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Potential effects of colostrum against some biochemical changes in alloxan-induced diabetic rats

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Abstract: Bovine colostrum (BC) has been reported to enhance immune functions and antioxidant defense systems, reduce oxidative stress and fat accumulation, and facilitate the movement of glucose to the muscle. However, very few attempts have been made to examine its anti-diabetic effects in experimental animals. Therefore, the present study aims to evaluate whether BC decreases blood glucose and oxidative stress as well as enhance the blood lipid profile in diabetic rats induced by alloxan. Treatment of animals with aloxane caused a significant increased ($p \leq 0.05$) in serum glucose concentration by the ratio 85.59% compared to normal controls. Supplementation of the rat diets with BC by the levels of 5 and10 ml/kg BW decreased this value which recorded 30.80 and 20.40%, respectively. The same behavior was recorded for some blood lipid profile parameters (triglycerides, total cholesterol, LDL and VLDL) and malonaldialdehyde (MDA, the biomarkers of oxidative stress and inflammation in liver). Also, improving in liver (albumin and globuline) and kidney (urea and creatinine) functions and antioxidant defense systems (SOD and GSH) in diabetic rats have been induced by different rates as the result of supplementation the diet with BC. All of these effects could be attributed to the strong immunological and antioxidant activities of BC as the result of its high bioactive compounds content. These findings provide a basis for the use of BC in prevention and early treatment of T2DM complications which include elevation the levels of blood glucose and oxidative stress, the disturbance in blood lipid profile, liver and kidney functions, and antioxidant defense systems.

Key words: Diabetes, blood glucose, kidney functions, oxidative stress, blood lipid profile, antioxidant defense systems**.**

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin

secretion, insulin action or both. Type 2 diabetes (non–insulin-dependent diabetes mellitus), the most prevalent form of the disease, is caused by a complicated interplay of genes, environment, lifestyle choices, insulin abnormalities, increased glucose production in the liver, increased fat breakdown and possibly defective hormonal secretions in the intestine (Neel, 1962). DM 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 DM 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 pre-milk substance that is produced immediately after birth. Within few minutes of birth, baby can suckle the breast. Colostrum is thick lemon yellow mammary secretion and is rich in proteins. This lasts for 2-4 days after the lactation has started. This is the source of primary components, immune factors (specific antibodies, immunoglobulins, prolin rich polypeptide, lactoferrin, cytokines, oligopolysaccharides, glycoproteins and trypsin inhibitors, lactalbumins) and growth factors (epithelial growth factor, EGF, transforming growth factors, TGF, platelet derived growth factor (PDGF), and Vitamins and Minerals). Colostrum is 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 cyanocobalamin (Kaushik *et al.*, 2000; Lin *et al.,* 2009 and Asger *et al.*, 2017).

Bovine colostrum (BC) contains useful ingredients which have been found to be beneficial in various diseases in human beings. In gastrointestinal tract (GIT) bovine colostrum has great role in terms of maintenance of integrity of mucosa, permeability, local immunity (secretory IgA), systemic immunity and antigen handling. There are clinical observations to support that bovine colostrum is effective in the treatment of bacterial and viral diarrhea in adults and children (Davidson et al., 1989; Kaushik *et al.,* 2002 and Thapa, 2005). Indeed, many studies have confirmed the presence of insulin-like growth factor-1 (IGF-1) in BC and indicated concentrations of IGF-1 and IGF-11 in the first colostrum that range from 289 to 902 pg/L. IGF-1 is suggested to have

beneficial effects on glucose homeostasis since it lowers blood glucose and increases insulin sensitivity (Campbell, P. and Baumrucker, 1989; Collier, et al., 1989 and Frystyk, 2004). Also, it was reported that IGF-1 levels are generally lower in Type 2 diabetic patients, and the progressive age-dependent decline of IGF-1 is higher in Type 2 diabetic patients than in healthy individuals (Janssen and Lamberts, 2002; Thapa, 2005 and Jun *et al.,* 2009). Additionally, leptin in bovine colostrum which works in concert with IGF-1, could be beneficial to people with elevated cholesterol and TG levels, because it is linked to fat breakdown in muscle. Interestingly, Type 2 diabetic patients were shown to have significantly lower leptin levels compared to nondiabetic subjects after controlling for age and percent body fat (Dagago-Jack *et al.*, 2000 and Jun *et al.,* 2009). Although various studies on the beneficial effects of colostrum have been performed, there are few reports on its antidiabetic effects. Therefore, the present study was carried out to investigate the potential effects of colostrum against some biochemical changes in alloxan-induced diabetic rats.

Materials and Methods

Materials

Colostrum: Bovine colostrum (BC) used in the present study was fresh collected secretion as the earliest phases of lactation period which collected from healthy cows from three private farms in Kuwait

Chemicals: Alloxan, used for induction of diabetes mellitus among rats and reduced glutathione (GSH) were obtained from Sigma Chemical Co., St. Louis, Mo. Casein, as main source of protein from Morgan Company for Chemicals. Cairo, Egypt and Vitamins and salts mixtures, all organic solvents and other chemicals were of analytical grade were purchased from El-Ghomhorya Company for Drugs, Chemicals and Medical instruments Trading, Cairo, 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.

Biological experiments

Experimental animals

A total of 28 male Sprague-Dawley rats (age, 8 weeks; weight 100 ±10 g) were provided from Kuwait Research Institute, Kuwait.

Basal Diet

The basic diet prepared according to the following formula as mentioned by (AIN, 1993) as follow: protein (10%), corn oil (10%), vitamin mixture (1%), mineral mixture (4%), choline chloride (0.2%), methionine (0.3%), cellulose (5%), and the remained is corn starch (69.5%). The used vitamin mixture component was that recommended by (Campbell, 1963) while the salt mixture used was formulated according to (Hegsted, 1941).

Induction of diabetes

Diabetes was induced in sixty three normal healthy rats by injection into operationally with freshly prepared alloxan monohydrate in saline at a dose level of 150 mg/ kg body weight (Lazarow and Palay, 1954). Immediately after injection animals were received 5% glucose solution over night to overcome drug induced hypoglycemia (Wohaieb and Godin, 1987and Kakkar *et al.*,1998). After five days blood glucose was analyzed by a drop of blood was obtained from tail vein and subjected to a strip of haemogluco test. All rats with fasting blood sugar > 126 mg/dl were considered to be diabetics and included in the experiment.

Experimental design

All biological experiments performed complied with the rulings of the Institute of Laboratory Animal Resources, Commission on life Sciences, National Research Council (NRC, 1996). Rats (n=28 rats), were housed individually in wire cages in a room maintained at 25 ± 2 ^{0}C and kept under normal healthy conditions. All rats were fed on basal diet for one-week before starting the experiment for acclimatization. After one week period, the rats were divided into divided into two main groups, the first group (Group 1, 7 rats) still fed on basal diet and the other main group (21 rats) was injected subcutaneous by alloxan monohydrate to induce diabetic rats then classified into three sub groups as follow:

- Group (2): Fed on standard diet only as a positive control (rats with diabetes).
- Group (3): fed on the basal diet plus consuming cows colostrum (5ml/kg b.w) twice daily.
- Group (4): 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

Blood sampling

At the end of experiment period, 6 weeks, blood samples were collected after 12 hours fasting using the abdominal aorta and rats were scarified under ether anesthetized. Blood samples were received into glass centrifuge tubes, containing oxalate solution (1.34 %) as anticoagulant. After centrifugation at 3000 rpm for 10 min., plasma was with drown and used for the hematological analysis.

Hematological analysis

Blood glucose levels were performed in plasma by the method of Teuscher and Richterich, (1971). Serum total protein and albumin were determined 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), respectively. Superoxide dismutase (SOD) activity was determined according to Dechatelet *et al.,* (1974). Malondialdehyde (MDA) and glutathione (GSH) were determined according to Stocks and Donnandy (1971) and Beutler ., 1984), respectively. 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).

Statistical Analysis

The results were expressed as means ± S.D. and analyzed for statistical significance by two-way ANOVA followed by tukey's post-hoctest 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

Chemical composition (%) of BC after 12 h of parturition

Data in Table (1) showed the chemical composition of BC after 12 h of parturition . From such data it could be noticed that total protein and whey protein content of first milking BC 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). Such data are in accordance with that reviewed by Thapa (2005).

Table (1). Chemical composition (%) of BC after 12 h of parturition

Variables	Total protein	Whey protein	Crude fat	Ash	Lactose	Total solids
Value	11.00	8.50	6.30	0.87	2.00	20.17

Body weight gain (BWG), food intake (FI), food efficiency ratio (FER), and the relative weight of liver, kidneys and pancreas of control and diabetic rats groups treated with BC

Data in Table (2) showed the BWG, FI, FER and the relative weight of liver, kidneys and pancreas of control and diabetic rats groups treated with BC. From such data it could be noticed that treatment of animals with alloxan caused a significant decreased ($p \leq 0.05$) BWG and FER. by the ratio -24.40 and -1.44%, respectively compared to normal controls. Supplementation of the rat diets with BC by the ratio of 5 and 10 ml/kg BW increased the BWG and FER by the ratio o19.40, and -9.60; and (-1.14 and -0.52% in comparison with the control group, respectively.

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 BC 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 that obtained by (Ragab 2002) who reported that diabetic animals had lower body weight compare with controls. Sadek, *et al.* (2011) observed that diabetic 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. BC 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. Also, Sadek *et al.* (2011) observed that diabetic animals had higher relative liver weight as compared with non-diabetic control group.

Table (2): Body weight gain (BWG), food intake (FI), food efficiency ratio (FER), and the relative weight of liver, kidneys and pancreas of control and diabetic rats groups treated with BC (means ± SD)

Groups	Bodyweigh t gain (g)	Daily food intake (g/d)	Food efficiency ratio (FER)	Relative weight of liver	Relative weight of kidneys	Relative weight of pancreas
Group 1: Control (-Ve)	12.80 ±9.39c	17.99 ±1.86a	0.71 ±0.56c	2.16 ±0.22a	0.66 ±0.03a	0.16 ±0.03a
Group 2: Control (+ve)	9.67 ±4.39a	16.91 ±2.11a	0.69 ±0.43a	4.44 ±1.11d	0.89 ±0.19c	0.22 ±0.09bc
Group 3: Control (+ve) + BC (5 ml/kg BW)	10.32 ±8.53a	16.98 ±1.68a	0.69 ±0.52a	3.86 ±0.46bc	0.86 ±0.٠6c	0.21 ±0.05c
Group 4: Control (+ve) + BC (10 ml/kg BW)	11.57 ±4.56b	17.45 ±1.59a	0.70 ±0.22b	3.02 ±0.50b	0.88 ±0.05c	0.13 ±0.02b

* Values with different letters by the same column means significant different at $p \leq 0.05$.

Plasma glucose levels (mg/dl) in control and diabetic rats groups treated with BC

Data in Table (3) were shown the Initial and final plasma glucose levels (mg/dl) in control and diabetic rats groups treated with BC. From such data it could be noticed that treatment of animals with alloxan caused a significant increased ($p \leq 0.05$) in serum glucose concentration by

the ratio 23.03% compared to normal controls. Supplementation of the rat diets with BC decreased this value by the rate of -30.80 and -20.4% for 5 and 10 ml/kg BW of BC, respectively. Such data are inaccordance with that observed by Kuipers *et al*. (2002) who reported that BC has been shown to balance blood sugar levels this is due to a growth factor known as IGF-1 (insulin like growth factor). It 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 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 (3): Initial and final plasma glucose levels (mg/dl) in control and diabetic rats groups treated with BC (means ± SD)

Groups	Initial plasma glucose level (mg/dl)	Final plasma glucose level (mg/dl)	Plasma glucose level gain (mg/dl)	Plasma glucose level gain (%)
Group 1: Control (-ve)	94.80 ±3.96a	98.40 ±8.41a	3.60 ±4.82c	3.8 ±4.80c
Group 2: Control (+ve)	317.20 ±86.50b	391.00 ±71.62c	73.80 ±59.48d	23.03 ±28.16d
Group 3: Control (+ve) + BC (5 ml/kg BW)	310.00 ±122.52b	214.40 ±74.86b	-95.60 ±51.66a	-30.80 ±5.84a
Group 4: Control (+ve) + BC (10 ml/kg BW)	310.60 ±72.41b	247.20 ±72.44b	-63.40 ±52.71ab	-20.4 ±14.19ab

* Values with different letters by the same column means significant different at $p \leq 0.05$.

Effect of BC on cholesterol, triglyceride, HDL, LDL and VLDL of control and diabetic rats groups treated with BC

Data in Table (4) were shown the TG, TC, LDL-c and VLDL-c levels (mg/dl) in control and diabetic rats groups treated with BC. From such data it could be noticed that treatment of animals with alloxan

Table (4): Effect of BC on cholesterol, triglyceride, HDL, LDL and VLDL of control and diabetic rats groups treated with BC (means ± SD)

Groups	TG (mg/dl)	TC (mg/dl)	LDL-c (mg/dl)	HDL-c (mg/dl)	VLDL-c (mg/dl)
Group 1: Control (-ve)	83.40 ±12.03 c	79.60 ±7.70 c	22.12 ±5.08 d	40.80 ±8.25a	16.68 ±2.40 d
Group 2: Control (+ve)	117.80 ±19.94 a	121.00 ±25.20 a	73.24 ±22.44 a	24.20 ±3.63d	23.56 ±5.04 a
Group 3: Control (+ve) + BC (5 ml/kg BW)	90.00 ±16.79 b	99.20 ±15.41b	47.20 ±15.46 b	34.00 ±7.10 b	18.00 ±3.35 b
Group 4: Control (+ve) + BC (10 ml/kg BW)	92.40 ±11.63b	98.00 ±12.04b	47.32 ±10.58 b	32.20 ±5.49 bc	18.48 ±2.32 b

* Values with different letters by the same column means significant different at $p \leq 0.05$.

caused a significant increased ($p \leq 0.05$) in TG, TC, LDL-c and VLDL-c serum concentration by the ratio 41.25, 52.01, 231.25 and 41.25% compared to normal controls. Supplementation of the rat diets with BC decreased these values by significant different rates. The opposite direction was recorded for the HDL-c. Such data are in accordance with that observed by Johar, (2002) and Josepha (2010) who reported that the hyperglycemia caused a significant increases in total lipids, cholesterols, 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 TG enriched VLDL-c from the circulation. Also, Hany, (2011) reported that BC can efficiently decrease TG and total cholesterol level in Type 2 diabetic patients. A significant ($p \leq 0.05$) decrease in cholesterol concentration was also shown a recent report on rats that received 10% BC. 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). Furthermore, Ragab, (2002) Yassin *et al*. (2004) and Hany, (2011) 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.

In this context, coronary heart disease (CHD) is a major health problem in both industrial and developing countries including Egypt. Many studies have now shown that blood elevated concentrations of total or low density lipoprotein (LDL) cholesterol in the blood are powerful risk factors for CHD, whereas high concentrations of high density lipoprotein (HDL) cholesterol or a low LDL (or total) to HDL (reviewed in Bedawy, 2008). The composition of the human diet plays an important role in the management of lipid and lipoprotein concentrations in the blood. Reduction in saturated fat and cholesterol intake has traditionally been the first goal of dietary therapy in lowering the risk for cardiovascular disease. In recent years, however, the possible hypocholesrerolemic effects of several dietary components, such as found in BC (Jun *et al.*, 2009).

Total protein, albumin, globulin, urea and creatinine of control and diabetic rats groups treated with BC

Data in Table (5) were shown the total protein, albumin, globulin, urea and creatinine of control and diabetic rats groups treated with BC. From such data it could be noticed that treatment of animals with alloxan caused a significant decreased ($p \leq 0.05$) in total protein, albumin, globulin serum concentration by the ratio -31.56, -36.06 and 58.67% compared to normal controls, respectively. Supplementation of the rat diets with BC decreased these values by significant different rates. The opposite direction was recorded for the kidney function parameters (urea and creatinine) Such data are in accordance with that reviewed by Thapa (2005).

In general, albumin is an important metal binding protein. It is a sacrificial antioxidant that can bind copper tightly and iron weakly to its surface serving as a target for their related free radical reactions. Thus it inhibits copper ion dependent lipid peroxidation (Gutteridge and Wilkins, 1983). It was reported that hypo-albuminaemia is most frequent in the presence of advanced chronic liver diseases. Hence decline in total

protein and albumin can be deemed as a useful index of the severity of cellular dysfunction in chronic liver diseases. So, it is worthy to report that feeding with BC produced significant improvement in serum albumin compared to diabetic group. Such enhancement in serum proteins including albumin and globulin occurred in treated grope could be attributed to the high level and activity of the immunological components found in the BC (Thapa, 2005).

Table (5): Total protein, albumin, globulin, urea and creatinine of control and diabetic rats groups treated with BC (means ± SD)

Groups	Total protein (g/dl)	Albumin (mg/dl)	Globulin (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)
Group 1: Control (-ve)	7.16 ±0.70 c	4.16 ±0.49 b	3.00 ±0.40 b	26.80 ±2.58 b	0.86 ±0.17b
Group 2: Control (+ve)	4.90 ±0.57 a	2.66 ±0.46 a	1.24 ±0.18 a	36.40 ±8.90a	1.15 ±0.48a
Group 3: Control (+ve) + BC (5 ml/kg BW)	6.90 ±1.00 b c	3.86 ±0.59 ab	2.6 ±0.68 b	29.60 ±5.52b	0.98 ±0.13ab
Group 4: Control (+ve) + BC (10 ml/kg BW)	6.14 ±0.69 bc	4.02 ±0.68 b	2.9 ±0.19 b	28.00 ±5.52b	0.90 ±0.26ab

* Values with different letters by the same column means significant different at $p \leq 0.05$.

Urea is formed in the liver as the end product of protein metabolism. During ingestion, protein is broke down into amino acids. In the liver, these amino acids are catbolized and free ammonia is formed. The ammonia is combined to form urea (Pagana and pagana, 1997). Urea, the major product of protein catabolism measuring urea is the most popular laboratory procedure for assessing renal function (Bennett *et al*., 1995 and Pagana and pagana, 1997). Creatinine is a catabolic product of creatine phosphate, which is used in skeletal muscle concentration (Pagana and pagana, 1997). In the skeletal muscle serum creatinine levels are elevated by renal disease and dehydration. The decreasing in serum uric acid and creatinine as the result of feeding BC could be attributed to their higher content of many bioactive compounds which exhibited immunological and antioxidant activities (Thapa, 2005).

Oxidative stress and antioxidant defense systems parameters of control and diabetic rats groups treated with BC

Data in Table (6) were shown the oxidative stress (MDA) and antioxidant defense systems (GSH and SOD) parameters of control and diabetic rats groups treated with BC. From such data it could be noticed that treatment of animals with alloxan caused a significant increased ($p \leq 0.05$) in serum MDA concentration by the ratio of 70.52% compared to normal controls, respectively. Supplementation of the rat diets with BC by the ratios 5 and 10 ml/kg BW decreased these values by significant ($p \leq 0.05$) rates, 24.33 and 28.33% , respectively. The opposite direction was recorded for the antioxidant defense systems parameters (GSH and SOD). Such data are in accordance with that reviewed by Thapa (2005) Jun et al., (2009).

Table (6): Oxidative stress and antioxidant defense systems parameters of control and diabetic rats groups treated with BC (means ± SD)

Groups	Malondialdehyde MDA (U/mL)	Glutathione GSH (U/mL)	Superoxide dismutase SOD (mg/L)
Group 1: Control (-ve)	11.26±1.4 c	9.27±0.6 c	0.54±0.12 b
Group 2: Control (+ve)	19.2±0.8 a	4.22±1.54 a	0.26±0.09 a
Group 3: Control (+ve) + BC (5 ml/kg BW)	14.0±1.2b	6.25±0.03 b	0.67±0.05c
Group 4: Control (+ve) + BC (10 ml/kg BW)	14.45±2.5 b	5.66±0.79 b	0.65±0.17c

* Values with different letters by the same column means significant different at $p \leq 0.05$.

Oxidative stress occurs when the generation of free radicals and active intermediates in a system exceeds the system's ability to neutralize and eliminate them (Sies, 1985). Diabetes results in the production of ROS that in turn cause mutations to the DNA which if not repaired helps in promotion of carcinogenesis (Samarth *et al.,* 2006). ROS initiates lipid peroxidation (LPO) i.e. formation of MDA directly by reacting with the lipids of membranes or by acting as second messengers for the primary free radicals (Rajendran *et al.*, 2008). In the present study, we observed a significant rise in the LPO levels as well as ROS levels upon diabetes. Several reports have documented the potent antioxidant capacity of BC

where by mitigation of lipid peroxidation and oxidative stress in several tissues were demonstrated (Thapa, 2005 and Jun *et al.,* 2009).

GSH is an important biological antioxidant. It is normally play the role of an intracellular radical scavenger and is the substrate of many xenobiotic elimination reactions. A marked decreased level of GSH is reported in the plasma of diabetic patients (Elmaadawy, *2016).* GSH systems may have the ability to manage oxidative stress with adaptational changes in enzymes regulating GSH metabolism i.e link between hyperglycemia and GSH depletion. It could be interpreted by Lee *et al.,* (1995) who reported that, in hyperglycemia conditions, glucose is preferentially used in polyol pathway that consumes NADPH necessary for GSH regeneration by the GSH-reductase enzyme. Hyperglycemia is therefore indirectly the cause of GSH depletion. In the present study, it was reported that feeding the diabetics rats with beef meatballs supplemented with BC removed some of the metabolic disorders induced by T2DM in liver cells through increasing the GSH synthesis.

To cope with the oxidative stress elicited by aerobic metabolism, animal and human cells have developed a ubiquitous antioxidant enzymatic defense system, which consists of glutathione peroxidase (GSH-Px), glutathione reductase (GSH-Rd), catalase (CAT) and superoxide dismutase (SOD) together etc. SODs are responsible for the reduction of $O_2^{\cdot-}$ to H_2O_2 and multiple enzymes will remove H_2O_2 including GSH-Px and CAT. Also, the GSH reduces the selenium and the reduced form of the enzyme then react with hydrogen peroxide (Harmon, 1986).

Conclusion

Diabetes mellitus is widely distributed all over the world including Kuwait. Oxidative stress, lipid toxicity and low- grade inflammation as major causes on diabetic complications. Several strategies to improve diabetic complications have been proposed, because early treatment and prevention play a pivotal role in reducing the population burden of diabetes. The present study demonstrated that BC has several properties for lowering the levels blood glucose, improve liver and kidney functions and antioxidant defense systems and enhance the blood lipid profile in rats with Type 2 diabetes. It is notable that BC may have therapeutic potentials as an anti–Type 2 diabetes agent.

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التاثيرات المحتملة للبأ البقرى على بعض التغيرات الحيوية لفئران التجارب المصابة بمرض السكرى المستحث بالالوكسان

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لقد أثبتت العديد من الدراسات أن اللبأ البقري قد إستخدم على نطاق واسع فى تعزيز وظائف المناعة وأنظمة الدفاع المضادة للأكسدة، والحد من الإجهاد التأكسدي وتراكم الدهون، وتسهيل حركة الجلوكوز إلى العضلات.. ومع ذلك، فإنه لم تبذل سوى محاولات قليلة جدا لدراسة آثاره المضادة للسكري في حيوانات التجارب. لذلك، تهدف الدراسة الحالية إلى تقييم ما إذا كان اللبأ البقرى يقلل من نسبة السكر في الدم والإجهاد التأكسدي، فضلا عن تحسين المقاييس الخاصة بصورة دهون الدم فى الفئران المصابة بالسكري المستحث بالألوكسان . ولقد أدت معاملة حيوانات التجارب بالألوكسان الى حدوث زيادة معنوية ($p\leq0.05$) في تركيز الجلوكوز في الدم بنسبة ٨٥.٥٩٪ مقارنة بالمجموعة الضابطة الطبيعية .كما أدى تدعيم وجبات الفئران باللبأ البقرى بمقدار ٥ ، ١٠ مل / كجم من وزن الجسم الى حدوث إنخفاض فى هذه القيمة بنسب ٣٠.٨٠ و ٢٠.٤٠٪ على التوالي . كما تم تسجيل نفس السلوك لبعض المقاييس المتعلقة بصورة دهون الدم والتى تشمل الدهون الثلاثية، الكوليسترول الكلي، الليبوبروتينات منخفضة الكثافة، الليبوبروتينات منخفضة الكثافة جدا والمالونالدالدهيد وكذلك المؤشرات الحيوية للإجهاد التأكسدي وإلتهاب الكبد (المالونالدهيد). أيضا أدت التغذية على اللبأ الى حدوث تحسن في وظائف الكبد (الألبومين والجلوبيولين) والكلى (اليوريا والكرياتينين) وأنظمة الدفاع المضادة للأكسدة (الجلوتاثيون والسوبرأكسيد ديسميوتيز) في الفئران المصابة بالسكري مقارنة بمجموعة الفئران الضابطة .ويمكن أن تعزى جميع هذه الآثار إلى الأنشطة المناعية والمضادة للأكسدة القوية من قبل اللبأ نتيجة لمحتوه العالى من المركبات النشطة بيولوجيا لذلك توفر هذه النتائج أساسا لاستخدام اللبأ في الوقاية والعلاج المبكر للمضاعفات الخاصة بمرض السكرى من النوع الثانى T2DM والتي تشمل ارتفاع مستويات الجلوكوز في الدم والإجهاد التأكسدي، والخلل في فى صورة دهون الدم ووظائف الكبد والكلى، وأنظمة الدفاع المضادة للأكسدة.

الكلمات المفتاحية: السكرى، جلوكوز الدم، وظائف الكلى، الاإجهاد التأكسدى، صورة دهون الدم، أنظمة الدفاع المضادة للأكسدة.