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Potential Effects Of Colostrums Against Some Biochemical Changes In Diabetic Rats Induced Alloxan

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Abstract

The present work was concerned with the investigation of colostrums potential effects on some biochemical changes in diabetic rats. The results showed the impact of oral administration of colostrum in diabetic rats. The biochemical measurements showed an improvement in plasma glucose levels in groups consumed cow colostrum (5&10 ml/kg bw). The decrement was reach 30.80% and 20.40%. On the other hand there were highly significant increases in serum total proteins, albumin and globulin in diabetic rat groups consumed colostrums compared to their corresponding control group. Cow colostrum has positive effect on reducing both urea and creatinine in groups consumed colostrum.

While diabetic rats consumed colostrums levels at (5&10 ml/kg bw) it resulted in significant reduction in lipids pattern, total cholesterol, triacylglycerol, LDL-c and superoxide dismutase in association with the increase in HDL-c, malondialdehyde and glutathione compared to their corresponding control group. In summary, the results of this study indicated that some of the abnormalities that accompany the development of diabetes mellitus in rats given alloxan are ameliorated and improved metabolic parameters by dietary cow colostrum intake.

Key words: Diabetes, Cows colostrums, Hyperglycemia, Antioxidants.

Introduction

Diabetes mellitus (DM) is one of the most serious chronic diseases which is linked with hyperglycemia that occurs either when the

pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces (**Bliss, 2000 and Ramachandran et al., 2010**). Diabetes have several acute and chronic complications that greatly affect human health and some of them considering as life threatening such as diabetic ketoacidosis (DKA) and hyperosmolar coma. World Health Organization (WHO) indicates that diabetes mellitus is one of the major killers nowadays, with Southeast Asia and Western Pacific populations being most at risk (**King et al. 1998, Takeshi et al. 2002 and American Diabetes Association, 2008**).

Colostrum is breast milk produced after the birth of the newborn and lasts for 2-4 days. It is viscous lemon yellow color and rich in minerals salts (zinc and selenium) and fat soluble vitamins; vitamin A, E, and slightly D, while it is poor in lactose, fat, and contains considerable amount of the water soluble vitamins whereas bovine colostrum contains higher relative concentrations of thiamine, riboflavin, niacin, folic acid and cobalamin (**Kaushik et al. 2000, Lin et al. 2009 and Asger, et al., 2017**). The most important bioactive components in colostrum include growth and antimicrobial factors. Assessment of microbial community structure in human colostrum and mature milk based on geographical location and delivery mode Growth factors promote the growth and development of the newborn, while antimicrobial factors provide passive immunity and protect against infections during the first weeks of life. Colostrum is a possible natural food which may have hypoglycemic properties and thus help in the control of diabetes mellitus (**Or-Rashid, et al., 2010 and Xiaoxia, et al. 2017**). Colostrum has been shown to maintain blood glucose levels to serve the brain due to its high content of insulin like growth factors that cross the blood brain barrier to help nerve synapse in the brain and therefore enhancing mental acuity (**Kuipers et al. 2002**). Several bacterial pathogens can be transmitted in colostrum and milk, whether by direct shedding from the mammary gland, postharvest contamination, or bacterial proliferation in improperly stored colostrum (**Stewart et al., 2005**). Heating colostrum at 60°C for 60 min should be sufficient to maintain fluid characteristics (**Johnson et al. 2007**). The present work identifies colostrum as a dietary factor which plays a key role in the development of diabetic rats.

Materials and Methods

Materials:

- **Colostrum:** colostrum used in the present investigation was fresh collected secretion as the earliest phases of lactation period which collected from healthy cows from three private farms in El-Dakahlia.
- **Animals:** A total of 28 male Sprague-Dawley rats (age, 8 weeks; weight 100 ± 10 g) were provided from of National Research Center, Cairo, Egypt. Rats were housed as groups in wire cages under the normal laboratory conditions. The basal diet prepared according to (NRC 1995). The vitamin and mineral mixture had the prepared according to (Campbell 1963).
- **Alloxan:** was obtained from El Gomhoria Company, Egypt.

Methods :

- Total solids, ash and lactose were analyzed according to the method of (AOAC, 2000) while total or whey protein and fat as described by British Standards Institution (BSI, 1990) and (Ling 1963), respectively.

Induction of diabetes: Diabetes was induced by intraperitoneally injection of a freshly prepared aqueous solution of alloxan monohydrate in saline at a dose level of 100 mg/kg-body weight (Al-Zuhair et al., 1996).

Experimental design: A total of 28 male healthy rats were divided into 4 equal groups, all rats were subcutaneous injected by alloxan as 100 mg/kg body weight rats to induce hyperglycemic. Animal blood was extracted from the tail vein for glucose analysis and rats with fasting glucose ranging from 210-220 mg/dl, showing clear signs of polyuria, polyphagia and polydipsia were considered diabetic and were analyzed 48 hours after alloxan treatment. Animals with fasting blood glucose less than 150 mg/dl were rejected. The rats were divided into the following groups of 4 animals each: **Group I:** negative control rats fed on the basal diet. **Group II:** positive control diabetic rats fed on the basal diet. **Group III:** diabetic rats fed on the basal diet plus consuming cows colostrum (5ml/kg b.w) twice daily. **Group IIII:** diabetic rats fed on the basal diet plus consuming cows colostrum (10ml/kg b.w) twice daily.

Food intake was measured every day by subtracting the residual and refusal diet from served diet. Daily food intake (g) = Diet given - (Residual diet + Refusal diet)

The animals were weighted weekly to monitor the body weight changes and feed efficiency ratio (FER) was calculated as described by (Guo et al., 2002).

Relative weight of organs = Weight of organ / Final body weight × 100

Biochemical analysis of serum: At the end of experimental period (6 weeks), and after overnight fasting rats were scarified and blood samples were collected from hepatic portal vein in two centrifuge tubes. Blood glucose levels were performed in plasma by method of (Teuscher and Richterich, 1971). All diabetic rats with baseline blood sugar level about 249.05 ± 5.42 mg/dl. In serum total protein and albumin by (Weissman et al., 1950: and Dumas and Biggs 1972) respectively. Total cholesterol, triacylglycerol, and high density lipoprotein were determined according to Roeschlau et al. (1974); Trinder, (1969) and Arcol, (1989). After decapitation of animals, liver, kidney and pancreas were dissected immediately, rinsed and washed by saline solution, then blotted on filter paper to remove water residue and weighed to calculate the relative organs weight as described by (Guo et al., 2002). Superoxide dismutase (SOD) activity according to (Dechatelet et al., 1974). Determination of malondialdehyde (MDA) in red blood cells RBCs by the method described by Stocks and Donnandy (1971). Glutathione (GSH) according to (Beutler ., 1984).

Statistical Analysis: The results were expressed as means \pm S.D. and analyzed for statistical significance by two-way ANOVA followed by tukey's post-hoc test for multiple comparisons, using SPSS program for windows version 15.0 (SPSS Inc, Chicago, USA). Values were considered statistically significant at $P < 0.05$.

Results and Discussion

Table (1) showed chemical composition of cow colostrums. Total protein and whey protein content of first milking cow colostrums were observed very high, which could be due to high concentration of globulin than serve as the carrier of antibodies for suckling calf against disease producing organism (Tsioulpas and Grandison 2007).

Table (2) showed that alloxanized rats showed a highly significantly decrement in the values of body weight cow colostrums 5&10ml consumption by diabetic rats, showed increase in body weight gain reached (-19.40, and -9.60) in comparison with the diabetic control

group -24.40g. The mean values of FER were being in case of control (-ve) (0.71), while diabetic group consuming cow colostrums showed (-1.14 and -0.52) as compared to control (+ve) (-1.44). The relative weight of liver, kidneys and pancreas was observed; the positive control suffered from marked liver, kidneys and pancreas enlargement compare to the control (-ve). While diabetic rats fed on the base diet with cow colostrums showed marked reduction in relative weight of liver and pancreas. No significant difference was observed between relative weights of kidneys diabetic rat groups fed the base diet or colostrum. This result similar to the results of (**Ragab 2002, Antonio et al. 2001 and Ene et al. 2007**) who reported that diabetic animals had lower body weight compare with controls. **Sadek, et al. (2011)** observed that alloxanized rats showed a highly significantly decrement in the values of body weight, and the decrement reached (15.25%) as compared to the initial body weight (145±5g). Colostrum consumption by diabetic rats, showed marked augment in body weight gain reached (22.57%) in comparison with the diabetic control group fed the balanced diet with drinking water. **Ene et al. (2007) and Sadek et al.(2011)** observed that diabetic animals had higher relative liver weight as compared with non-diabetic control group.

Biochemical measurements revealed that, the control (+ve) rats showed significant increase in final blood glucose level, blood glucose gain and blood glucose percent in comparing with the negative control group. While, cow colostrums groups showed significant decrease on final blood glucose level, blood glucose gain and blood glucose percent in comparing with the positive control. These results were agreed with many authors as **Kuipers et al. (2002) and Boudry et al. (2008)** who reported that colostrum has been shown to balance blood sugar levels this is due to a growth factor known as IGF-1 (insulin like growth factor). Colostrum can completely eliminate the need for insulin. It balances the pancreas just like it does the thymus so that blood sugar levels are able to normalize. **Jahantigh et al. (2011) and Sadek et al. (2011)** reported that colostrum insulin like growth factor IGF which has an important role to control glucose metabolism. IGF closely related to synthesis of adiponectin in adipocytes. Adiponectin may be augment and mimic the metabolic actions of insulin by increasing fatty acid oxidation

and insulin-mediated glucose disposal in skeletal muscle as well as by decreasing hepatic glucose output.

Table (4) showed that positive control rat group showed significant increase in total cholesterol (T.Ch), triglyceride (TG), LDL_C and VLDL_C but significant decrease in HDL_C in comparing with the control (-ve). The cow colostrums group consumed (5&10ml) showed significant decrease in cholesterol, triglyceride, LDL_C and VLDL_C but significant increase in HDL in comparing with the control (+ve). This results agree with **Barakat, 2006, Johar, 2002 and Josepha (2010)** who reported that the hyperglycemia caused a significant increases in total lipids, cholesterol, free fatty acids, and triglyceride contents. This may be attributed to an overproduction of the lipid by the gastrointestinal tract. The increased plasma triglyceride (TG) level of diabetic animals can be traced to the markedly depressed tissue lipoprotein lipase activity and clearance of TAG enriched VLDL-c from the circulation. **Schernhaner, (2005) and Hany, (2011)** reported that cow colostrum can efficiently decrease TG and total cholesterol level in Type 2 diabetic patients. A significant decrease in cholesterol concentration was also shown a recent report on rats that received 10% cow colostrums. Positive control rat group showed significant decrease in total protein and albumin but showed increase in urea, however non-significant deference in globulin and creatinine ratio in comparing with the negative control rat group. Cow colostrums rat groups showed significant increase in total protein and albumin but showed decrease in urea, however non-significant deference in globulin and creatinine in comparing with the control (+ve) (table 5). These results agree with **Ragab, (2002) Yassin et al. (2004) Hany, (2011)** who reported that highly significant decrease in serum total protein and albumin was recorded in diabetic rats through the study with percentage decrease of (21.74% and 20.19%) respectively as compared to control levels. The estimated level of globulin in diabetic rats showed significant decrease with a percentage of (24.17%) compare to control(+ve). The results of the present work showed that there was significant amelioration in plasma lipid profile in healthy and diabetic rats when consuming the balanced diet plus colostrums.

Data in Table (6) revealed decrease significantly in malondialdehyde (MDA) and a significant elevation in superoxide

dismutase (SOD) and glutathione (GSH) were observed in the diabetic groups treated with cow colostrums (5&10ml) when compared with diabetic control. As evident from Table (9) significant decrease in malondialdehyde (MDA) were observed in cow colostrums (5&10ml) were (14 and 14.45) when compared with control (+ve) was (19.2 u\ml). Data present in Table (9) revealed increase significantly in superoxide dismutase (SOD) was observed in Cow colostrums (5&10ml) rats (0.67 and 0.65mg\lL), also increase significantly in glutathione GSH was observed in cow colostrums(5&10ml) rats reached to (6.25 and 5.66u\ml) as compared to control (+ve) (4.22).

Conclusion

This study shows that cow colostrums intake is effective in up-regulating the antioxidant defense mechanism by attenuating (MDA) and (SOD). Changes in the cholinergic system, the improved that may be due to its on inflammatory effect in alloxan-induced diabetes. It also can improve the lipid profile, insulin sensitivity, hyperglycemia control and the GSH with relieving of the oxidative stress.

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Table (1) chemical composition (%) of cows colostrums after 12 h of parturition

Variables	protein	Whey protein	Fat	Ash	Lactose	Total solids
Cow colostrums	11.00	8.50	6.30	0.87	2.00	20.17

Table(2)Body weight gain, food intake, food efficiency ratio (FER), and the relative weight of liver, kidneys and pancreas of control and diabetic rats groups treated with raw and heated cow and buffalo colostrums (means \pm SD)

Variables	Bodyweight gain (g)	Daily food intake (g/d)	Food efficiency ratio (FER)	Relative weight of liver	Relative weight of kidneys	Relative weight of pancreas
Control (-ve)	12.80 \pm 9.39c	17.99 \pm 1.86a	0.71 \pm 0.56c	2.16 \pm 0.22a	0.66 \pm 0.03a	0.16 \pm 0.03a
Control (+ve)	-24.40 \pm 4.39a	16.91 \pm 2.11a	-1.44 \pm 0.43a	4.44 \pm 1.11d	0.89 \pm 0.19c	0.22 \pm 0.09bc
Cow Colostrums	5ml/kg b.w	-19.40 \pm 8.53a	16.98 \pm 1.68a	-1.14 \pm 0.52a	3.86 \pm 0.46bc	0.86 \pm 0.06c
	10ml/kg b.w	-9.60 \pm 4.56b	17.45 \pm 1.59a	-0.52 \pm 0.22b	3.02 \pm 0.50b	0.88 \pm 0.05c

Values with the same letters by column indicate no significant different ($p < 0.05$) and vice versa

Table (3) Initial plasma glucose level, final plasma glucose level, plasma glucose level gain and plasma glucose level gain (mg/dl) (means \pm SD)

Variables	Initial plasma glucose level (mg/dl)	Final plasma glucose level (mg/dl)	Plasma glucose level gain (mg/dl)	Plasma glucose level gain (%)	
Control (-ve)	94.80 \pm 3.96a	98.40 \pm 8.41a	3.60 \pm 4.82c	3.8 \pm 4.80c	
Control (+ve)	317.20 \pm 86.50b	391.00 \pm 71.62c	73.80 \pm 59.48d	23.03 \pm 28.16d	
Cow Colostrum	5ml/kg b.w	310.00 \pm 122.52b	214.40 \pm 74.86b	-95.60 \pm 51.66a	-30.80 \pm 5.84a
	10ml/kg b.w	310.60 \pm 72.41b	247.20 \pm 72.44b	-63.40 \pm 52.71ab	-20.4 \pm 14.19ab

Values with the same letters by column indicate no significant different ($p < 0.05$) and vice versa

Table (4): Effect of cow colostrums on Cholesterol, Triglyceride, HDL, LDL and VLDL of diabetic rat groups (means \pm SD)

Variables		TG (mg/dl)	Tch (mg/dl)	LDL-c (mg/dl)	HDL-c (mg/dl)	VLDL-c (mg/dl)
Groups						
Control (-ve)		83.40 \pm 12.03 c	79.60 \pm 7.70 c	22.12 \pm 5.08 d	40.80 \pm 8.25a	16.68 \pm 2.40 d
Control (+ve)		117.80 \pm 19.94 a	121.00 \pm 25.20 a	73.24 \pm 22.44 a	24.20 \pm 3.63d	23.56 \pm 5.04 a
Cow Colostrums	5ml/kg b.w	90.00 \pm 16.79 b	99.20 \pm 15.41b	47.20 \pm 15.46 b	34.00 \pm 7.10 b	18.00 \pm 3.35 b
	10ml/kg b.w	92.40 \pm 11.63b	98.00 \pm 12.04b	47.32 \pm 10.58 b	32.20 \pm 5.49 bc	18.48 \pm 2.32 b

Values with the same letters by column indicate no significant different ($p < 0.05$) and vice versa

Table (5):Effect of cow colostrums on total protein, albumin, globulin, urea and creatinine (means \pm SD)

Variables		Total protein (g/dl)	Albumin (mg/dl)	Globulin (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)
Groups						
Control (-ve)		7.16 \pm 0.70 c	4.16 \pm 0.49 b	3.00 \pm 0.40 b	26.80 \pm 2.58 b	0.86 \pm 0.17b
Control (+ve)		4.90 \pm 0.57 a	2.66 \pm 0.46 a	1.24 \pm 0.18 a	36.40 \pm 8.90a	1.15 \pm 0.48a
Cow Colostrums	5ml/kg b.w	6.90 \pm 1.00 b c	3.86 \pm 0.59 ab	2.6 \pm 0.68 b	29.60 \pm 5.52b	0.98 \pm 0.13ab
	10ml/kg b.w	6.14 \pm 0.69 bc	4.02 \pm 0.68 b	2.9 \pm 0.19 b	28.00 \pm 5.52b	0.90 \pm 0.26ab

Values with the same letters by column indicate no significant different ($p < 0.05$) and vice versa

Table (6): Effect of cow colostrums on some blood antioxidant parameters (means \pm SD)

Variables Groups		MDA (U/mL)	SOD (mg/L)	GSH (U/mL)
Control (-ve)		11.26 \pm 1.4 c	0.54 \pm 0.12 b	9.27 \pm 0.6 c
Control (+ve)		19.2 \pm 0.8 a	0.26 \pm 0.09 a	4.22 \pm 1.54 a
Cow Colostrums	5ml/kg b.w	14.0 \pm 1.2b	0.67 \pm 0.05c	6.25 \pm 0.03 b
	10ml/kg b.w	14.45 \pm 2.5 b	0.65 \pm 0.17c	5.66 \pm 0.79 b

Values with the same letters by column indicate no significant different ($p < 0.05$) and vice versa
 MDA:malondialdehyde SOD:superoxide dismutase GSH: glutathione

التأثيرات المحتملة للبا البقرى على بعض التغيرات الحيوية لفئران التجارب المصابة بمرض السكرى بالالوكسان

على مناحى نزال الشمري

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الملخص العربي

هدفت هذه الدراسة ببحث التأثير المحتمل للبا على بعض التغيرات الحيوية لفئران التجارب المصابة بمرض السكرى حيث اجريت الدراسة على عشرين من فئران التجارب المصابة بالالوكسان. ولقد أظهرت النتائج أثر تناول الفئران المصابة للبا عن طريق الفم. تحسن مستوى الجلوكوز فى الدم فقد أنخفض بنسبة ٣٠,٨% للفئران المصابة و تغذت على لبا بقرى طازج بنسبة ٥ مل لكل كجم و بنسبة ٢٠,٤% لمن تغذت على لبا بقرى بنسبة ١٠ مل لكل كجم من وزن الفار. و على الجانب الأخر لوحظ زيادة معنوية فى مستوى البروتين الكلى و الألبومين و الجلوبيولين فى سيرم الدم فى الفئران المصابة و تغذت على اللبا. كما أظهرت النتائج الأثر الواضح فى انخفاض كلا من اليوريا و الكرياتينين و الكوليستيرول الكلى، و الجليسيريدات الثلاثية ، و الليبوبروتينات منخفضة الكثافة، وأنزيمات SOD و مع ارتفاع مستوى الليبوبروتينات مرتفعة الكثافة، المالونالدهيدات (مؤشر أكسدة الدهون)، و الجلوتاثيون للفئران المصابة و تغذت على اللبا. وقد توصلت النتائج للتأكيد على أن التغيرات الشاذة التى لازمت الفئران المصابة بالسكرى قد تحسنت و تطورت مؤشرات الأيض نتيجة تناول اللبا البقرى الطازج