[bc]
G4	5.6±0.3[d]	168.5±6.6[c]	377.5±4.2[a]	10.1±0.7[bd]	116.6±11.9[d]	7.9 ±0.9[a]

Means with the same superscript letter in each column are not significantly different ($P > 0.05$).
Means with different superscript letters in each column are significantly different ($P \leq 0.05$).

Table 2. Effect of insulin and camel milk on lipid profile (mg dl^{-1}) in experimentally induced diabetic rabbit (Mean ±SEM)

groups	TG	TC	HDL-C	LDL-c	PLs
G1	412.7±32.7[d]	366.7±15.4[a]	34.2±1.1[cd]	210.7±1.8[a]	145.3±3.1[cd]
G2	603.4±9.6[b]	274.2±6.6[cd]	52.1±1.0[a]	119.7±0.4[d]	214.5±41.3[c]
G3	682.5±5.1[a]	350.7±28.2[ab]	45.1±2.3[b]	149.9±0.4[c]	555.5±72.2[a]
G4	524.8±14.2[c]	295.9±7.9[c]	36.4±3.8[c]	168.8±0.4[b]	364.2±38.4[b]

Means with the same superscript letter in each column are not significantly different ($P > 0.05$).
Means with different superscript letters in each column are significantly different ($P \leq 0.05$).

TC in G2 was significantly ($P \leq 0.05$) lower than that in G1. HDL-c in G2 was significantly ($P \leq 0.05$) higher than that in G1.While LDL-c in G2 was significantly lower ($P \leq 0.05$) than that in G1. In G3, TC was not significantly ($P > 0.05$) lower than that of G1, but it was found significantly ($P \leq 0.05$) higher than that in G2. TC of G4 was significantly ($P \leq 0.05$) lower than that G3 and control one (Table 2). HDL in G2 was significantly higher ($P \leq 0.05$) than that in normal G1. Although the serum mean value of LDL in G2 was significantly lower ($P \leq 0.05$) than that in G1 (Table 2), in G3 HDL level was significantly higher ($P \leq 0.05$) than that of G1. LDL in G3 was significantly lower ($P \leq 0.05$) than that of G1. HDL in G4 was not significantly ($P > 0.05$) differed from that in G1 (Table 2). However, LDL G4 was significantly lower ($P \leq 0.05$) than that in G1.

Phospholipids in G2 were not significantly ($P > 0.05$) different from that in G1. In G3 phospholipids was significantly higher ($P \leq 0.05$) than that in G1 (Table 2). In G4 phospholipids was significantly higher ($P \leq 0.05$) than that in G1.

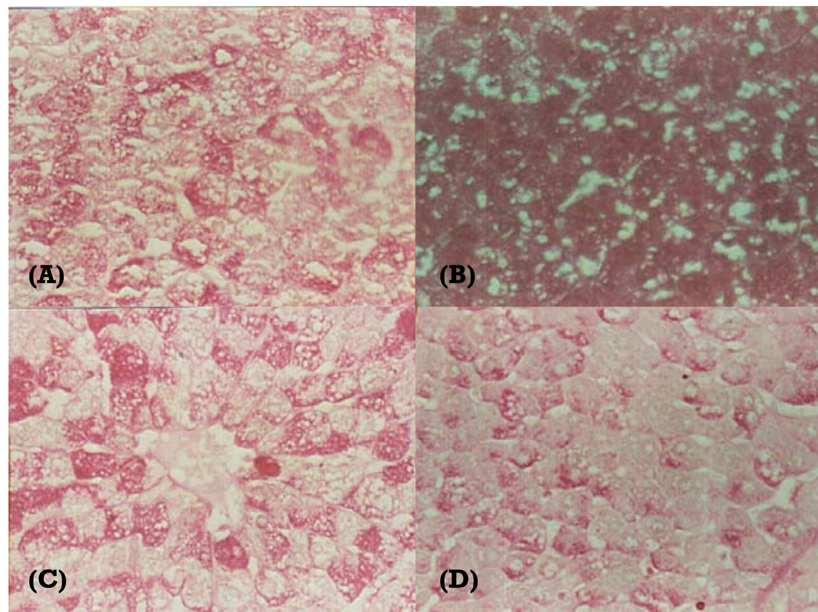

Fig 2. Photomicrographs of the PAS stained liver samples; **(A)** group I showed normal glycogen content of hepatocytes; **(B)** group II showed severe glycogen infiltration, which stained red; **(C)** group III showed moderate glycogen infiltration; **(D)** group IV showed mild glycogen infiltration (H&E, 10×).

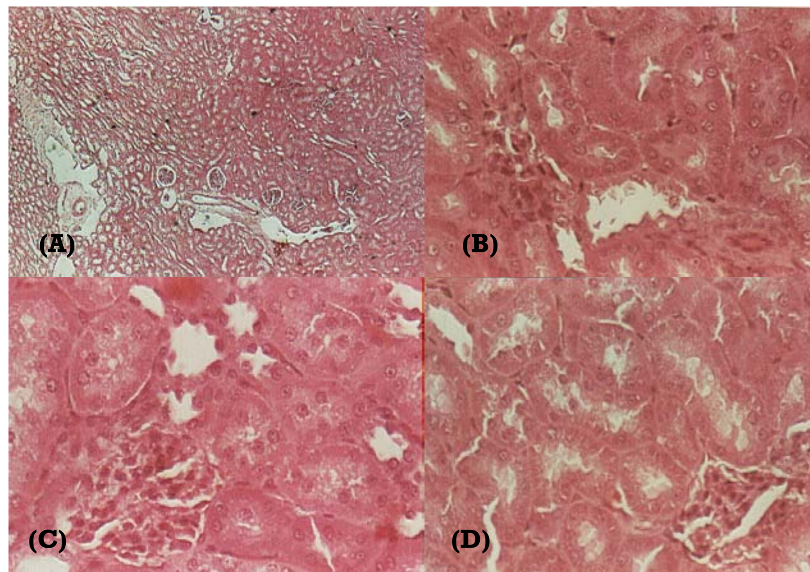

Fig 3. Photomicrographs of the kidney medulla in: **(A)** group I showed normal renal tubules; **(B)** Group II demonstrated a severe cloudy swelling with focal necrosis of some renal tubules; **(C)** Group III represented a moderate cloudy swelling; and **(D)** Group IV showed a mild cloudy swelling with focal necrosis of some epithelial cells of the renal tubules (H&E, 10×).

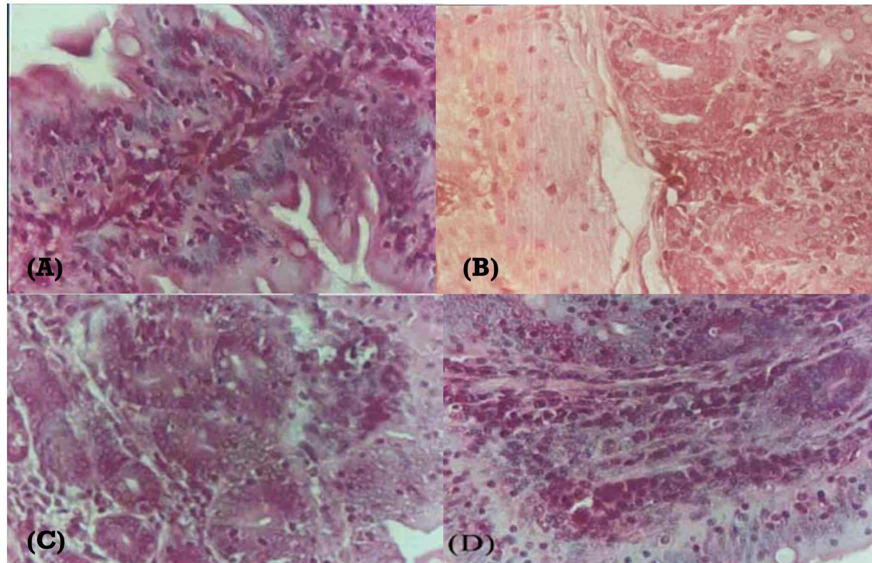

Fig 4. Photomicrographs of the pancreas in: **(A)** group I showed islets of Langerhans among the pancreatic acini; **(B)** Group II represented necrotic cells of the endocrine portion of the islets of Langerhans among the exocrine portion of the pancreatic acini; **(C)** Group III demonstrated the restoration of islets of Langerhans among the pancreatic acini; and **(D)** Group IV showed the high number of islets of Langerhans among the pancreatic acini (H&E, 10×).

Discussion

In diabetes, oxidative stress is caused by both increased production of ROS, sharp reduction in antioxidant defenses and altered cellular redox status.[7] Hyperglycemia increases the generation of free radicals via several mechanisms. Oxidative stress can be increased before clinical signs of diabetic complications.[6] Therefore, cells must be protected from this oxidative injury by antioxidant enzymes.[29]

Our findings about the MDA content are in agreement with previous reports.[30,29] These results also are in agreement with those of Santini *et al*. (1997) who reported that after treatment with insulin, the values of MDA were lower than that in the control group.[31]

Our results about the SOD activity supported the previous reports.[32-34] In diabetes mellitus, a decrease in SOD activity coupled with increasing superoxide or H_2O_2 production,[35] which has the ability to penetrate membranes of the cells. Consequently, erythrocytes are subjected to continuous flux of O_2 and H_2O_2 arising from hemoglobin oxidation.[36] SOD has an important role in combating this process, since it can catalyze the dismutation of two superoxide radicals in to H_2O_2.[33] SOD is decreased in diabetes due to its consumption in conversion of superoxide anions into H_2O_2 protecting the cell from harmful effect of superoxide anions. Van Dam *et al*. (1996) observed that the insulin treatment of diabetic rats caused restoration of altered enzymes activities.[37] Moreover, Sindhu *et al*. (2004) showed that insulin treatment of STZ-diabetic rats normalized the activities and protein expression of all antioxidant enzymes.[34] Nevertheless, this result was in disagreement with Knoess, (1979) recording that vitamin C levels were three times that of cow milk and one-and-a-half that of human milk. In addition, Yagil *et al*. (1994) who reported that camel milk contains high minerals (sodium, potassium, iron, copper, zinc and magnesium) and high vitamin C level which considered a strong antioxidant in combating free radicals.[38,39]

The finding of current study concerning the GSH content of serum agreed with Varvarovská *et al*. (2004).[8] In addition, Wohaieb and Godin, (1987) reported that hepatic GSH content was lower in diabetic rats which was restored by insulin treatment.[32] This decrease may be due to a decline in its formation which requires NADPH+H^+ and glutathione reductase.[40] The reduced availability of NADPH+H^+ could be because of reduced synthesis in HMP shunt resulted due to decreased activity of glucose-6-phosphate dehydrogenase as this enzyme plays a very important role to maintain high ration of NADPH+H^+/$NAPDP^+$ in the cell and plays a crucial role in regeneration of GSH from GSSG .[41]

Our results agreed with Srinivasan *et al*. (1997) reporting that hyperglycemia reduces transmembrane ascorbate transport mechanisms in vitro, although in vivo results are controversial.[42] Ascorbate depletion is dependent on free radicals generation as this molecule specifically traps oxyradicals, such as superoxide, hydroxyl and peroxyl, to protect the lipids from detectable oxidative damage.

The result of this study regarding the catalase activity are in agreement with that of Wohaieb and Godin, (1987); Sindhu *et al*. (2004) who noticed that the activity of hepatic catalase in diabetic rats was decreased.[32,34] Yagil *et al*. (1994) showed that camel milk contains high minerals (sodium, potassium, iron, copper, zinc and magnesium) and high vitamin C level, which considered as a strong antioxidant in combating free radicals confirmed these results.[39] Among others zinc plays a vital role in a variety of antioxidant enzymes including catalase enzyme.[43] Moreover, previous reports indicate that zinc itself has a potential antioxidant effect in diabetes.[44]

These results were supported by histopathological examination of liver (Fig. 1-C and Fig. 1-D), kidneys (Fig.3-C and 3-D) and pancreas (Fig. 4-C and 4-D). Our histopathological findings are in agreement with other as it has been reported that the alterations in the activities of the antioxidant enzymes are accompanied by significant changes in the ultra structure of the liver tissue.[45]

Acute[46] and chronic[47] hyperglycemia increased the production of reactive oxygen species (ROS). Various mechanisms suggested that the formation of reactive oxygen-free radicals and the glucose oxidation are the main source of free radicals.[47] In the same aspect, Catherwood *et al*. (2002) suggested that plasma lipid peroxidation was a good indicator for glucose-induced oxidative stress.[48] Granner, (2000) explained the metabolic effect of insulin on glucose metabolism by stimulation of glycolysis through increasing activity of glucokinase, phosphofructokinase and pyruvate kinase enzyme, stimulation of glycogenesis by stimulation of glycogen synthase and inhibition of gluconeogenesis through inactivation of phosphoenolpyruvate carboxykinase (PEPCK).[49]

Our results in terms of glucose level in serum are supported by previous reports.[12,50,51] There was a marked improvement in diabetes quality of camel milk treatment group due to good glycemic control or anabolic effect of camel milk.[52] Agrawal *et al*. (2004) concluded that the hypoglycemic effect of camel milk in streptozotocin-induced diabetic rats attribute to β-cell functions improvement.[13] Additionally, Agrawal *et al*. (2007) explained that this may be due to: i-euglycemia possibly reduces β-cell work, leading to β-cell rest, preserving β-cell function; ii- tolerance induction in the body due to high concentration of circulating insulin; iii- camel milk immunoglobulins with relatively small size and weight, might offer an interplay with host cell protein leading to an induction of regulatory cells and finally leading to a downward regulation of immune system and β-cell salvage, and iv- the presence of half-cystine, lactoferrin or insulin like factor in camel milk.[11] The

biochemical findings of present study are confirmed with histopathological alterations observed in the animals treated with either insulin or camel milk.

Although our findings regarding the insulin level of serum in animals treated with insulin are not in accordance with some previous reports,[53] Chaillous *et al.* (2000) observed that oral administration of insulin did not prevent the deterioration of beta cell function.[54] Other reports also are indicating that insulin therapy prevents diabetes in animal models.[55-58] Animal studies have suggested that insulin may be acting metabolically by restoring the beta cells. The mean value of serum insulin of G4 (7.9 ± 0.9 µIU ml^{-1}) was significantly higher ($P \leq 0.05$) than that of G2, and G3. Furthermore, the camel milk returned the level of insulin near to the normal level (Table 1).This result confirms Agrawal *et al*, (2007) who had studied the traditional use of camel milk in treating diabetes.[11]

These biochemical findings are supported by histopathological examination of pancreas, indicating the necrosis in the pancreas "endocrine portion" of diabetic rabbits, and then the restoration of islets of Langerhans among the pancreatic acini in insulin treated diabetic rabbits. The pancreas of rabbits receiving camel milk showed the high restoration number of islets of Langerhans among the pancreatic acini. Previous reports showed that the camel milk contains a high concentration (52 units/liter) of insulin .[59]

Triacylglycerols (TG) in G2 (603.4 ± 9.6 mg dL^{-1}) was significantly ($P \leq 0.05$) higher than that G1 (412.7 ± 32.7 mg dL^{-1}) (Table 2). This result agreed with that of Arkkila *et al.* (2001), who found that the abnormalities in the lipid metabolism may be due to insulin deficiency. Since a significant increase in TG may be due to the lack of insulin under diabetic condition, while insulin activates the enzyme lipoprotein lipase, which in turn hydrolysis TG under normal condition.[60]

TG in G3 (682.5 ± 5.1 mg dl^{-1}) was found significantly higher ($P \leq 0.05$) than that in normal G1 (412.7 ± 32.7 mg dL^{-1}), and in G2 (603.4 ± 9.6 mg dL^{-1}) (Table 2)which were not in agreement with Arkkila *et al.* (2001).[60] Gupta *et al.* (1999)found that the insulin treatment of diabetic rats restored the altered lipid levels in livers of diabetic rats and altered enzymes activities to normal level.[61] TG in G4 (524.8±14 mg dL^{-1}) was significantly ($P \leq 0.05$) lower than that in G2, but significantly ($P \leq 0.05$) higher than that in G1 (Table 2). These results are supported with those of Hull, (2004); Agrawal *et al.* (2007), showing that a high insulin concentration ofcamel milk can cause the activation of lipoprotein lipase enzyme.[62,11]

The obtained results regarding TC are not in agreement with Newairy *et al.* (2002), while agree with the result of Young *et al.* (1988) who reported that in streptozotocin-induced diabetic animals, cholesterol absorption is elevated and its synthesis is down regulated.[63,64] These alterations however can be produced not only from lack of insulin, but also from gut hypertrophy that is present in these animals. The reduced synthesis of cholesterol in starving animals is accompanied with a decrease in the activity of the enzyme. Insulin or thyroid hormones increase HMG-CoA reductase activity, whereas glucagon or glucocorticoids decrease it. Its activity is reversibly modified by phosphorylation-dephosphorylation mechanisms, some of which may be cAMP-dependent and therefore immediately responsive to glucagon.[65]

Although these findings are in agreement with early studies,[38] there are reports which do not support these findings.[59] In the same aspect, Anderson *et al.* (1999) reported that the vitamin C supplementation significantly reduced lipid profile in diabetic rats when compared to untreated diabetic rats and

prevents oxidation of LDL-cholesterol decreasing total and LDL-cholesterol and triacylglycerol; and raising HDL-cholesterol level.[66]

Horowitz *et al*. (1993) reported that reduced HDL level found in diabetes has several reasons such as that of an increase concentrations of plasma VLDL drive the exchange of triglycerides from VLDL for the cholesteryl esters found in HDL.[67] Moreover, the triacylglycerol in HDL is a substrate for plasma lipases, especially hepatic lipase that converts HDL to smaller particle that is more rapidly cleared from the plasma. Additionally Goldberg, (2001) observed a defective lipolysis leads to reduced HDL production.[68]

Our findings in case of LDL level are not in agreement with Gupta *et al*. (1999).[61] This is due to the fact that insulin treatment of diabetic rats caused restoration of altered lipid levels in livers of diabetic rats and restored altered enzymes activities to the control level. Previous studies suggested that the improvement in lipoproteins was due to the antioxidant effect of vitamin C and zinc in the camel milk.[69]

Cooper *et al*. (1990) reported that insulin therapy increased the synthesis of phospholipids, diacylglycerol and protein kinase C activity in rat hepatocytes. Our results are in agreement with previous reports.[70,71]

In short; it is concluded that the camel milk contains insulin like peptides, vitamin C and zinc in addition to other minerals and vitamins that are effective in the treatment of diabetes. Beside its hypoglycemic effect it also reduces the oxidative stress which is often accompanied with diabetes mellitus.

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