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Full Length Research Paper

Preventive effect of ordinary and hyperimmune bovine colostrums on mice diabetes induced by alloxan

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In the present study, the anti-diabetic effect of ordinary and hyperimmune bovine colostrum were evaluated in diabetic mice induced by alloxan. The results indicated that blood glucose levels were significantly decreased after administration of colostrum for 30 d, and the glucose tolerance was strengthened in a dose-dependent manner. In addition, the hyperimmune colostrum was more efficient than ordinary colostrum in decreasing the blood glucose level and improving glucose tolerance in diabetic mice (P<0.05). Furthermore, total levels of serum cholesterol (TC) and triglycerides (TG) were significantly decreased, and serum high density lipoprotein cholesterol (HDL-c) was significantly increased in a dose-dependent manner compared with the control; the hyperimmune colostrum was also more efficient than ordinary colostrum in reducing the serum levels of TC and TG, and increasing the serum levels of HDL-c in diabetic mice (P<0.05). These results suggest that bovine colostrum could modify the diabetic phenotype of mice induced by alloxan.

Key words: Colostrum, diabetic mice, blood glucose, blood lipids.

INTRODUCTION

Diabetes mellitus is a chronic disease that is often undiagnosed or inadequately treated. Nowadays, the prevalence of diabetes is growing at an alarming rate. Currently there are over 150 million people with the disease worldwide and the number is likely to increase to 300 million or more by the year 2025 due to the increase in sedentary lifestyles, consumption of energy rich diets, and obesity (King et al., 1998). Diabetes mellitus is classified into two types, insulin dependent (Type 1) and non-insulin dependent (Type 2). The two types of diabetes have distinct pathogenesis but hyperglycemia and various life-threatening complications resulting from long-term hyperglycemia are the most common features (Abraira et al., 1995; Ohkubo et al., 1995).

In diabetes mellitus, uncontrolled elevated blood glucose is often associated with lipid and lipoprotein disorders that predispose susceptible individuals to cardiovascular problems such as atherosclerosis (Durrington, 1993; Ross and Harker, 1976). Previous studies have shown that the risk of developing atherosclerosis and hence coronary heart disease is high in individuals with elevated serum cholesterol and low levels of serum high density lipoprotein cholesterol (Castelli et al., 1986). Sustained reductions in hyperglycemia will decrease the risk of developing microvascular complications, and most likely reduce the risk of macrovascular complications (Gaster and Hirsch, 1998). Therefore, effective control of the blood glucose levels is a key step in preventing or reversing diabetic complications in diabetic patients (Diabetes Control and Complications Trial Research Group, 1993). However, due to the limited efficacy and adverse side effects of currently available therapies, it is difficult to maintain good glycemic control in most diabetic patients (Prout, 1974; Grover and Vats, 2001; Kameswara et al., 1997; De-Fronzo, 1999). Therefore, there is a strong incentive to develop new hypoglycemic agents, especially those derived from natural sources, such as plant and animal products, because these sources are usually considered to be less toxic with fewer side-effects than synthetic ones.

Colostrum is the initial 3~4 days of milk produced by mammals after giving birth. It is not only a good source of nutrients such as protein, carbohydrate, fat, vitamins and

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minerals, but also many biologically active constituents included, which play important roles in the protection and development of newborns. These constituents include immunoglobulins, antimicrobial proteins, growth factors, antiinflammatory, antioxidant and immune enhancing components. They may act by stimulating the immune system, or by providing passive protection (Kulkarni and Pimpale, 1989; Playford, 2001). Immunization of cows with pathogens as antigens could raise the concentration of specific antibodies in colostrum by stimulating immune response in vivo of B lymphocytes, thereby resulting in a relative increase in succession. Interest in using hyperimmune colostrum as an immunotherapy agent is increasing.

Administration of bovine colostrum has been shown to affect some biochemical and physiological functions; control some fundamental life processes, such as cell division, cell differentiation or apoptosis; stimulate the growth and development of the gastrointestinal tract of new-born animals and boost immune function (Kurokowa et al., 1987; Xu, 1996; Uruakpa et al., 2002). However, the function of bovine colostrum has not been thoroughly examined. Herein, we have used a diabetic mice model induced by alloxan to study the hypoglycaemic effects of bovine ordinary and hyperimmune colostrum.

MATERIALS AND METHODS

Vaccine preparation

The vaccine was prepared using three different species of pathogenic bacteria including four strains of enterotoxigenic *Escherichia coli*, five strains of enteropathogenic *E. coli*, three strains of enteroinvasive *E. coli*, two strains of Salmonella typhi, three strains of Shigella dysenteriae, Shigella sonnei and Shigella flexneri originnating from human intestinal tract (National Institute for the Control of Pharmaceutical and Biological Products, Beijing 100050, PR China). After growing separately in Bacto Synthetic Broth (BSB) for 24 h at 37^{o}C, the bacteria were killed by 4.0% formaldehyde for 24 h. The killed bacteria were harvested by centrifugation at 4500 rpm for 15 min and washed three times with 0.9% NaCl solution, then suspended in saline and mixed with each other in a ratio of 1:1. After the absence of viable cells was conformed by planting aliquots of the suspension on BSB agar plate which was incubated for 3 days at 37oC, they were emulsificated using a 2.0% aluminum stearate solution as the adjuvant to produce a multivalent vaccine consisting of whole cells of 17 strains of pathogenic diarrhea bacteria (1×109 cfu/ml for each bacteria cells).

Preparation of bovine hyperimmune and ordinary colostrum powder

Pregnant Holstein cows were injected intramuscularly to both sides of the necks with 10 ml (2×5 ml) of vaccine. Immunization was started at the onset of drying off, about 2 months before the predicted day of parturition. Three booster injections (2×5 ml) were given in 2-week intervals starting 2 weeks after the initial injection. The cows were healthy and did not receive any antibiotics during the immunization procedure. Colostrum of the first milking on the first day was collected from cows at parturition, cooled to 4^{o}C, and fat was removed via centrifugation at 5,000 rpm for 15 min at 4^{o}C. The skim colostrum was lyophilized, stored at 4^{o}C and used as the skim hyperimmune colostrum powder sample. The ordinary colostrum from non- hyperimmune cows was similarly pooled and treated.

Preparation of alloxan-induced diabetic animal model

All experiments were performed on male Kunming mice (4 weeks old, 18~22 g) purchased from Qinglongshan Animal Resources Centre (Nanjing, PR China) and left to acclimatize for one week before the experimental period. The animals were housed under a daily cycle of 12 h light and 12 h darkness room with temperature 22±2^{o}C and relative humidity 75±10% throughout the experimental period, with free access to commercial pellet food purchased from Nanjing Qinglongshan Animal Resources Centre (PR China) and water. Animals were randomly divided into two groups (control and diabetic induced). Diabetes was induced by an intraperitioneal injection of 200 mg/kg•bw of alloxan monohydrate (0.90% NaCl) after overnight fasting. The control group received only 0.90% (w/w) NaCl in the same way. One week later, the fasting blood glucose levels of the mice were measured by three consecutive determinations after fasting for 6 h; the mice with blood glucose level of above 11.10 mmol/L were taken as successful diabetic model of hyperglycemia and used for the experiments.

Colostrum on diabetic mice blood glucose and serum lipids levels

The mice were divided randomly into six groups of 10. Group 1 consisted of normal mice that received ordinary skim milk powder at the dose of 133.40 mg/kg•bw (bw, body weight) and served as a normal control mice, group 2 consisted of diabetes mice that received ordinary skim milk powder at the dose of 133.40 mg/kg•bw and served as diabetic control mice, group 3 and 4 consisted of diabetes mice that received ordinary skim colostrum powder at the dose of 133.40 and 266.80 mg/kg•bw, respectively, group 5 and 6 consisted of diabetes mice that received hyperimmune skim colostrum powder at the dose of 133.40 and 266.80 mg/kg•bw, respectively. The skim milk powder and colostrum powder were dissolved in sterilized water and given by gastric intubation once a day throughout the experimental period of 30 d. During the experimental period, body weight was measured every 10 days. On the day 0 and 30 after fasting for 6 h, blood samples were taken by capillary glass tubes from the eye venous pool of mice after light anesthetized with ether, and the serum was separated for the measurement of fasting blood glucose, triglyceride (TG), total cholesterol (TC) and high density lipoprotein cholesterol (HDL-c) levels. Levels of serum glucose, triglyceride, total cholesterol and high density lipoprotein cholesterol were determined by the oxidase method with commercially available kits (Sigma Co., Shanghai) according to Trinder (Trinder, 1969).

Colostrum on diabetic mice glucose tolerance

For the test of colostrum on diabetic mice glucose tolerance, mice of group 2~6 were given glucose with a dose of 2.50 g/kg•bw by gastric intubation on day 30 of experiment after 6 h fasting. Blood glucose levels were determined from the tail vein at 0, 0.5, 1.0, and 2.0 h after the glucose administration, and the changes in plasma glucose were also determined as the area under the curve (AUC) by the method of AUC = 0.25 × (blood glucose value at 0 h + 4 × blood glucose value at 0.5 h + 3 × blood glucose value at 2 h) (Zheng et al., 2006).

Statistical analysis

Results were presented as mean ± standard error of mean for all

Table 1. Body weight gain of mice after 30 d administration.

Dosage mg/Kg·b w	Initial weight (g)	Final weight (g)	Gain of body weight (g)
133.40 (group 1)	18.43±2.3	27.16±2.2	8.73
133.40 (group 2)	18.38±2.4	18.72±2.31	0.34 *
133.40 (group 3)	18.60±2.0	19.25±2.3	0.65 *
266.80 (group 4)	18.32±2.6	21.37±2.6	3.05 *,†
133.40 (group 5)	18.18±2.4	19.87±2.5	1.69 *,†,Δ
266.80 (group 6)	17.95±2.1	22.09±1.9	4.14 *,†,Δ

Dietary treatments: Group 1 consisted of normal mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw (bw, body weight) and served as a normal control mice, group 2 consisted of diabetes mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw and served as diabetic control mice, group 3 and 4 consisted of diabetes mice that received ordinary skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively, group 5 and 6 consisted of diabetes mice that received hyperimmune skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively. Data are mean ± SD of measurements from 10 mice. Significant and greatest differences denote $p<0.05$ and $p<0.01$. $^{*}p<0.01$ compared to normal mice control (group 1); $^{\dagger}p<0.05$ compared to diabetic control mice (group 2); $^{\Delta}p<0.05$ compared to ordinary bovine colostrum group (group 3 or 4).

groups. Student t-test was used for test of significance between two groups.

RESULTS

Effects of bovine colostrum on body weights of diabetic mice

Results of body weight gain after bovine colostrum administration for 30 d in Kunming mice are shown in Table 1. The body weight gain of diabetic mice (groups 2~6) was significantly lower than that of normal control mice (group 1, p<0.01). Weight gain in the 266.80 mg/kg•bw dose of bovine colostrum groups (groups 4 and 6) was greater than those in the 133.40 mg/kg•bw dose of bovine colostrum groups (groups 3 and 5) and in the diabetic control group (group 2). In the 133.40 mg/kg•bw dose of hyperimmune bovine colostrum group was obviously greater than those in 133.40 mg/kg•bw dose of ordinary bovine colostrum and diabetic control groups. At the 266.80 mg/kg•bw dose in the hyperimmune bovine colostrum group's weight gain was greater than that in the ordinary bovine colostrum group, and there was a little but no significant difference in weight gain between the 133.40 mg/kg•bw dose of ordinary bovine colostrum group and the diabetic control group.

The above results suggest that diabetes could inhibit body weight gain in mice and bovine colostrum could significant improve body weight gain in diabetic mice in a dose-dependent manner, and that hyperimmune bovine colostrum was more efficient than ordinary bovine colostrum in increasing the body weight gain of diabetic mice. compared with control group (group 2), and the AUC was18.36 and 22.73% in group 3, 4, 5 and 6 respectively,

Effects of bovine colostrum on blood glucose levels

Results of serum glucose levels after bovine colostrum administration for 30 d in Kunming mice are shown in Table 2. Diabetic control mice (group 2) demonstrated 3 fold increase in blood glucose concentrations over normal control mice (group 1) throughout the experimental period. However, following 30 days of bovine colostrum treatment, elevated blood glucose levels in diabetic mice were significantly reduced (p<0.05 or 0.01). The serum glucose levels of diabetic mice were significantly lower in the hyperimmune colostrum group than that in ordinary colostrum group at dose of 133.4 or 266.8 mg/kg•bw, and lower in the higher dose of bovine colostrum (group 4 or 6) than in low dose of bovine colostrum (group 3 or 5). This implies bovine colostrum could decrease the serum glucose levels of diabetic mice in a dose-dependent manner and hyperimmune colostrum is more efficient than ordinary colostrum in decreasing the serum glucose levels of diabetic mice.

Effects of bovine colostrum on blood glucose tolerance

In order to investigate the effects of administration of bovine colostrum after 30 days on glucose tolerance in diabetic mice, the fasting blood glucose levels of diabetic mice were measured after a dose of 2.50 g/kg•bw glucose loading. As presented in Table 3, serum glucose in diabetic mice exhibited significantly higher level during all time points measured. The maximum rise in blood glucose occurred 0.5 h after the glucose loading. Colostrums significantly suppressed the rise in blood glucose at 0.5, 1.0 and 2.0 h (p<0.05) compared to the control (group 2). The area under the curve (AUC) of blood glucose decreased by approximately 7.52, 13.39, significant lower of group 4, 5 and 6 than 2, group 5 than 3, group 6 than 4, group 4 and 6 than 3 and 5. It indicated that bovine colostrum could obviously strengthen the glucose tolerance of diabetic mice induced by alloxan in a dose-dependent manner, and hyperimmune bovine colo-

Table 2. Serum glucose level of mice after 30 d administration.

Dosage (mg/kg·bw)	0 d Glucose (mmol/L)	30 d Glucose (mmol/L)
133.40 (group 1)	4.92±0.54	5.38±0.27
133.40 (group 2)	15.72±1.02	16.07±0.53
133.40 (group 3)	16.09±0.54	14.70±0.49*
266.80 (group 4)	16.21±0.89	12.40±0.84†
133.40 (group 5)	15.86±0.75	12.28±0.70$^{*,\Delta}$
266.80 (group 6)	16.14±0.68	10.08±0.55$^{\dagger,\Diamond}$

Dietary treatments: Group 1 consisted of normal mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw (bw, body weight) and served as a normal control mice, group 2 consisted of diabetes mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw and served as diabetic control mice, group 3 and 4 consisted of diabetes mice that received ordinary skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively, group 5 and 6 consisted of diabetes mice that received hyperimmune skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively. Data are mean ± SD of measurements from 10 mice. Significant and greatest differences (analysis of variance) denote $p<0.05$ and $p<0.01$. $^{*}p<0.05$ compared to positive control (group 2); † $p<0.01$ compared to positive control (group 2); $^{\Delta}$ $p<0.05$ compared to low dose ordinary colostrum (group 3);$^{\Diamond}$ $p<0.05$ compared to high dose ordinary colostrum (group 4).

Table 3. Glucose levels of diabetic mice after a dose of 2.50g/kg·bw glucose load.

Treatment	Levels of serum glucose m mol/L				AUC
	0 h	0.5 h	1 h	2 h	
Group 2	16.21 ± 1.27	29.78 ± 1.22	28.75 ± 1.15	23.88±1.26	51.74
Group 3	14.36 ± 1.46	27.86 ± 1.07	25.63±1.16	21.87±1.27	47.85*
Group 4	12.51 ± 1.38	26.09 ± 1.26*	23.94±1.12*	20.79±1.18*	44.81$^{*,\Delta}$
Group 5	12.23 ± 1.15	24.98 ± 1.05*	23.59±1.20*	18.93±1.11*	42.24*,†
Group 6	10.10 ± 1.09	23.70 ± 1.13*	21.45±1.03*	18.34±1.12*	39.98$^{*,\dagger,\Delta}$

Treatments: Group 2 consisted of diabetes mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw and served as diabetic control mice, group 3 and 4 consisted of diabetes mice that received ordinary skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively, group 5 and 6 consisted of diabetes mice that received hyperimmune skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively. The area under the curve (AUC) by the method of AUC=0.25 × (Blood glucose value at 0 h + 4 × Blood glucose value at 0.5 hour + 3×Blood glucose value at 2 h). Data are mean ± SD of measurements from 10 mice. Significant and greatest differences denote $p<0.05$ and $p<0.01$. $^{*}p<0.05$ compared to control (group 2); $^{\dagger}p<0.05$ compared to normal colostrum (group 3, 4); $^{\Delta}p<0.05$ compared to low dose colostrum (group 3, 6).

trum is more efficient than ordinary bovine colostrum in improving the diabetic mice glucose tolerance.

Effects of bovine colostrum on serum lipid concentrations

Results of serum lipids concentrations after 30 days bovine colostrum administration in Kunming mice are presented in Table 4. There were significant differences in most of the lipid profiles between the diabetic mice and normal control mice (group 1), and a significant decrease in triglyceride (TG) and total cholesterol (TC) levels and increase in HDL-cholesterol level in colostrum treated mice compared to the control diabetic mice (group 2) . The triglyceride (TG) and total cholesterol (TC) levels of diabetic mice treated by 266.80 mg/kg•bw dose of colostrum (groups 4 and 6) were obviously lower than those treated by 133.40 mg/kg•bw dose of colostrum (groups 3 and 5); those treated by hyperimmune colostrum (groups 5 or 6) were obviously lower than those treated by ordinary colostrum (group 3 or 4) in the same dose, and normal control mice (group 1) were obviously lower than those in control diabetic mice (group 2), respectively. Whereas the total concentration of serum high-density lipoprotein cholesterol (HDL-c) in high dose colostrum (groups 4 and 6) was obviously higher than those in the low dose colostrum (group 3 and 5), hyper-immune colostrum groups (group 5 or 6) were obviously higher than those of same dose ordinary colostrum (group 3 or 4), and normal control mice (group 1) were obviously higher than those in diabetic control mice (group 2), respectively

The above results suggest that diabetes could induce hyperlipidemia and bovine colostrum could obviously decrease the serum TC and TG levels and increase se-

Table 4. Serum lipids levels of mice after 30 d administration.

Dosage (mg/kg·bw)	TC (mmol\L)	TG (mmol\L)	HDL-c (mmol\L)
133.40 (group 1)	2.56±0.56	1.57±0.15	1.54±0.21
133.40 (group 2)	3.51±0.09$^{\blacklozenge}$	3.24±0.74$^{\blacklozenge}$	0.91±0.14$^{\blacklozenge}$
133.40 (group 3)	3.38±0.36*	1.94±0.48†	1.41±0.37†
266.80 (group 4)	3.06±0.60$^{\dagger,\blacktriangle}$	1.66±0.29$^{\dagger,\blacktriangle}$	1.79±0.51$^{\dagger,\blacktriangle}$
133.40 (group 5)	3.23±0.43$^{\dagger,\Delta}$	1.76±0.50$^{\dagger,\Delta}$	1.58±0.41$^{\dagger,\Delta}$
266.80 (group 6)	2.84±0.41$^{\dagger,\Diamond,\blacktriangle}$	1.56±0.23$^{\dagger,\Diamond,\blacktriangle}$	2.06±0.25$^{\dagger,\Diamond,\blacktriangle}$

Treatments: Group 1 consisted of normal mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw (bw, body weight) and served as a normal control mice, group 2 consisted of diabetes mice that received ordinary skim milk powder at the dose of 133.40 mg/kg·bw and served as diabetic control mice, group 3 and 4 consisted of diabetes mice that received ordinary skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively, group 5 and 6 consisted of diabetes mice that received hyperimmune skim colostrum powder at the dose of 133.40 and 266.80 mg/kg·bw, respectively. Data are mean ± SD of measurements from 10 mice. Significant and greatest differences denote $p<0.05$ and $p<0.01$. $^{*}p<0.05$ compared to diabetic control (group 2); $^{\dagger}p<0.01$ compared to diabetic control (group 2); $^{\Delta}p<0.05$ compared to low dose normal colostrum (group 3) ; $^{\Diamond}p<0.05$ compared to high dose normal colostrum (group 4); $^{\blacktriangle}p<0.05$ compared to low dose colostrum (group 3, 5); $^{\blacklozenge}p<0.01$ compared to normal control (group 1).

rum HDL-c levels in diabetic mice. High doses of colostrum was more efficient than low dose of colostrum, and hyperimmune colostrum was more efficient than ordinary colostrum in reducing the serum TC, TG, and increasing serum HDL-c levels in diabetic mice.

DISCUSSION

Alloxan is widely used to induce diabetes in experimental animals, causing the selective destruction of insulin-secreting β cells of the islets of Langerhans, to which other cells (α, γ, δ) are resistant. The destruction of the insulin-secreting β cells is brought about by a redox cycle with the formation of superoxide radicals established by alloxan and the production of its reduction, dialuric acid. Superoxide radicals undergo dismutation to hydrogen peroxide, which produces the reactive hydroxyl radicals by the Fenton reaction. The action of reactive oxygen species with a simultaneous massive increase in cytosolic calcium concentration causes rapid destruction of β cells (Szkudelski, 2001). This is accompanied by typical and permanent hypoinsulinemia and hyperglycemia (Lenzen and Panten, 1988). As shown in Tables 2 and 4, diabetic control mice (group 2) induced by alloxan demonstrated significant increases in serum glucose, cholesterol and triglycerides, and decreases in serum high density lipoprotein cholesterol concentrations over normal control mice (group 1) values throughout the whole experimental period.

This study has demonstrated that the inclusion of ordinary and hyperimmune colostrum had a marked effect on the levels of serum glucose and serum lipids in diabetic mice induced by alloxan, and modified the diabetic phenotype. One possible mechanism for hypoglycaemic effect of bovine colostrum could be originated from the insulin-like growth factors and conjugated isomers of linoleic acid (CLA). Bovine colostrum is characterised by higher concentrations of insulin-like growth factor (IGF-1 and truncated IGF-1) and unsaturated fatty acids (such as oleic and CLA) compared with normal milk (Francis et al., 1988; Pakkanen and Aalto, 1997; Pierre et al., 2006; Banni et al., 1996). IGF-1, especially truncated IGF-1, has an obvious insulin function; they may interact with and activate the insulin receptor directly, enhance pronounce insulin function, act to increase insulin sensitivity, and improve glucose metabolism (Dozio et al., 1995; Sullivan and MacDonald, 1995; Zenobi et al., 1992; Rossetti et al., 1991). Evidence has been proved that CLA acts as an insulin sensitizing agent, normalizing glucose tolerance and lowering circulating free fatty acids, thus preventing or delaying the onset of hyperglycemia in diabetic rat model. The striking antidiabetic properties of CLA appear to be linked to CLA activation of peroxisome proliferator-activated receptors alpha (PPARα) and gamma (PPARγ) (Yoon et al., 2003; Han et al., 2006). The PPARs are members of the nuclear hormone receptor family and are distributed in a variety of tissues. PPARα ligands have shown to improve lipid profiles and increase insulin sensitivity. PPARα may indirectly improve insulin sensitivity by increasing β-oxidation of fatty acids, which reduces lipid accumulation and toxicity in muscle and liver tissues (Li and Glass, 2004; Michalik et al., 2006). PPARγ could induce the expression of genes involved with the insulin signaling cascade (Kintscher and Law, 2005). The ability of CLA to prevent the development of hyperglycemia in diabetic rats is strikingly similar to the effects of thiazolidinedione (TZD) (Houseknecht et al., 1998).

The other mechanism for bovine colostrum modifying the diabetic hyperlipidemia may be that bioactive components (such as IGF-I) modify digestion and absorption of fatty acids, by possibly altering lipase activity or fatty acids binding proteins, or that the unsaturated fatty acids

of bovine colostrum modify lipid metabolism in diabetic mice, such as non essential monounsaturated fatty acids have a beneficial effect on cholesterol metabolism and a protective role against cardiovascular diseases. Essential fatty acids could decrease triacylglycerols, total cholesterol and non-HDL-cholesterol levels. Polyunsaturated fatty acids have an important effect on the structure and physical properties of localized membrane domains. They modulate enzyme activities, carriers and membrane receptors (LDL receptors, insulin, antibodies neurotransmitters, drugs receptors), and are involved in the activetion of nuclear transcription factors (De-Lacruz et al., 2000; Gavino et al., 2000; De-Deckere et al., 1999; Spector, 1999; MacDonald, 2000; Faulconnier et al., 2004). CLA could increase adipose tissue and liver lipogenic enzyme activities and decrease plasma lipid concentrations. It has been proven that dietary CLA shares the potent of lowering lipids concentration. The mechanism by which CLA reduces plasma lipid concentrations may be via activation of hepatic PPARα. Fibrate hypolipidemic drugs such as gemfibrozil and clofibrate reduce plasma triglycerides presumably by activating PPARα in the liver, thereby increasing fatty acid oxidation. Consistent with being a peroxisome proliferator in rodent liver, CLA induced acyl-CoA oxidase expression (a marker of peroxisomal β-oxidation) in rats and is also a PPARα activator. Therefore, in addition to its effects on PPARγ related events such as adipocyte differentiation, CLA treatment may prevent diabetic symptoms in rats via a PPARα mediated effect in the liver (Houseknecht et al., 1998).

The goals of managing diabetes mellitus are to optimise the control of blood glucose and reduce the effects of normalise disturbances in lipid metabolism that could predispose patients to cardiovascular complications. This study shows that in addition to lowering blood glucose and improving glucose tolerance, bovine hyperimmune and ordinary colostrum could decrease serum TC and TG and increases HDL-c to diabetic mice. The above multiple effects provide evidence to support the use of bovine colostrum as functional food. These effects of hyperimmune colostrum and ordinary colostrum could make an efficient and economic contribution to treating diabetes if these effects could be confirmed in human volunteers. The mechanism by which hyperimmune colostrum was more efficient than ordinary colostrum in modifying the diabetic phenotype in mice needs further confirmation.

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