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PROTECTIVE EFFECTS OF CAMEL MILK ON INFLAMMATORY AND ANTIOXIDANT BIOMARKERS IN THE OFFSPRING WITH EXPERIMENTAL STREPTOZOTOCIN-INDUCED DIABETES

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ABSTRACT

Camel milk possess rich content of antioxidants help in ameliorating some chronic disease. The purpose of this study was to investigate the effects of supplemental camel milk on apoliproteins, leptin, hyperhomocyteinemia as well antioxidant status in rats subjected to induced-streptozotocin (STZ) diabetes. Pregnant rats were assigned to 3 groups of 12 rats in each group; Group 1: Control; Group 2: Diabetic with citrate and Group 3: Diabetic with camel milk. Diabetes was induced by STZ at a dose of 49 mg/kg dissolved in citrate buffer. Blood glucose concentrations was measured on a weekly basis after inducing diabetes and the concentrations exceeded 200 mg/dL is a confirmed diabetic rats. The study indicated that camel milk improved blood profile of the measured parameters and these effects are related to antioxidant properties. Current findings confirmed an increase in homocysteine (Hcy), cathepsin G and apolipoprotein B (ApoB) levels and decreases in apolipoprotein A (ApoA) and leptin levels in the group with no supplemental camel milk. Restoration of the elevated levels of biomarkers were found in the camel milk treated group. An improved in Total Antioxidant Status (TAS) and reduced Malondildehyde (MDA) is clearly seen in camel milk-treated offspring compared with non-treated group. Camel milk is suggested to have cardio protective effects as it improved these markers of inflammation associated with heart changes.

Key words: Antioxidant, camel milk, diabetes, inflammation, rats

In recent years, particularly in the Arabian countries there is a change in life style, with increasing consumption in refined sugar. Diabetes Mellitus (DM) is a global health issue with macro and micro vascular complications posing a threat to health sectors and productivity (Majid *et al,* 2016). There is greater consensus about the relationship between food and health and studies on functional food increased dramatically in recent years. The diabetic complications include not only hyperglycaemia, but also cardiomyopathy due to oxidative stress. There is an urgent need for non-conventional therapy for diabetes with less adverse effects. Therefore, the World Health Organisation recommended more research on herbal and medicinal plants (Ameh *et al,* 2010). The aim of this study was to examine the protective effects of camel milk in diabetic animal model of rats. It also tested whether treatment of camel milk can alter oxidative and inflammatory stress agents.

Materials and Methods

Pregnant rats were matched for body weight and assigned to 3 groups of 12 rats in each group (diabetic with citrate and diabetic with camel milk and control), of 15 each. Diabetes was induced by streptozotocin at a dose of 49 mg/kg dissolved in citrate buffer (STZ Sigma, USA) injection. Control rats received (i.v.) citrate buffer. Blood glucose concentrations was measured on a weekly basis after inducing diabetes and the concentrations exceeded 200 mg/dL is a confirmed diabetic rats (Volpato *et al,* 2009). Total antioxidant status was measured in the plasma as the ability of the plasma to prevent ABTS oxidation in comparison to Trolox (Cayman Chemical Co, USA). Malondialdehyde concentration was estimated in the plasma according to the method of Fernandez *et al* (1997). Apolipoprotein (ApoA) and B amounts were measured using the nephelometric method of Randox, UK. The amount of plasma leptin was measured using a commercial kit (Randox, UK). Plasma cathepsin and Hcy were measured using Randox, UK kits. The assays of plasma hormones (LH, FSH and T_3) were done in accordance with the manufacturer's instruction (EIA-5179; DRG Diagnostic, Marburg, Germany).

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The experimental plan followed the requirement of the National Committee of Bio and Medical Ethics, Saudi Arabia. Data were tested for normality and homogeneity of variance and the differences were tested by one way ANOVA, followed by a Turkey's post hoc test. P value < 0.05 was considered statistically significant.

Table 1. Nutritional composition of the experimental diets during pregnancy and lactation in rats.

Nutrients	
Fibre	48
Carbohydrate (% of total kcal)	61
Protein (% of total Kcal)	18
Fat (% of total Kcal)	16
Energy (Kcal/Kg)	3750

Table 2. Supplemental camel milk on antioxidant status and hormonal profile in rat offspring.

Variable	Control	Diabetes	Diabetes+ camel milk
TAS Trolox Equiv./L	0.53±0.08	0.34±0.071[a]	0.51±0.01[b]
MDA (Nmoles of MDA/mg protein)	1.63±0.39	4.12±0.13[a]	1.71±0.42[b]
LH (ng/mL)	6.34+1.00	5.11+1.01[a]	6.00+0.77[b]
FSH (ng/mL)	5.34+0.44	3.55+0.44[a]	4.85+0.65[b]
T_3 (ng/dL)	0.80+0.06	0.49+0.03[a]	0.74+0.03[b]

Values are presented as means±standard error for 10 rats per group

[a]Significant differences at P < 0.05 compared to the control group

[b]Significant differences at P < 0.05 compared to the diabetic group

Results and Discussion

The main components of diets given to experimental rats are shown in table 1. Malondialdehyde is one of the major products of oxidation of polyunsaturated fatty acids, causing damage to tissue and this is manifested in pathological conditions, including DM (Nguyen *et al,* 2016). As shown in table 2, a reduction in TAS as well as an increase in TBARS is indicated in diabetic rats, with camel milk ameliorated such effects. Similar trends were observed by medicinal plant extracts, as reported by Naseem *et al* (2016). The authors confirmed that Panax ginseng is effective in ameliorating diabetes via increasing antioxidant profile, catalase and lowering lipid peroxidation biomarker.

The influence of camel milk on the plasma concentrations of LH, FSH and T_3 as well as antioxidant status in rat offspring is presented in table 2. Diabetes resulted in a significantly decreased hormonal status compared with the control ones. However, supplemental camel significantly (P < 0.05) reversed the suppressive effects of diabetes, by normalising hormonal levels. Similar trend of adjusting the hormone in diabetic rats were observed by the work done by Adedara *et al* (2105), in which the authors identified *Garcinia kola* seed extract as anti-diabetic agent. In another study, *Ficus pumila Linn* extract altered serum hormonal levels in rats, reducing the negative effects of hyperprolactinemia in rats (He *et al,* 2016).

Table 3. Effect of camel milk on diabetes-induced changes in plasma apolipoproteins, leptin and Hcy of rat offspring.

	Control	Diabetes	Diabetes+ camel milk
ApoA (g/L)	138.2±1.9	103±2.9[a]	129±4.3[a,b]
ApoB (g/L)	109±4.3	168±4.3[a]	115±2.9[b]
Leptin (ng/mL)	4.2±0.13	2.9±0.2[a]	3.35±0.8[a,b]
Cathepsin	4.33±0.9	8.5±0.28[a]	5.4±0.36[b]
Hcy (µmol/L)	3.12±0.18	4.55±0.11[a]	2.81±0.23[b]

Values are presented as means±standard error for 10 rats per group

[a]Significant differences at P < 0.05 compared to the control group

[b]Significant differences at P < 0.05 compared to the diabetic group

As indicated in table 3, camel milk proved effective in normalising inflammatory biomarkers in diabetic rat offspring. Leptin adjust the energy balance and it has specific effects of cardiac function and in reported studies lack of its receptor is linked with diabetes (Friedman, 2016). The plasma leptin of the control group was lower than the rest of the groups and camel milk significantly increased its level.

Homocysteine is a non-protein alpha amino acid. Its high levels (hyperhomocysteinemia) leads to inflammation. It can alter innate immunity and can lead to disturbance in diabetes mellitus (Joshi *et al,* 2016). The apolipoprtien A and B are used to assess the risk for cardiovascular diseases (Sharma *et al,* 2017). Due to its antioxidant properties, 50 mg of daily dose of ginger extract significantly improved the status of apo, leptic, cathepsin and Hcy in wistar rats (Likhanizadeh *et al,* 2016). Similar protective effects against inflammatory biomarkers were observed in the study in which cloudy apple juice and apple peel extract were used (Fathy and Drees, 2016).

Inflammatory biomarker are differently expressed between control and diabetic rats (La

Fontaine *et al,* 2014). In another study, lycopene proved effective in enhancing the antioxidant status, by increasing SOD and also reducing the inflammatory response in diabetic rats (Li *et al,* 2016). The studies are comparable to that of camel milk and this could give extra support about the role of antioxidant in either the milk or medicinal plants in alleviating some markers.

This study outline similar effects in both camel milk and ginger extract in normalising some inflammatory biomarkers. Such biomarkers may produce cardiac abnormalities and thus future studies on camel milk and its cardio-protective properties may be recommended. In conclusion, the supplementation of rat offspring with camel milk restored the levels of inflammatory ApoA, ApoB, Hcy and leptin in the experimentally-induced diabetes in rats. Further studies are required to understand the mechanism behind these effects.

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