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Composition and hypoglycemic effect of camel milk in streptozotocin–induced diabetic rats

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ABSTRACT

This work studies the analysis of anti-diabetic effects of camel milk in streptozotocin (STZ)–induced diabetic rats which was conducted to assay liver and kidney clinical pharmacological function parameters. Diabetes was induced in the experimental groups of rats by intraperitonial administration (60 mg/kg b.wt.) of streptozotocin. The rats were fed daily with fresh camel milk by feeding bottles for 30 days. To investigate the effect on blood glucose serum proteins, uric acids, urea, creatinine, lipid profile and the effect of diagnostic marker function enzymes of liver and alkaline phosphate (ALP) were tested in the plasma/serum in control and experimental groups of rats. Camel milk supplemented to diabetic rats was manifested in reduced level of blood glucose, uric acid, urea, creatinine, and increase in the activities of albumin, albumin/globulin ratio and reduction in all liver activity function marker enzymes and lipid profile to approximately the control levels. Camel milk is considered to have medicinal benefit that can assist in treatment of varying illness due to its high vitamin and mineral content. Also, camel milk contains high level of mineral such as potassium, iron, zinc, magnesium, cooper, sodium and manganese; and lower sugar, lower lactose compared with cow milk. Cholesterol in camel milk is lower than in cow and goat milk. Camel milk is three times higher in vitamin C than cow milk and ten times higher in iron, low protein and large concentration of insulin that have a positive effect on immunity. The anti-diabetic activity of camel milk has been attributed to the camels' choice of gazing on natural vegetation. Other benefits of camel milk include precautionary in ulcers, regular intake camel milk helps to control blood sugar levels. The beneficial effects of camel are easily observable in prevention of infections such as tuberculosis, gastro-enteritis and cancer. It is also proposed to be a new Viagra. In conclusion, this study showed that supplementations of camel milk to diabetic rats has antihypoglycemic effects and prevent liver and renal damage associated with streptozotocin–induced diabetic rats.

Keywords: Composition, diabetes, streptozotocin, liver function, kidney, camel milk.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder resulting from a total destruction of beta cells which leads to deficiency in insulin secretion and in its action which is manifested in hyperglycaemia with modification of protein, fat and carbohydrate metabolism (Hovens et al., 2005). The expected worldwide prevalence of DM has increased dramatically in the past decades, which has been caused by change in lifestyle resulting in increase in prevalence obesity. The present studies indicate that there are 170 million people in the world with diabetes in the year 2010, and this is expected to increase to 360 million in the year 2030 (Wild et al., 2004). In traditional practices there is an increasing demand for natural products with antidiabetic activity to be used to control diabetes mellitus. In many countries, this has caused an increase in the number of experimental and clinical investigations towards the validation of natural products with anti-diabetic properties. This is because it has been confirmed that insulin and other oral hypoglycemic drugs show various side effects such as hypoglycaemic coma and hepatorenal disturbances (Suba et al., 2004). Moreover, such anti-diabetic products are not safe for

use during pregnancy (Rahman and Zaman, 1989). In this work, the search and testing was carried out using natural, safe and more effective hypoglycaemic agents, as well as identification of the substances responsible for their hypoglycaemia activity.

The World Health Organization (WHO) recommended that the research on the treatment by use of several medicine plants as diabetic remedies in the treatment of diabetic mellitus (World Health Organization, 1980), has led to an increase in the number of experimental and clinical investigations on other hypoglycaemic agents.

Camel milk has been known and deeply studied for their special and medicinal properties such as higher hepatoprotective, insulin like, antimicrobial and antiviral activities (Khan and Alzohary, 2011). Camel milk has other activity in comparison with other species such as bovine and contains a high level, concentration, factors of lysozyme, lactoferrin and immunoglobulins, and vitamin C, which has been shown to play an important and crucial role to explaining these properties (Konuspayeva, 2007; Elagamy et al., 1996).

Finally, the present study explains the analysis and investigated the diabetic effects of fresh camel milk in streptozotocin–induced diabetic rats in rats by studying parameters such as kidney functions; urea, uric acid and creatinine, and liver function test enzymes; alanine amines transfers (ALT), aspartate aminotransfese (AST), alkaline phosphate (ATA), protein, albumin and lipid profile.

MATERIALS AND METHODS

Experimental animals

Selected suitable healthy male albino Wister rats 200 to 250 g were used. They were kept in the laboratory for at least once a week before use in the assay and maintained on adequate and controlled diet, with water available at all times except during the assay when they were fasted for 18 to 24 h prior to the assays. They were divided into five groups of eight rats each as follow:

G1: Normal control rats (vehicle treated)
G11: Normal rats fed with camel milk for 30 days.
G111: Diabetic control group injected with STZ (60 mg/kg b.wt.).
G1V: Diabetic rats fed with camel milk.
GV: Diabetic rats treated with insulin by .i.p. injection (16 unit kg b. wt./day) (Gupta et al., 2004).

Induction of diabetes with streptozotocin

The animals were fasted overnight and diabetes were induced in rats by intraperitonieal injection with freshly prepared of STZ, 60 mg/mg b. wt, of rats in 0.1 M citrate buffer (pH. 4.5) (Khan and Alzohairy, 2011). The animals were allowed to drink 5% glucose solution overnight to maintain the drug induced diabetes by hyperglycaemia; whereas, the control rats were injected by control buffer alone. The animal were considered as diabetic, if their blood glucose values were above 250 mg/dl on the third day after STZ was injected, otherwise, the treatment was started on the fourth day after STZ injection and this was considered as the first day of treatment. The treatment takes 30 days or one month.

Collection of samples of blood and tissue

After 30 days, the animals were sacrificed and the blood samples were collected and divided for plasma and serum collection. The sterile tubes without any anticoagulants were used to collect blood, and then it was allowed to clot at room temperature for 30 min. The serum was submitted for centrifugation at 1000×g to be separated within 15 min at 4°C and was saved in aliquots, stored at -20°C for further analysis. However, the liver, kidney and pancreas were rapidly removed and washed with cold normal saline, after cut were preserved in 10% of neutral formalin for microscopic pathological studies.

Biochemical study of the serum

Blood glucose, parameters of liver activity (Alt, AST, ALP, protein, albumin and cholesterol) and kidney function test (urea, uric acid and creatinine) were studied by using the diagnostic kits as aforementioned.

Statistical analysis

Results were noted as means and standard deviation of three replicates. The significant of differences was calculated by using student t-test. $p < 0.05$ was considered statistically significant.

RESULTS

Administration of STZ dose (60 mg/kg b.wt) to the experimental groups rats results can be obtained in a marked detectable modifications. A significant lowering body weight (24.6 g) was noted in diabetic rats in compared to control rats. Treatment of diabetic group animals with camel milk showed a significant increased in body weight to approximately near normal rats. However, a significant increase in the level of blood glucose was showed in diabetic rats (560 mg/dl) if compared to control and insulin treated rats. Supplementations of diabetic rats with camel milk significantly decreased were observed in the levels of blood glucose within 235 mg/dl (Table 1).

The level of protein, plasma albumin and albumin/globulin rats in control and STZ-DM rats were also assayed for comparative study. The level of protein in plasma was observed to be decreased in diabetic rats ($p < 0.05$) compared to control rats. The lowered level of protein in plasma after camel milk supplementation showed a significant increased to near control.

Main trance the level of albumin and albumin/globulin (A/G) ratio in plasma were also showed to be decreased in diabetic animals treated with camel milk (Table 1).

In case of urea, uric acid and creatinine levels showed a significant increased in STZ-DM rats ($p < 0.05$) were detected when compared to control animals (Table 2). Feeding of diabetic animals with camel milk for 30 days indicate a significantly decreased urea, uric acid and creatinine levels in STZ-DM rats.

Table 1. Effect of camel milk treatment of control, and experimental rats, blood glucose and serum proteins.

Parameter	Groups				
	1	2	3	4	5
Glucose mg/dl)	115.63 ± 5.60	121.76 ± 4.30	520.46 ± 8.90[a]	235.61 ± 7.10[ab]	135.32 ± 5.20
Protein (g/dl)	6.83 ± 0.96	7.13 ± 086	4.52 ± 0.38[a]	6.34 ± 0.40[ab]	7.06 ± 0.34
Albumin (g/dl)	3.86 ± 0.45	3.98 ± 0.38	2.36 ± 0.34[ad]	3.34 ± 0.21[ab]	3.51 ± 0.41
AG ratio	1.31 ± 0.18	1.40 ± 0.13	0.86 ± 0.10[a]	1.12 ± 0.09[ad]	1.21 ± 0.06

Values are given as ± SD for groups of eight animals, values are statistically significant, [a]$p < 0.05$ compared to control, [b]$p < 0.05$ compared to diabetic.
a: The data expressed in mean± S.D n = 8 in each group.
b: Represent statistical significant vs. diabetic control ($p < 0.0$ 5).

Table 2. Effect of camel milk treatment on liver and kidney diagnostic markers on control and experimental groups of rats.

Parameter	Groups				
	1	2	3	4	5
ALT (U/L)	45.28 ± 4.2	48.39 ± 3.9	138.23 ± 8.4[a]	70.76 ± 3.2[ab]	58.31 ± 3.2
AST (U/L)	75.76 ± 5.4	76.29 ± 4.9	122.43 ± 8.6[a]	98.29 ± 7.3[nd]	83.22 ± 4.2
ALB (U/L)	92.76 ± 4.7	95.36 ± 5.4	149.25 ± 7.9[nd]	110.46 ± 6.9[ab]	103.32 ± 4.5
Urea (mg/dl)	21.23 ± 2.3	22.07 ± 1.8	38.25 ± 2.5[a]	31.30 ± 2.0[ab]	26.14 ± 1.2
Uric acid (mg/dl)	2.71 ± 0.6	2.52 ± 0.5	4.64 ± 0.8[nd]	3.21 ± 0.4[nd]	3.07 ± 0.7
Creatinine (mg/dl)	0.91 ± 0.08	0.98 ± 0.06	2.27 ± 0.13[a]	1.54 ± 0.1[ab]	1.03 ± 0.2

Values are given as ±SD for groups of eight animals, values are statistically significant, [a]$p < 0.05$ compared to control, [b]$p < 0.05$ compared to diabetic, nd: Not determined, AST: Aspartate aminotransferase, ALP: Alanine aminotransferase, ALT: Alanine transaminase.

Table 2 shows the activities of AST, ALT and ALP in plasma of control and STZ-DM rats. The efficacy of these enzymes was found to be directly increased ($p < 0.05$) in the plasma of diabetic rats. Supplementation of rats with camel milk for 30 days showed a dramatic shift, towards normal values of these liver function which tested enzymes in STZ-DM rats groups.

Modification in the levels of lipid profile was also assayed to assess the STZ-induced diabetic impairment and protective result of camel milk against dyslipidemia. The results of this study explained that levels of cholesterol, low density lipoprotein and high density lipoprotein-cholesterol and triglycerides (TG) were significantly higher ($P < 0.05$) in diabetic control groups of rats and these levels were significantly reduced in the group of rats treated with camel milk (Table 3).

DISCUSSION

Diabetes mellitus is a dangerous disease with complications and prevalence of mortality accounting for at least 10% of total health care (King et al., 1998). Three fourth of the world population cannot afford the products of allopathic medicine and thus have to resolve to the use of anti-diabetic evidences reported for traditional mediums, which are being sourced from natural products of animals and plants (Hays et al., 2008). Some of these substances indicate anti-diabetic effects by directly influencing B-cells to stimulate insulin and restore insulin sensitivity (Lombardo and Chicco, 2006).

Nowadays, camel milk is gaining popularity because of its scientific justification for high nutritional qualities and therapeutic ally value (Strasser et al., 2006). Camel milk has been used by certain diabetic patients as a treatment in many parts of the world. Camel milk contains approximately 53 unit/l insulin, also does not react to acid and form coagulation in the stomach (Abu-Lehia, 1987). Camel milk has a powerful antibacterial and antiviral activity which could demodulate the immune system. However, drinking non-pasteurized camel milk indicated its therapeutic efficacy to be beneficial to infection of the alimentary canal and autoimmune disease (Shabo et al., 2008).

Literature overview shows that camel milk is a quality drink for many people and it is the most actively used milk for curing a number of diseases (Shabo et al., 2005; Agrawal et al., 2007; Redwan and Tabll, 2007). The findings of the present study confirmed the glycemic control in streptozotocin-induced diabetic rats, so high concentration of insulin of camel milk may be responsible for anti-diabetic effect (Agrawal et al., 2003).

Streptozotocin is a selective B-cells genotoxicant and when administrated in a single high dose it produced a

Table 3. Effect of camel milk treatment on lipid profile on control and experimental groups of rats.

Parameter	Groups				
	1	2	3	4	5
Cholesterol (mg/dl)	131.26 ± 10.4	138.45 ± 8.7	298.31 ± 12.4[a]	196.27 ± 11.9[ab]	105.21 ± 4.8
LDL-C (mg/dl)	70.21 ± 4.5	71.25 ± 5.3	191.31 ± 8.4[a]	128.34 ± 5.9[nd]	105.34 ± 6.3
HDL-C (mg/dl)	41.37 ± 5.1	42.43 ± 6.2	58.43 ± 6.8[a]	52.37 ± 5.6[ab]	49.31 ± 5.3
TG (mg/dl)	74.32 ± 7.1	76.43 ± 6.5	167.43 ± 5.8[a]	109.23 ± 6.3[ab]	84.36 ± 6.1

Values are given as ±SD for groups of eight animals, values are statistically significant, [a]$p < 0.05$ compared to control, [b]$p < 0.05$ compared to diabetic, nd: Not determined, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, TG: Triglycerides.

rapid onset of diabetes by generating sufficient levels of DNA which led to high activities of poly adenosine diphosphate ribose synthetase in the base excision repair pathway of insulin (Burns and Gold, 2007).

The current study showed a significant rise in the blood glucose level in diabetic rats (Table 1). This may indicate the total destruction of all pancreatic beta cells by STZ, resulting in STZ induced diabetes (Gupta et al., 2004). The increase of glucose in STZ treated rats is due to an oxidative stress initiated in the pancreas, resulting to a single strand break in pancreatic islets DNA (Yamamoto el al., 1981; Sboui et al., 2010).

The protective efficacy of camel milk could be attributed to its antioxidants (Al-Humanid et al., 2010). It has been noted that camel milk contains high concentration of vitamins (A, B, C and E) and is rich in magnesium (Knoess, 1979). It is reported that the antioxidant vitamins play an important role in preventing tissue injury caused by toxic agents like CCl4, CALCL3 and STZ. In addition, camel milk is rich in zinc (Knoess, 1979). Moreover, many elements essential for living organs require zinc for their actions and it has a relationship with many enzymes in the body and can prevent cell damage through activation of antioxidant system (Powell, 2000; Ozturk et al., 2003; Ozdemir and Inanc, 2005).

The final results of this study are in agreement with others such as Al-Humaid et al. (2010) who observed that treatment of rats with camel milk poisoned with lead acetate restores the raised levels of liver function enzymes (ALT and AST), urea and triglycerides to normal. After treatment camel milk has been justified to be antitoxic and antioxidant.

In other studies, we showed that the concentration of aminotransferases, alkaline phosphatase, protein and cholesterol level in rats poisoned with cci4 restore to almost normal level after treatment with camel milk. Pharmacological study of the liver observed that there is a decrease in fatty modification, inflammatory cell inflammation and necrosis after treatment with camel milk (Khan and Alzohairy, 2011).

Uric acid, urea and creatinine levels are significantly raised in STZ-DM rats as compared with control groups. Supplementation of diabetic rats with camel milk for 30 days result in significantly reduced kidney function parameters (Table 2). Al-Hashem (2009) showed that the rats poisoned serum levels of urea, creatinine, albumin, bilirubin, AST, ALT, ALP, LDH (lactate dehydrogenase), cholesterol and TG. The amount of albumin and protein were also significantly has been lowered with ALCl3 toxicity.

Agrawal et al. (2009) showed that there was a significant improvement of microalbuminuria after administration of camel milk and insulin injected was significantly lowered results in a glycemic control. A significant decrease in lipid profile was also showed after camel supplementation.

CONCLUSION

The therapeutic activity of the fresh camel milk on streptozotocin-induced diabetic rats was found in the present study. Camel milk shows a significant therapeutic value in the treatment of diabetes produced metabolic disorders due to the presence of insulin/insulin-like proteins. This result may have an implication in the clinical management of diabetes mellitus in humans. So, camel milk would be beneficial for healthy drink.

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