رقم البحث (7)

EFFECT OF CAMELS MILK FEEDING ON OXIDATIVE STRESSES IN EXPERIMENTALLY INDUCED DIABETIC RABBITS

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ABSTRACT

Diabetes mellitus is a multi-factorial disorder that characterized by hyperglycemia, lipoprotein abnormalities resulting from malfunction in insulin secretion and/or insulin action causing impaired metabolism of glucose, lipids and protein. In addition, generation of free radicals often worsen the complications of diabetes mellitus such as hypertension, atherosclerosis and microcirculatory disorders. A group of scientists reported the effect of camel milk on diabetes, referring to its importance in treatment of diabetes and patients who drink camel milk daily, their need to insulin decrease. Therefore, this study aimed to throw light on the effect of camel milk in comparison to insulin treatment. This study was carried out on forty male New Zealand rabbits, divided into four equal groups each group contained ten rabbits. The first group (G1) was considered as control non diabetic group injected with normal saline solution. The other animals were injected intravenously with alloxan for induction of experimental diabetes mellitus and then divided into three equal groups ten rabbits each as the follows: (G2) considered as control diabetic left untreated, (G3) was considered as diabetic insulin treated group, (G4) was considered as diabetic camel milk treated group. After the end of the experiment (4 weeks), blood (whole blood & serum) in addition to 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.It was observed that the effect of camel milk containing insulin like peptides, vitamin C and zinc in addition to other minerals and vitamins that are effective in the treatment of diabetes in comparison to insulin treatment alone. In addition to its hypoglycemic effect and improvement of oxidative stress accompanied with diabetes mellitus.It was observed that there is regeneration in β cells and

high number of islets of Langerhans among the pancreatic acini in rabbits receiving camel milk. There is a wide similarity between camel milk and goat milk. So, from this study, camel milk administration in case of insulin dependant diabetes mellitus is recommended as oral anti diabetic drug.

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 lipid occur. (**Rameshkumar *et al*., 2004)**. Despite the great studies that have been made in the understanding and management of diabetes, the disease and the disease related complications are increasing unabated (**Tiwari & Madhusudana, 2002**). 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 (**Virella-Lopes & Virella, 2003)**.

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 (**Rosen *et al.,* 2001**).The source of oxidative stress is a cascade of reactive oxygen species (ROS) leaking from the mitochondria (**Knight, 1998**), 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 (**Bonnefont-Rousselot *et al.,* 2000)**. Onset of diabetes is a complex mechanism because hyperglycemia may be the cause and effect of increased oxidative stress (**West, 2000).**

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. Type I diabetes demonstrated increased oxidative stress (lower SOD and GSH) when compared with normal, this was reported by **Varvarovská *et al.,* (2004).** The most prominent indicators of oxidative stress are the increased level of lipid peroxidation products (in particular malondialdehyde - MDA).

Camel milk possesses insulin like activities, which decrease the requirement of exogenous insulin in type 1 diabetic patients **(Agrawal *et al.,* 2005)**.

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 **(Agrawal *et al.* 2007)**. Adding that 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**.**

Agrawal *et al.*, (2004) have reported the hypoglycemic activity of camel milk in streptozotocin induced diabetic rats.

This study aimed to evaluate the effect of insulin and camel milk administration on diabetic rabbits type I. Therefore, serum insulin, glucose, malondialdehyde 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 examination on liver, kidneys and pancreatic tissues was carried out.

MATERIAL AND METHODS

The present study was carried out on forty male New Zealand Male White (NZW) Rabbits of 1.8 and 2.0 kg average body weight. 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. Rabbits were transferred and housed and fed on a formulated ration ad-libitum according to **NRC, (1994)**. Fresh clean tap water was available at all times from automatic nipple drinkers. Single dose of alloxan monohydrate (90 mg/kg), dissolved in 5cm of normal saline given intravenously on the marginal ear vein as described by **Gomes *et al.*, (2007)** for induction of experimental diabetes mellitus typeI. Biosynthetic human insulin (HuNil ®U40 was purchased from Elli Lilly Company Egypt, and it was administrated daily subcutaneously in a dose rate of 1.5 IU/kg body weight **(Guyton et al., 2000**). Fresh she camel milk was obtained from Ismailia desert (Manaief El-Mataiea) weekly, administrated with feeding syringe daily in a dose rate of 7ml/kg according to **Agrawal *et al.*, (2003a).**

Rabbits were fasted for 12 to 14hr before induction of diabetes by alloxan and divided into four groups; each group contained ten rabbits as the following: **Group I (G1)** is a control non diabetic group injected with normal saline solution. **Groups II-IV**(G2-G4) Included the other thirty rabbits injected with a single intravenous dose of alloxan (hydrate) $C_4H_2N_2O_4.H_2O$ on the marginal ear vein 90 mg/kg dissolved in 5cm of normal saline **(Gomes *et al.*, 2007).**

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 was considered diabetic. Any rabbit were not diabetic was repeatedly injected with the same dose of alloxan until the blood glucose level was in the range of diabetes. **Group II (G2):** is an untreated diabetic group and left untreated for four weeks. **Group III (G3** is a diabetic group was treated with biosynthetic human insulin (HuNil®) daily in a dose rate of 1.5 IU/kg body weight subcutaneously for four weeks (**Guyton *et al.*, 2000). Group IV (G4):** It is a diabetic group was given camel milk daily by feeding syringe in a dose rate of 7ml /kg body weight (**Agrawal *et al.*, 2003a)** for four weeks.

After the end of the experiment, the animals were sacrificed by decapitation for collection of blood and tissue samples after 12 hours from the end of fasting (overnight).The collected blood sample was divided into two parts: the first one fresh blood was collected in heparinized tube to prevent blood coagulation and used for determination of superoxide dismutase activity (SOD) **(Nishikimi *et al.*, 1972),** catalase activity (CA) **(Aebi *et al.*, 1984)** and reduced glutathione "GSH"level **(Beutler *et al.*, 1963)**.

The second blood sample was collected in sterile vial without anticoagulant and centrifuged at 3000 r.p.m. for collection of clear serum sample used for analysis of malondialdehyde (MDA) **(Ohkawa, *et al.*, 1979)**, glucose **(Berth and Delanghe, 2004),** insulin **(Chevenne *et al.*,1998),** triacylglycerols (TG) **(Fassati and Prencipe. 1982),** total cholesterol (TC) **(Allain, *C.C. et al., 1974)***, HDL-cholesterol **(Lopez-Virella, 1977),** LDL-cholesterol **(Friedewald *et al.*, 1972)** and phospholipids (PLs) **(Connerty *et al., 1961).***

Tissue samples were collected from liver, pancreas and kidney and were dissected and separated, kept in formalin 20% for histopathological examination **(Woods and Ellis, 1994).**

Table (1): Effect of insulin treatment and camel milk feeding on some biochemical parameters in experimentally induced diabetic rabbits

animal groups	MDA (nmol/ml	SOD (U/ml)	CA (U/L)	GSH (mg/dL)	Glucose (mg/dL)	Insulin (µIU/ml
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 differed (P>0.05). Means with different superscript letters in each column are significantly differed (P≤0.05).

Table (2): Effect of insulin treatment and camel milk feeding on lipid profile (mg/dl) in experimentally induced diabetic rabbit (Mean ±SEM)

animal 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 differed (P>0.05). Means with different superscript letters in each column are significantly differed (P≤0.05).

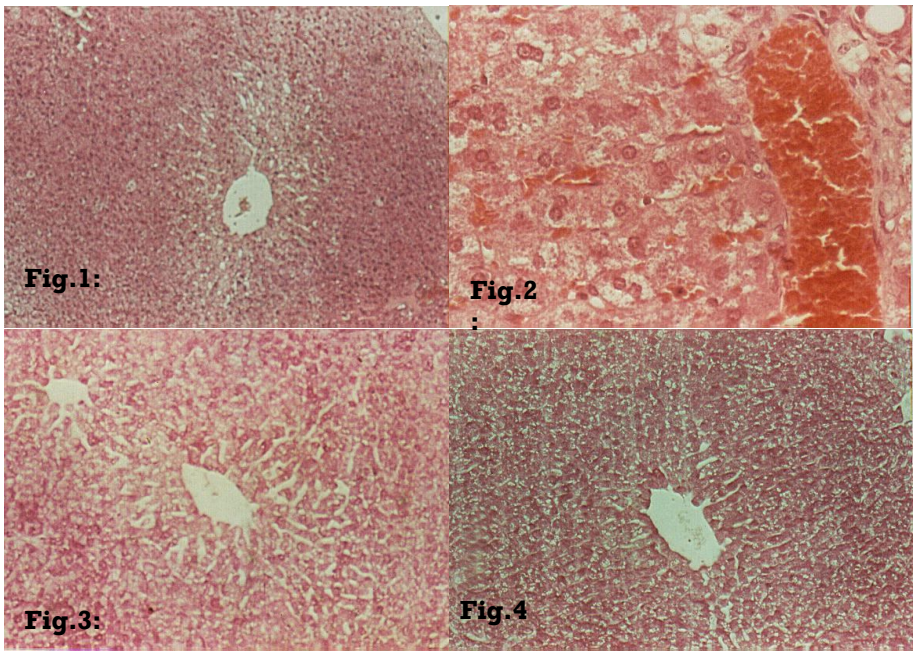

Fig.1: Liver group I showed normal hepatic plates. **(H&E)X52**

Fig.2: Liver group II showed sever congestion of the hepatic sinusoids resulted in focal hepatic necrosis, besides telangiectasis. **(H&E)X 520**

Fig.3: Liver group III showed moderate hydropic degeneration. **(H&E)X130**

Fig.4: Liver group IV showed mild vacuolation. **(H&E) X130**

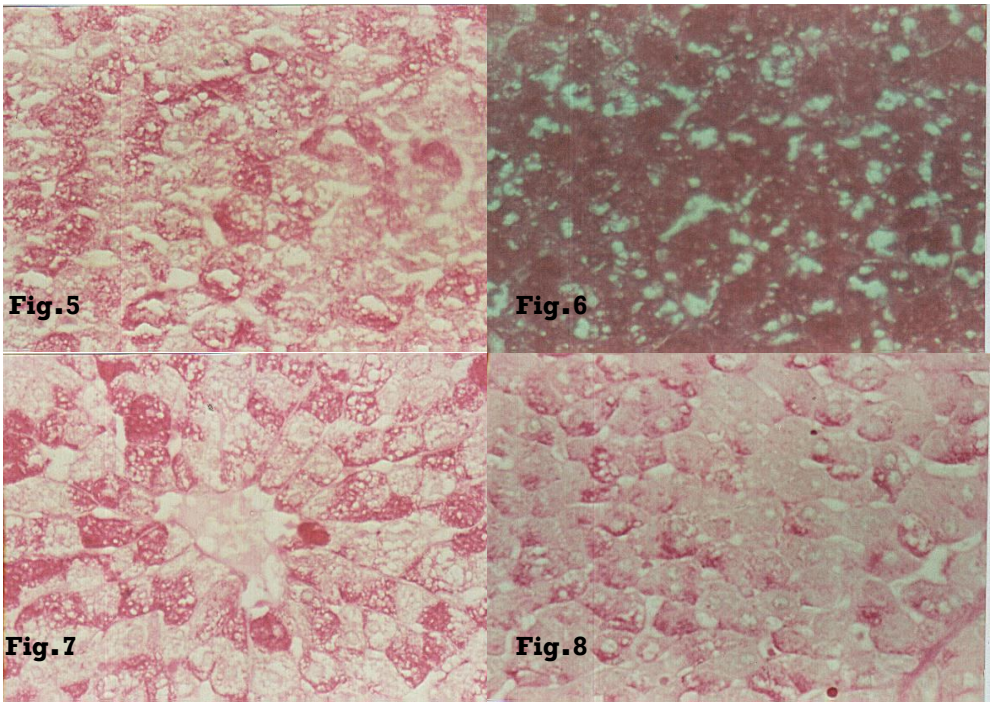

Fig.5: Liver group I showed normal glycogen content of hepatocytes. **(PAS)X 520**
Fig.6: Liver group II showed sever glycogen infiltration which stained red. **(PAS)X 520**
Fig.7: Liver group III showed moderate glycogen infiltration. **(PAS)X 520**
Fig.8: Liver group IV showed mild glycogen infiltration. **(PAS)X 520**

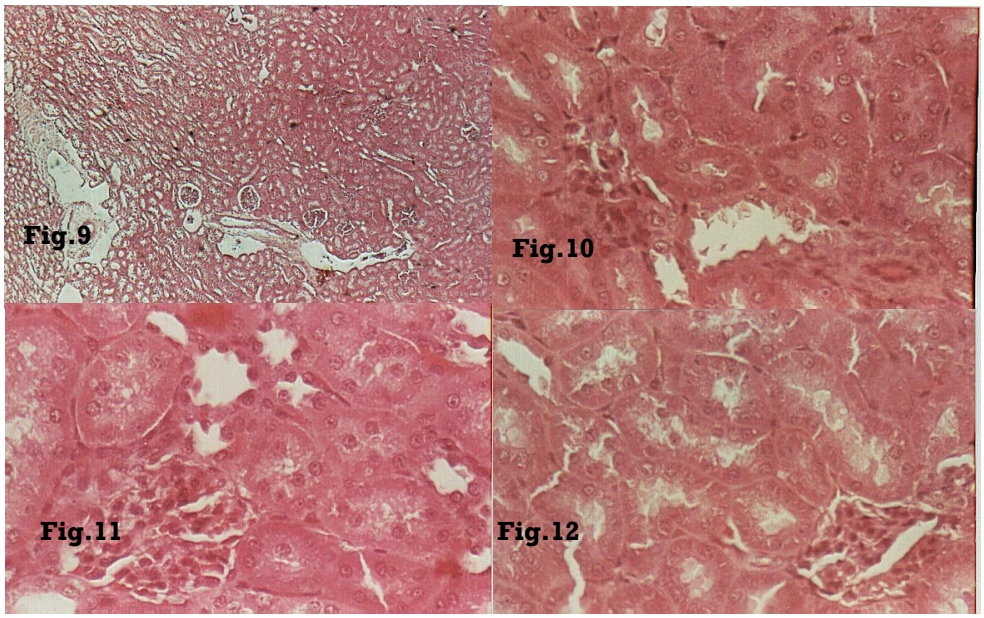

Fig.9: Renal medulla in group I showed normal renal tubules. **(H&E)X52**
Fig.10: Kidney group II showed sever cloudy swelling with focal necrosis of some renal tubules. **(H&E)X 520**
Fig.11: Kidney group III showed moderate cloudy swelling. **(H&E)X 520**
Fig.12: Kidney group IV showed mild cloudy swelling with focal necrosis of some epithelial cells of the renal tubules. **(H&E)X 520**

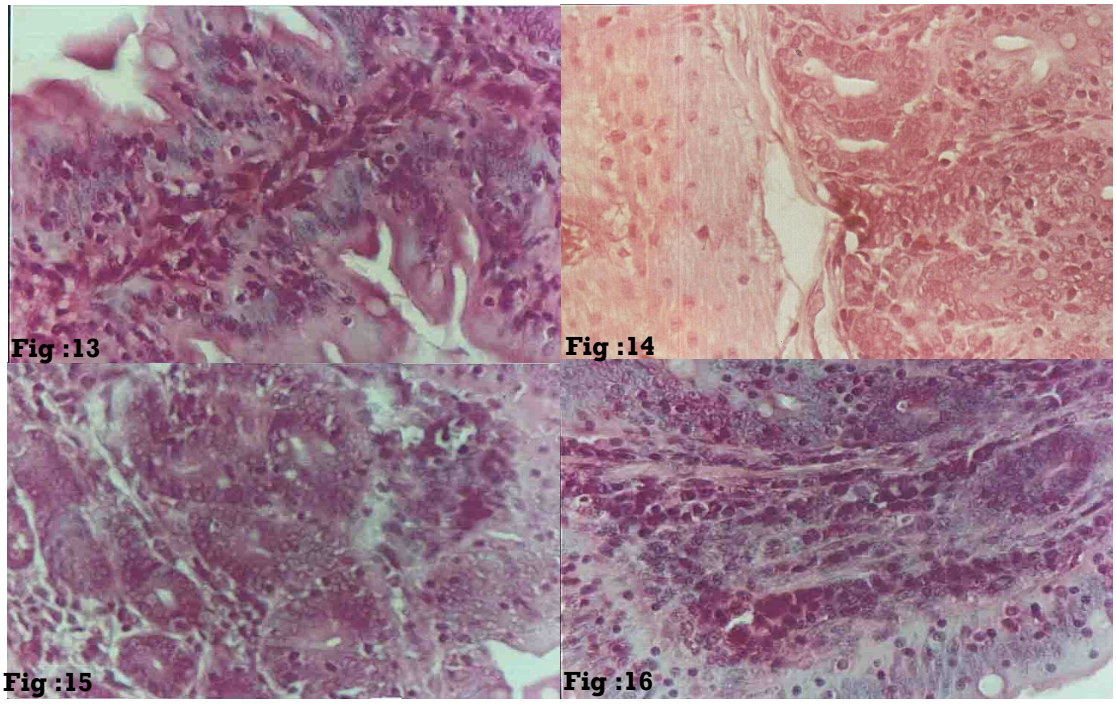

Fig.13: Pancreas group I showed islets of Langerhans among the pancreatic acini. **(H&E)X520**

Fig.14: Pancreas group II showed necrotic cells of the endocrine portion" islets of Langerhans" among the exocrine portion "Pancreatic acini". **(H&E)X 520**

Fig.15: Pancreas group III showed restoration of islets of Langerhans among the pancreatic acini. **(H&E)X 520**

Fig.16: Pancreas group IV showed high number of islets of Langerhans among the pancreatic acini. **(H&E)X 520**

DISCUSSION

In diabetes, oxidative stress seemed to be caused by both increase production of ROS, sharp reduction in antioxidant defenses and altered cellular redox status (**West, 2000**). Hyperglycemia increased generation of free radicals via several mechanisms. Oxidative stress can be increased before clinical signs of diabetic complications (**Bonnefont-Rousselot *et al.*, 2000**). Therefore, cells must be protected from this oxidative injury by antioxidant enzymes (**Qujeq *et al*., 2004).**

MDA content in serum of G2 (8.7±0.2 nmol/ml) was significantly higher($P \leq 0.05$) than that of G1 (6.5±0.3 nmol/ml) as shown in table (1).These results were in agreement with those of **Koo and Vaziri, (2003); Qujeq *et al.*, (2004).**

The increase in MDA content might be due to an increase in oxygen free radicals that could be due to either increased production or decreased its destruction. Increased lipid

peroxidation is attributed to chronic hyperglycemia which causes increased production of reactive oxygen species (ROS) due to autoxidation of monosaccharides which lead to the production of superoxide and hydroxyl radical **(Wolff and Dean, 1987)**, which cause tissue damage by reacting with polyunsaturated fatty acids in membranes **(Das *et al.,* 2000).** MDA content in serum of G3 (7.9±0.1 nmol/ml) was significantly lower (P ≤0.05) than that G2 (8.7±0.2 nmol/ml), but significantly higher (P ≤0.05) than that of G1 (6.5±0.3 nmol/ml) as shown in table (1).These results in agreement with those of **Santini *et al.,* (1997) who** reported that after treatment with insulin, the values for parameters were lower; although still higher than in the control group. In G4, MDA content in serum (5.6±0.3 nmol/ml) was significantly lower (P ≤0.05) than that of G3 (7.9±0.1 nmol/ml) as shown in table (1).These results agree with those of **Yagil *et al.,* (1994**). These results were supported by histopathological examination in liver (Fig. 2 & 6), kidneys (Fig. 10) and pancreas (Fig.14).

SOD activity in control rabbits group G1 is 222.1±18.6 U/ml, while in G2 is 161.0±12.5 U*/ml*, in G3 is 224.3±9.0 *U/m,* while in the last group G4 168.5±6.6 U/m. SOD activity in G2 showed a significant decrease than that of G1, as shown in table (2). This was in agreement with **Andallu and Varadacharyulu, (2003).** In addition **Wohaieb and Godin, (1987); Sindhu *et al.,* (2004)** who reported that in diabetic rats, hepatic SOD activity was lower than normal control animals.

In diabetes mellitus, the decrease in SOD activity coupled with the increase superoxide or H_2O_2 production **(Wolff et al., 1991)**, 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 **(Arai *et al.,* 1989).** SOD has an important role in combating this process, since it can catalyze the dismutation of two superoxide radicals in to H_2O_2 **(Andallu and Varadacharyulu, 2003**). 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.

SOD activity G3 (224.3±9.0 *U/ml)* was not significantly higher (P>0.05) than that of G1 (222.1±18.6 *U/ml*) but significantly higher (P≤0.05) than G2 and injection of insulin in G3 returns the SOD level to G1, as shown in table (1). This result was in agreement with **Van Dam *et al.,* (1996).**

SOD activity in G4 (168.5±6.6 *U/ml)* was not significantly higher than (P>0.05) than that of G1 (222.1±18.6 *U/ml*), but significantly lower (P≤0.05) than the G3 (224.3±9.0 *U/ml),* as shown in table (1). This result was in disagreement with **Knoess, (1979)** recording that

vitamin C levels are three times that of cow milk and one-and-a-half that of human milk In addition to **(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.

Catalase activity in G2 (204.7±17.9 U/L) was not significantly lower (P >0.05) G1 (237.9±15.4 U/L**)**. Blood catalase activity in G2 was significantly lower (P ≤0.05) than that G3 (374.6±15.7 U/L) as shown in table (1)).This result agree with that of **Wohaieb and Godin, (1987); Sindhu *et al.,* (2004)** who noticed that the hepatic catalase in diabetic rats was decreased. **Van Dam *et al.,* (1996)** observed that the insulin treatment of diabetic rats caused restoration of altered enzymes activities. Moreover, **Sindhu *et al.,* (2004)** showed that insulin treatment of STZ-diabetic rats normalized the activities and protein expression of all antioxidant enzymes.

Catalase activity in G4 (377.5±4.2 U/L) was not significantly higher (P >0.05) than that of G3 (374.6±15.7 U/L), but significantly higher (P ≤0.05) than that of G2 **Yagil *et al.,* (1994**) exhibited that camel milk contained high minerals (sodium, potassium, iron, copper, zinc and magnesium) and high vitamin C level which considered a strong antioxidant in combating free radicals confirmed these results. Zinc is a necessary factor for in a variety of antioxidant enzymes including catalase enzyme **(Sumovski *et al.,* 1992)**. Moreover, **Bray and Bettger, (1990)** observed that zinc has a potential antioxidant effect in diabetes.

GSH content in G2 (8.6±0.6 *mg/ dL*) was significantly lower (P≤0.05) than that of G1 (16.9±1.9 *mg/dL*) as shown in table (1).This result agreed with **Varvarovská *et al.,* (2004).** In addition, **Wohaieb and Godin, *(1987)*** reported that hepatic GSH content was lower in diabetic rats which was restored by insulin treatment. This decrease may be due to a decline in its formation which requires $NADPH+H^+$ and glutathione reductase **(Garg *et al.,* 1996*).*** The reduced availability of $NADPH+H^+$ could be due to 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 **(Jain, 1998).** The mean value of whole blood GSH content G2 (9.8±1.5 *mg/ dL*) was significantly decreased (P≤0.05) that that G1 (16.9±1.9 *mg/dL*) as shown in table (1). This result was disagreeing wit those of **Wohaieb and Godin, (1987)**.

GSH content in rabbits G4 (10.1±0.7 *mg/dL)* was a non significantly higher (P>0.05) than G2 nor the G3 (9.8±1.5 *mg/ dL*), but significantly lower than (P≤0.05) that of G1 as

shown in table (1).This result agreed with **Srinivasan *et al.*,(1997)** reporting that hyperglycemia is known to reduce transmembrane ascorbate transport mechanisms in vitro, although in vivo results are controversial, 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. Vitamin C metabolic disorders in erythrocytes of diabetes and its model, STZ-induced diabetes so this explains the impairment in the vitamin C absorption of camel milk. These results were supported by histopathological examination in liver (Fig. 3&4), kidneys (Fig.11&12) and pancreas (Fig.15&16). These results in agreement with **Belgin *et al.*, (2005)** who explained the alterations in the activities of the antioxidant enzymes are accompanied by significant changes in the ultra structure of the liver tissue; mainly intercellular bleary canaliculi were distended and contained stagnant bile, swollen mitochondria in hepatocytes and disoriented and disintegrating cristae, dilatation of the rough endoplasmic reticulum (rER) with detachment of ribosomes, and dissociation of polysomes. But the treatment of diabetic rats improved significantly diabetes-induced alterations in liver antioxidant enzymes.

Acute **(Kosoa *et al.*, 2000)** and chronic **(Kyselova *et al.*, 2002)** hyperglycemia increased the production of reactive oxygen species (ROS). Various mechanisms suggested that formation of reactive oxygen-free radicals and glucose oxidation was believed to be the main source of free radicals **(Kyselova *et al.*, 2002).** In the same aspect, **Catherwood *et al.*, (2002)** suggested that plasma lipid peroxidation was a good indicator for glucose-induced oxidative stress. **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).

Serum glucose of G4 (116.6±11.9 *mg/dL)* was not significantly differ from ($P > 0.05$) that of G1 (135.0±9.2 *mg/dL)*, but significantly lower ($P \leq 0.05$) than that G3 ((205.7±15 *mg/dL)* as shown in table (1).These results in explained by **Agrawal *et al,* (2003a, b); Breitling (2002).**There was a marked improvement in diabetes quality of camel milk treatment group due to good glycemic control or anabolic effect of camel milk **(El Agamy *et al.,* 1992). Agrawal *et al.,* (2004)** concluded the hypoglycemic activity of camel milk in streptozotocin induced diabetic rats to the hypoglycemic effect of camel milk and β-cell functions improvement and **Agrawal *et al.,* (2007)** explained that this 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- The presence of half-cystine, lactoferrin or insulin like factor in camel milk**.** These results were supported by histopathological examination in liver (Fig.6, 7 and 8) showed liver cells normal fill with glycogen, liver sever glycogen infiltration due to experimental diabetes.

Serum insulin of G3 (5.6 ±0.4 µIU/ml) was significantly higher (P >0.05) than that of G2 (2.4 ±0.1 µIU/ml) as shown in table (6). This result was disagree with the result of **Engl, (2002*)***, reported that in some diabetic cases insulin at the various dosage not delay or prevent type I diabetes, moreover, **Chaillous *et al*., (2000)** observed that oral administration of insulin did not prevent the deterioration of beta cell functionn in agreement with **Gotfredsen *et al.*,(1985); Vlahos *et al.*, (1991); Bowman *et al.*, (1996); Füchtenbusch *et al.*, (1998)**,explaining that insulin therapy prevents diabetes in animal models. Moreover, pilot studies have suggested that insulin therapy also delays diabetes in humans. Animal studies have suggested that insulin may be acting metabolically by causing the beta cells to rest or immunologically.

The mean value of serum insulin of G4 (7.9 ±0.9 µIU/ml) was significantly higher (P ≤0.05) than that of G2, and G3 . Furthermore, the camel milk returned the level of insulin near to the normal level as shown in table (2).This result was in agreement with **Agrawal *et al,* (2007)** stating that the milk of the camel has traditionally been used to treat diabetes.

These results were supported by histopathological examination in pancreas (Fig.13, 14 and 15) showed 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. In (Fig. 16) pancreas of rabbits receiving camel milk showed high restoration number of islets of Langerhans among the pancreatic acini, in agreement with **Singh, (2001)** reporting the radioimmunoassay of insulin in camel milk which revealed high concentration i.e.(52units/liter).

Triacylglycerols in G2 (603.4±9.6 *mg/dL)* was significantly higher (P ≤0.05) than that G1 (412.7±32.7 *mg/dL)* as shown in table (2). This result is agreed with that of **Arkkila *et al.*, (2001).** They added that the abnormalities in the lipid metabolism may be due to insulin deficiency since the significant increase in TG may be due to the lack of insulin under

diabetic condition, while insulin activates the enzyme lipoprotein lipase and hydrolysis TG under normal condition**.**

TG in G3 (682.5±5.1 *mg/d)* was significantly higher (P ≤0.05) than that of normal G1 (412.7±32.7 *mg/dL*), and G2 (603.4±9.6 *mg/dL)* as shown in table (2).These results was in disagreement with **Arkkila *et al., (2001).* Gupta *et al., (1999)*** found that insulin treatment of diabetic rats restored the altered lipid levels in livers of diabetic rats and the altered enzymes activities to control level.

TG in G4 (524.8±14 *mg/dL)* was significantly lower (P ≤0.05) than that of G2, but significantly higher (P ≤0.05) than that of G1 as shown in table (2). These results were agree with those of **Hull, (2004)**; **Agrawal *et al.,* (2007),** showing that high insulin units presented in camel milk caused activation of lipoprotein lipase enzyme.

TC in G2 (274.2±6.6 *mg/dL)* was significantly lower (P ≤0.05) than that of G1 (366.7±15.4 *mg/dL)*. HDL-c in G2 (52.1±1.0 *mg/dL)* was significantly higher (P ≤0.05) than that of G1 (34.2±1.1 *mg/dL).*While*,* LDL-c in G2 (119.7±0.4 *mg/dL)* was significantly lower (P ≤0.05) than that of G1 (210.7±1.8 *mg/dL)*. In G3, TC (350.7±28.2 *mg/dL)* was not significantly decreased (P >0.05) than that of G1 (366.7±15.4 *mg/dL)*, but it significantly higher (P ≤0.05) than that of G2 (274.2±6.6 *mg/dL)* as shown in table (2). These results were in disagreement with **Newairy *et al*., (2002*)***, and agree with the result of **Young *et al*., (1988)** who reported that in streptozotocin induced diabetic animals, cholesterol absorption is elevated and synthesis down regulated, but these alterations can result 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 by a decrease in the activity of the enzyme. Insulin or thyroid hormone increases HMG-CoA reductase activity, whereas glucagon or glucocorticoids decrease it. Activity is reversibly modified by phosphorylation-dephosphorylation mechanisms, some of which may be cAMP-dependent and therefore immediately responsive to glucagon, explained by **Ness and Chambers, (2000).**

TC of G4 was (295.9±7.9 *mg/dL)* significantly (P ≤0.05) lower than that G3 (350.7±28.2 *mg/dL)* and control one as shown in table (2).On the opposite to the result of **Singh, (2001)**. Although it was agree with **Knoess, (1979).** In the same aspect, **Anderson *et al* (1999)** reported that vitamin C supplementation significantly reduced lipid profile in diabetic rats when compared to untreated diabetic rats and prevents oxidation of LDL-cholesterol; decreases total and LDL-cholesterol and triacylglycerol; and raises HDL-cholesterol level.

HDL in G2 (52.1±1.0 *mg/dL)* was significantly higher (P ≤0.05) than that of normal G1 (34.2±1.1 *mg/dL)*. Although, the serum mean value of LDL in G2 (119.7±0.4 *mg/dL)* was significantly lower (P ≤0.05) than that of G1 (210.7±1.8 *mg/dL)* as shown in table (2). These results disagree with **Horowitz *et al.*, (1993)** reporting that reduced HDL level found in diabetes has several reasons. Increased concentrations of plasma VLDL drive the exchange of triglycerides from VLDL for the cholesteryl esters found in HDL. 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. In addition to **Goldberg, (2001)** observing a defective lipolysis leads to reduced HDL production.

In G3 HDL level (45.1±2.3 *mg/dL)* was significantly higher (P ≤0.05) than that of G1 (34.2±1.1 *mg/dL)* as shown in table (2). LDL in G3 (149.9±0.4 *mg/dL)* was significantly lower (P ≤0.05) than that of G1 (210.7±1.8 *mg/dL)* as shown in table (2).These results were in disagreement with **Gupta *et al.*, (1999*).*** This is due to that insulin treatment of diabetic rats caused restoration of altered lipid levels in livers of diabetic rats and restored altered enzymes activities to control level.

HDL in G4 (36.4±3.8 *mg/dL)* was not significantly (P> 0.05) differed from that of G1 (34.2±1.1 *mg/dL)* as shown in table (2). Although, LDL G4 (168.8±0.4*mg/dL)* was significantly lower (P ≤0.05) than that G1 (210.7±1.8 *mg/dL***.** These results were in agreement with those **Wu *et al.*, (2004)** who suggested that the improvement in lipoproteins was due to the antioxidant effect of vitamin C and zinc in the camel milk.

Phospholipids in G2 (214.5±41.34 *mg/dL)* was not significantly (P> 0.05) differed from that of G1 (145.3±3.1 *mg/dL)* as shown in table (2). In G3 (555.5±72.2 mg/dL) was significantly higher (P ≤0.05) than that of G1 (145.3±3.1 *mg/dL)* as shown in table (2). **Cooper *et al.*, (1990)** reporting that insulin therapy increases the synthesis of phospholipids, diacylglycerol and protein kinase C activity in rat hepatocytes. In G4 (364.2±38.4 *mg/dL)* was significantly higher (P ≤0.05) than that G1 (145.3±3.1 *mg/dL)* as shown in table (2),these results are In agreement with **Kurowska *et al.*, (2000)**.

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