Colostrums Immunoglobulin Potential Effects Against Some Biochemical Changes In Diabetic Rats.

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Abstract: Diabetes mellitus is one of the most distributed public health problem which increases the ability of other diseases and risks. The present work was concerned with the investigation of colostrum immunoglobulin potential effects on some biochemical changes in diabetic rats. The results showed the impact of oral administration of colostrum in healthy and diabetic rats. Regarding to fecal characteristics reflected the improvement of gastrointestinal tract function as increase the absorption which result in decrease fecal weights in association with minimized its volume that significantly effect on the fecal density with slightly increased in pH mean value in case of consuming colostrum. Hematological measurements reflected the positive effects of consuming colostrum on RBCs, WBCs counts, hemoglobin concentration and hematocrit values; as well as erythrocytes indices; such as erythrocyte size or hemoglobin contents. The biochemical measurements showed an improvement in insulin level as well as plasma glucose level in colostrum consumed group. The decrement was reach 21.94% in diabetic rats group compared with healthy group consumed water. On the other hand there were highly significant increases in serum total proteins, albumin and globulin which affect A/G ratio in both healthy and diabetic rat groups. When diabetic rats consumed colostrum it resulted in significant reduction in lipids pattern, the decrement reached 29.53%, 6.90%, 25.09 % and 17.39% for total lipids, total cholesterol, triacylglycerol, and LDL-c, respectively in association with the increase in the percentage of HDL-c by 57.99% compared to their corresponding control group that drank water. Data showed that colostrum has positive effect on reducing the oxidative stress risk accompanied with diabetes mellitus including decreased plasma malondialdehyde level with increase in both erythrocytes SOD enzyme activity and increase in hepatic reduced glutathione level. Positive immunological responses were also observed in the levels of immunoglobulin classes IgG and IgA when healthy or diabetic rats received colostrum.

Key words: Diabetes mellitus, Immunity, Blood glucose, oxidative stress.

INTRODUCTION

Diabetes mellitus (DM) is defined simply as a metabolic disease characterized by hyperglycemia and glucosuria resulting from the inability of cells to utilize glucose and also in term of metabolic abnormalities in fat and protein metabolisms which increases the risks of oxidative stress and ketosis. These are the principal early symptoms usually related to the metabolic abnormalities and accumulation of some of its metabolic residues…..later developments involve complications with blood vessels such as retinopathy, nephrosclerosis and atherosclerosis (Wjłowicz et al., 2004 and Hamden et al., 2008 b). Colostrum is the first food naturally ingested by the newborn infants of any mammalians. This is the secretion of mammary glands during the earliest phases of lactation (true colostrum persist for about 5 days after parturition) (Boudry et al., 2008). 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; and Lin et al., 2009). It is also rich in proteins containing more significantly globulins and albumin and less casein than in mature milk and for this reason colostrum is heat coagulable (Panchuk, 2005; Navratilova et al., 2006 and Kehoe et al., 2007).

Immunoglobulin (IgA) has been identified in colostrum which appears after three hours in blood of newborn fed colostrum. Moreover the presence of interleukins as trypsin inhibitor regulate the intensity and duration of immune response, boost T-cell function, regulate lymph activity, stimulate production of immunoglobulins and elevate the immune response as anti-infectious factor (Janeway, 1999; Korhonen et al., 2000. and (Tripathi and Vashishtha, 2006). The presence of security molecule in γ globulin in colostrum aids to delay the digestive hydrolysis of colostrum bioprotein in gastrointestinal tract as passive alimentary immunization, as well as colostrum contains interleukins that regulate the duration and intensity of the immune response are responsible for cell to cell communication, boost T-cell activity and the reproduction of immunoglobulins (Rona, 1998).
Colostrum is a possible natural food which may have hypoglycemic properties and thus help in the control of diabetes mellitus (Swantson-flatt et al., 1991). Bovine 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). The probable mechanism of hypoglycemic action of bovine colostrum could be referred to delaying gastric emptying with direct interference with glucose absorption at that carried out in some antidiabetic plants (Willatgamuwa, 1998). Another explanation for plasma glucose reduction by bovine colostrum may have been ascribed to increased glucose clearance from plasma by peripheral tissues and decreased hepatic output of glucose (Kim et al., 2008). Its effect in improving the general immunity of human diabetic subjects was due to its high contents of natural antibodies and other antimicrobial fractions (Mero et al., 2002 and Solomons, 2002).

So this is a renewed interest in the present work to identify bovine colostrum as a natural food for improving the general health conditions of diabetic rats, through its pronounced potent hormone modulation effects in addition to its offering the protective effects against many of infectious diseases associated with immunity weakness that could appear in diabetes.

**MATERIALS AND METHODS**

Throughout this study a total number of 32 rats were subjected to experimentation. Rats were randomly housed individually with constant controlled environments in stainless steel cages; temperature 25°C ± 5°C, air humidity 55% ± 10% and 12/12 hr light /dark cycle were held. All rats were offered the balanced diet with drinking water for 4 days for adaptation on the environment conditions before starting the experiment. Then experimental animals were divided into two main groups, the healthy rats and the diabetic one. For diabetes induction, rats were fastened overnight and were injected intraperitonally with freshly prepared alloxan monohydrate in saline at a dose level of 100 mg/kg-body weight (Al-Zuhair et al., 1996). Injected animals were kept on the control, balanced diet plus consuming water, this followed by monitoring random blood glucose level. Monitoring random blood glucose levels were performed following enzymatic method of (Teuscher and Richterich, 1971). All diabetic rats with baseline blood sugar level about 249.05±5.42 mg/dl. Then the healthy group was classified into two subgroups (1, 2) and the diabetic group was classified into two subgroups (3, 4), the number of rats in each subgroup was 8 rats.

**Experimental design:**


The balanced diet was given for each rat while water or tested colostrum was provided ad libitum. The tested colostrum used in the present investigation was the sample of the fresh collected secretion as the earliest phases of lactation period which collected from a good quality of 20 healthy cows from three private farms in Sharqia Governorate. Colostrum was kept at -20°C in deep freezer until used and analysis. 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).

\[
\text{FER} = \frac{\text{Gain in body weight}}{\text{Food intake}}
\]

Feces were collected daily for each group in the last week of the experiment for determination of the fecal characteristics e.g. dry weight, volume, density and pH as described by (Proskey et al., 1985).

At the end of experimental period (6 weeks), and after overnight fasting rats were scarified under ether anesthesia and the blood samples were collected from hepatic portal vein in three centrifuge tubes. The first tube contain EDTA was used in separation of RBCs for the determination of the superoxide dismutase enzyme activity by (Winterbourne et al., 1975), as well as hematological parameters according to (Dacie and Lewis, 1984); the second tube (EDTA free) for separation of serum by allowing blood samples left for 15 minutes at temperature of 37°C then centrifuged at 4000 rpm for 20 minutes, then the sera were removed, and kept in plastic vials at -20°C until analysis of total protein and albumin by Weissman et al.,1950 and Dumas and Biggs 1972 respectively and its fraction as well as immunoglobulin classes (IgG and IgA) by Berne (1974), the third tube contain ethylene diaminetetraacetic acid (EDTA) for separation of plasma by centrifuging at 4000 rpm for 20 minutes to separate plasma and then kept in plastic vials at -20°C until analysis of insulin by (Judzewitsch et al., 1982).
Plasma total lipids, total cholesterol, triacylglycerol, high density lipoprotein and MDA were determined according to Folch et al., 1957.; Roeschlau et al., 1974.; Trinder, (1969), Arcol, 1989.; and Draper and Hadley (1990). Fresh plasma was used for the determination of blood glucose level by the same assay described above. After decapitation of the animals, liver, kidney and spleen 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).

\[
\text{Relative weight of organs} = \frac{\text{Weight of organ}}{\text{Final body weight}} \times 100
\]

Liver was then stored frozen at –20°C until used for the determination of hepatic reduced glutathione according to Beutler et al., (1982).

**Statistical Analysis:**

The results were expressed as means ± 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**

The biological study data in general confirmed the impact of oral administration of colostrum for both healthy and diabetic subjects. The current results revealed that the replacement of water by colostrum led to significant decrease in food intake mean values at (P>0.05), and the percentage of decrement reached 49.73% and 48.25% in case of healthy and diabetic groups consuming colostrum respectively in comparison with their corresponding controls that consuming water. The body weight gain of healthy rats fed the balanced diet plus consuming colostrum instead of water increased by 41.71% in comparison with healthy group consumed water. While 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. The mean values of FER were being 0.21±0.03, vs. 0.07±0.01 in case of healthy group and it being 0.02±0.02 vs. -0.04±0.01 in case of diabetic group. With respect to the relative weight of liver, it was observed that alloxan-injected rats group fed on the balanced diet with consuming water suffered from marked liver enlargement compare to the corresponding healthy control consuming water. The values being 5.41±0.49g vs. 3.61±0.43g, while diabetic rats fed on the balanced diet with consuming colostrum showed marked reduction in relative weight of liver. No significant difference was observed between relative weights of kidney and spleen of healthy or diabetic rat groups fed the balanced diet either with drinking water or colostrum.

Consuming colostrum instead of water by both healthy and diabetic rats resulted in significant reduction in the values of fecal dried weight (P<0.05) comparing to their corresponding control groups that drinking water. The percentages of decrement were, 36.68% and 47.82%, respectively. Also there is a marked reduction in fecal volume of the groups that consuming colostrum either in healthy or diabetic rats. While the results of calculated fecal density markedly affected for far by fecal dry weight and fecal volume. Fecal pH values showed no significant differences between the mean values of healthy control groups either that drank water or colostrum. Alloxanized rats showed significant reduction in their pH mean value (5.68±0.01), while no marked changes were observed when colostrum was consumed instead of water in case of diabetic rats group.

The hematological analyses indicate that the numerical counting of RBCs was significantly higher in healthy rats consumed colostrum than their corresponding control rats that consumed water. Induction of diabetes mellitus resulted in a marked reduction in WBCs and RBCs mean values while consuming colostrum instead of water resulted in significant increase (P<0.05) in the mean counts of RBCs and WBCs. Also the current results showed that the levels of hemoglobin and hematocrit were go hand in hand with the values of RBCs in healthy and diabetic rats either consuming water or colostrum.

Biochemical measurements revealed that:

a) Healthy rats consuming colostrum instead of water showed no significant difference in plasma glucose level. Alloxan injection caused significant increase in glucose level (249.50±5.42 mg/dl), accompanied by decreased in plasma insulin by 61.89% in comparison with its level in healthy rats fed the balanced diet plus water. The results also revealed that when water replaced by colostrum in case of diabetic rats led to marked decrease in the level of plasma glucose level. The level being 194.75±2.86 mg/dl with insensible effect in insulin concentration (12.27±0.48 µlU/ml).

b) The values of total protein and its fractions; albumin and globulins and A/G ratio increased significantly by about 5.17%, 6.15%, 3.17% and 2.92% respectively in healthy rats fed colostrum in comparison with healthy rats drank water. On the other hand, induced diabetes mellitus resulted in reduced total protein as
well as albumin and globulin levels, and the percentage of decrement reached 21.59%, 22.63% and 19.45% respectively in comparison with the corresponding healthy rats fed the balanced diet plus consuming water. Consuming colostrum by diabetic rats affected positively on serum total protein and its fractions; and the increment reached 12.45%, 11.36% and 14.60% for total protein, albumin and globulin respectively. While there was slight change in the mean values of A/G ratios between the two diabetic rats fed the balanced diet with either consuming water or colostrum.

c) With respect to the values of lipid profile measurements, it is clear that colostrum intake leads to significant decrease in plasma lipid patterns. Induction of diabetes caused significant increase in total lipids, triacylglycerols, total cholesterol, and LDL-c by about 47.92%, 44.50%, 19.71% and 103.44% respectively, accompanied with significant decrease in HDL-c by 50.08% comparing with healthy rats consumed water. The replacement of water by colostrum in diabetic group resulted in marked reduction in values of these lipid patterns by about 29.53%, 25.09%, 6.90% and 17.39% for total lipids, triacylglycerols, total cholesterol, and LDL-c respectively, accompanied with an increase in HDL-c by 57.99% as compared with diabetic rats consumed water.

d) With respect to oxidative stress status, the present results indicated that induction of diabetes resulted in marked increment in plasma MDA by about 42.68% and reduction in both erythrocytes SOD enzyme activity and hepatic reduced glutathione by about 48.70% and 27.78% respectively as compared with healthy rats consumed water. The function role of colostrum to decrease the risk of oxidative stress in diabetes was shown in the significant decrement in plasma MDA concentration. The percentage of decrement was being 22.99% while there were significant increment reached 35.75% and 20.94% in case of erythrocytes SOD activity and hepatic reduced GSH respectively in comparison with diabetic rats fed the balanced diet plus consuming water.

The mean corpuscular hemoglobin (MCH) in pigogram was determined by the following formula:-

\[
\text{MCH} = \frac{\text{Hemoglobin in g per 1,000cc blood}}{\text{Red blood cells count in million per cu.mm}}
\]

Table 1: Effect of consuming colostrum instead of water on some biological parameters in healthy and diabetic rats fed balanced diet.

<table>
<thead>
<tr>
<th>Rat groups Parameters</th>
<th>Healthy consuming H2O</th>
<th>Healthy consuming colostrum</th>
<th>Diabetic consuming H2O</th>
<th>Diabetic consuming colostrum</th>
<th>L.S.D. t (0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food intake (g)</td>
<td>a 528.28±17.33</td>
<td>b 265.56±18.74</td>
<td>a 518.37±19.41</td>
<td>b 268.21±8.81</td>
<td>14.14</td>
</tr>
<tr>
<td>Body weight gain (g)</td>
<td>b 39.87 ± 7.18</td>
<td>a 56.50 ± 10.71</td>
<td>d -22.12 ± 1.35</td>
<td>c 5.62 ± 0.74</td>
<td>5.52</td>
</tr>
<tr>
<td>Feed efficiency ratio (FER)</td>
<td>0.07 ± 0.01</td>
<td>a 0.21 ± 0.03</td>
<td>d -0.04 ± 0.01</td>
<td>c 0.02 ± 0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Relative weight of liver (g%)</td>
<td>c 3.61 ± 0.43</td>
<td>c 3.96 ± 0.41</td>
<td>a 5.41 ± 0.49</td>
<td>b 4.33 ± 0.36</td>
<td>0.36</td>
</tr>
<tr>
<td>Relative weight of kidney (g%)</td>
<td>0.76 ± 0.15</td>
<td>0.75 ± 0.16</td>
<td>0.94 ± 0.06</td>
<td>0.84 ± 0.16</td>
<td>N.S</td>
</tr>
<tr>
<td>Relative weight of spleen (g%)</td>
<td>0.46 ± 0.10</td>
<td>0.46 ± 0.08</td>
<td>0.55 ± 0.15</td>
<td>0.48 ± 0.09</td>
<td>N.S</td>
</tr>
</tbody>
</table>

- There was no significant difference between means have the same letter in the same row.
Table 2: Effect of consuming colostrum instead of water on fecal characteristics in healthy and diabetic rats fed on the balanced diet (means ± SD).

<table>
<thead>
<tr>
<th>Rat groups Parameters</th>
<th>Healthy consuming water</th>
<th>Healthy consuming colostrum</th>
<th>Diabetic consuming water</th>
<th>Diabetic consuming colostrum</th>
<th>L.S.D. t (0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry weight (g/day)</td>
<td>a 5.37 ± 0.17</td>
<td>c 3.40 ± 0.11</td>
<td>b 4.60 ± 0.19</td>
<td>d 2.40 ± 0.25</td>
<td>0.17</td>
</tr>
<tr>
<td>Volume (cm³)</td>
<td>a 10.65±0.22</td>
<td>c 6.61±0.17</td>
<td>b 9.63±0.12</td>
<td>d 5.42±0.21</td>
<td>0.17</td>
</tr>
<tr>
<td>Density (g/cm³)</td>
<td>a 0.50±0.02</td>
<td>a 0.51±0.03</td>
<td>c 0.47±0.02</td>
<td>b 0.44±0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>pH</td>
<td>a 6.49±0.06</td>
<td>a 6.51±0.07</td>
<td>b 5.68±0.01</td>
<td>b 5.72±0.04</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* There was no significant difference between means have the same letter in the same raw.

Table 3: Effect of consuming colostrum instead of water on RBCs, WBCs, hemoglobin and hematocrit in healthy and diabetic rats fed balanced diet (means ± SD).

Mean corpuscular hemoglobin concentration (MCHC %) the following formula was used to determining its value:-

\[
\text{MCHC} = \frac{\text{Hemoglobin per 1000cc. blood}}{\% \text{ Volume of erythrocytes (hematocrit)}} \times 100.
\]

Saturation index (SI) was determined by the following formula:-

\[
\text{SI} = \frac{\% \text{ Hemoglobin}}{\% \text{ Hematocrit}}
\]

Table 4: Effect of consuming colostrum instead of water on the indices of erythrocytes; constants relating to size and to hemoglobin content in healthy and diabetic rats fed balanced diet (means ± SD).

<table>
<thead>
<tr>
<th>Rat groups Parameters</th>
<th>Healthy consuming</th>
<th>Healthy consuming colostrum</th>
<th>Diabetic consuming water</th>
<th>Diabetic consuming colostrum</th>
<th>L.S.D. t (0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCV  cµ</td>
<td>a 83.97±0.18</td>
<td>a 84.30±0.22</td>
<td>c 69.95±0.22</td>
<td>b 82.70±0.28</td>
<td>0.19</td>
</tr>
<tr>
<td>VI</td>
<td>a 1.00±0.03</td>
<td>a 1.00±0.02</td>
<td>c 0.80±0.05</td>
<td>b 0.84±0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>MCH  pg</td>
<td>a 28.78±2.22</td>
<td>a 29.52±2.28</td>
<td>c 21.22±1.15</td>
<td>b 24.51±1.74</td>
<td>1.62</td>
</tr>
<tr>
<td>MCHC %</td>
<td>a 34.09±2.56</td>
<td>a 35.16±2.92</td>
<td>b 29.63±2.92</td>
<td>b 30.34±1.80</td>
<td>2.20</td>
</tr>
<tr>
<td>SI</td>
<td>a 1.00±0.02</td>
<td>a 1.00±0.08</td>
<td>d 0.91±0.03</td>
<td>c 0.96±0.03</td>
<td>0.04</td>
</tr>
</tbody>
</table>

* There was no significant difference between means have the same letter in the same raw.
Effect of consuming colostrum instead of water on plasma levels of glucose and insulin in healthy and diabetic rats fed balanced diet (means ± SD).

<table>
<thead>
<tr>
<th>Rat groups</th>
<th>Healthy consuming H₂O</th>
<th>Healthy consuming colostrum</th>
<th>Diabetic consuming H₂O</th>
<th>Diabetic consuming colostrum</th>
<th>L.S.D. (0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma glucose level (mg/dl)</td>
<td>c 87.25 ± 2.76</td>
<td>c 86.88 ± 2.53</td>
<td>a 249.50 ± 5.42</td>
<td>b 194.75±2.86</td>
<td>3.06</td>
</tr>
<tr>
<td>Plasma insulin level (µU/ml)*</td>
<td>a 32.15 ± 0.96</td>
<td>a 32.21 ± 0.54</td>
<td>b 12.25 ± 0.65</td>
<td>b 12.27 ± 0.48</td>
<td>0.58</td>
</tr>
</tbody>
</table>

- There was no significant difference between means have the same letter in the same row.

Effect of consuming colostrum instead of water on serum levels of IgG and IgA in case of healthy and diabetic rats fed balanced diet (means ± SD).

<table>
<thead>
<tr>
<th>Rat groups</th>
<th>Healthy consuming H₂O</th>
<th>Healthy consuming colostrum</th>
<th>Diabetic consuming H₂O</th>
<th>Diabetic consuming colostrum</th>
<th>L.S.D. (0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma IgG (mg/dl)</td>
<td>b 134.26±0.47</td>
<td>a 143.20±1.54</td>
<td>d 118.40±1.04</td>
<td>c 121.06±1.70</td>
<td>1.09</td>
</tr>
<tr>
<td>Plasma IgA (mg/dl)</td>
<td>b 27.36 ± 0.71</td>
<td>a 33.94 ± 2.90</td>
<td>c 11.34 ± 0.43</td>
<td>b 21.58 ± 0.72</td>
<td>1.32</td>
</tr>
</tbody>
</table>

- There was no significant difference between means have the same letter in the same row.
Discussion:

Results of the present study revealed that diabetic rats showed a depletion in body weight gain and this may be due to degeneration of the adipocytes and muscle tissues to make up for the energy lost from the body due to frequent urination and over conversion of glycogen to glucose. Administration of colostrum by healthy and diabetic rats caused a significant increase in body weight gain, as compared with their corresponding controls consuming water. Such results are in agreement with those of Ene et al., (2007) who observed that diabetic animals had lower body weight, higher relative liver weight and kidney weights as compared with non-diabetic control group. In addition our results go hand in hand with (McDermott et al., 1995; Abd-El Hamid, 2005; Barakat, 2006; and Barakat et al., 2011), indicating that the relative weight of liver was significantly (P<0.01) increased in diabetic rats compare with controls. This finding agrees with that of Pluske et al., (1999) who observed an increase of 40% and 80% of the average daily gain in body weight with a starter diet supplemented with 50 and 100 g of bovine colostrum extract per kg of feed. Kuhne et al., (2000), found that increased body weight when feeding on both high and low feeding of colostrum. The body weight gain/dry matter intakes in both groups fed on low and high colostrum were greater (P< 0.05) than in groups fed milk replacer and King et al., (2001) confirmed that an increased in average daily gain in body weight of 20% with 60g of bovine colostrum /kg of feed.

In the present work administration of colostrum by healthy and diabetic rats resulted in a significant reduction in the values of fecal dried weight and volume accompanied with no marked changes in fecal pH values. Our findings are in good agreement with the findings of Kuhne et al., (2000) showed that fecal score was lower in groups fed colostrum than groups fed milk replacer. In addition Martin and Quigley, (2001) showed that fecal dry matter decreased in lambs fed on fresh colostrum. Boudry et al., (2008) suggested that the positive response of bovine colostrum might result from an improvement in the sanitary status of the colostrum treated piglets by a direct effect of colostrum on gut health.

Our results showed that the numerical counting of RBCs was significantly increased in healthy rats group consumed colostrum. These results go hand in hand with Lonerdal and Iyer (1995), Uruakpa et al. (2002) and Tripathi and Vashishtha (2006) who showed that lactoferrin is an enhancer of iron absorption while trypsin and chymotrypsin are remarkably ineffective in digesting lactoferrin particularly its iron- saturated form. Induction of diabetes mellitus resulted in a marked reduction in WBCs and RBCs mean values while replacement colostrum instead of water resulted in significant increase in the mean counts of RBCs and WBCs. The results showed that the levels of hemoglobin and hematocrit were go hand in hand with the values of RBCs in healthy and diabetic rats either consuming water or colostrum. Akku et al. (1996) showed that leukocytes of diabetics are affected by oxidative stress which might be a reason for decreased microbiidal activity. In addition Morigi et al. (1998) and Seghrouchni et al. (2002) illustrated that hyperglycemia in diabetic subjects leads to decrease total leukocytes count by increase number of adherent leukocytes to endothelial cells Martin and Quigley (2001), showed that total leukocytes count increased in all animals after colostrum intake. Remaining viable leukocytes may have played a role in supporting the immune response. Maneva et al., (2003) illustrated that lactoferrin is a glycolysis stimulator, leading to increased formation of ATP, which is necessary to maintain the ion gradient, membrane potential and morphology of the erythrocyte.

Kabalin et al., (2008) showed that changes in hematological parameters in newborn piglets are associated with organ maturation and development degradation of fetal erythrocytes and maternal globulins increase erythroposis by colostrum intake, the average of erythrocytes number at the end of suckling period was significantly higher than values obtained on the first day of life. The higher hemoglobin value at the end of suckling period was not significant regarding the first day of life, while hematocrit value increased at the same period significantly (P< 0.01). Moreover Grossin et al., (2009) found that red blood cell adhesion to endothelium is increased in diabetes mellitus and is correlated with the severity of vascular complications. Elevated glucose concentration increases the oxidation phenomenon and advanced glycation end product (AGE) formation. RBC proteins can be glycated such as glycated hemoglobin and RBC membrane proteins. They added that values of MCHC are inversely proportional to hematocrit value. Singh et al., (2009) reported that diabetes-related chronic hyperglycemia can lead to a hypoxic environment in the renal interstitium, which results in impaired production of erythropoietin by the peritubular fibroblasts and subsequent anemia.

The present work revealed alloxan injection caused significant increase in glucose level accompanied by decreased in the insulin by 61.89%. The results also illustrated that replacement of water by colostrum in case of diabetic rats resulted in marked decrease in the level of plasma glucose with insensible effect in insulin concentration. The good explanation for lowering blood glucose may be due to colostral interleukin-1 which can partially inhibit the phosphoenolpyruvate carboxykinase enzyme, the rate limiting enzyme in gluconeogenesis. As well as colostral insulin like growth factor IGF which has an important role to control glucose metabolism. IGF closely related to synthesis of adiponecint in adipocytes. Adiponecint 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. The good explanation for decreased insulin level is due
to the fact that injection of alloxan resulted in destruction of pancreatic β-cell which responsible for insulin secretion.

Our results agree the results of Ragab, (2002) reported that the probable mechanism of hypoglycemic action of bovine colostrum could be referred to its delaying of gastric emptying with direct interference with glucose absorption. In addition of the promoting activity of its insulin like growth factor that has an important role in glucose metabolism.

Our results confirmed by the results of Abd El-Hamid (2005), Barakat (2006), and Hamden et al., (2008a) illustrated that alloxan injection in rats lead to increase blood glucose level more than 200 mg/dl (hyperglycemia). In addition Sailaja Devi and Das, (2005) reported that almost all animals which received alloxan developed diabetes mellitus as evidenced by high blood glucose (350-400 mg/dl) and low plasma insulin levels compared to the control due to accumulation of alloxan in insulin producing cells result in destruction of pancreatic B-cells (Szkudelski, 2001).

Our results go hand in hand with Boudry et al., (2008) showed that colostrum has also been shown to balance blood sugar levels this is due, at least in part, 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.

In addition Hamden et al., (2008b) illustrated that the blood glucose level of diabetic rats increased by 167% (p<0.001) compare to the control animals. This is may be due to alloxan administration exert a deleterious effects on the function of pancreatic β-cells.

Our result match with the result of Kim et al., (2008) shown that as a whole, the rate of decrease in blood glucose level by bovine colostrum administration was highest among the subject with type 2 diabetes mellitus.

In the present work, induced diabetes mellitus has a risk factor that reduced the total proteins as well as albumin and globulin levels. Consuming colostrum by diabetic rats affected positively to increase total proteins and its fractions.

From biochemical manifestation of diabetes mellitus increase protein breakdown and oxidation of amino acids lead to negative nitrogen balance. Gabr (1998) and Barakat (2006) stated that alloxan injection caused a significant decrease in A/G ratio as compare with the normal control. While from the nutritional point of view, colostral insulin like growth factor stimulate amino acid uptake and reduced protein breakdown which incorporated with the positive production of globulin status. Also colostrum intake stimulates synthesis of albumin in liver. Fang et al., (1997) explained that IGF-1 has anabolic effect to stimulate amino acid uptake and reduce protein breakdown.

Our results in agreement with the results by Kuhne et al., (2000) shown that total protein and globulin concentrations increased rapidly in colostrum fed groups of calves as consequences of immunoglobulin absorption. Increased amounts of colostrum, higher concentrations of total protein and globulins in groups fed colostrum demonstrated the prolonged effects of high colostrum intake on globulin status. Albumin concentration rise in colostrum fed groups was probably the result of enhanced hepatic synthesis.

Our results are in good agreement with the results obtained by Ragab, (2002) reported that Streptozotocin - induced diabetes mellitus resulted in decrease plasma albumin and colostrum intake lead to marked increase in its level, and owed this result to the presence of significant levels of hormones and other transforming growth factor with the significant regulatory and modulating bio-function.

Our results match with the results recorded by Yassin et al., (2004) showed 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.

The results of the present work showed that there were significant amelioration in plasma lipid profile in healthy and diabetic rats when consuming the balanced diet plus colostrum. Colostrum contains biofunctional components which may play as regulatory lipid agent such as bioprotein IgG and lactoferrin as shown in the finding of Rey and Besedovsky, (1989) who observed that interleukin-1 can normalize triacylglycerol levels in advanced stages of chemically induced diabetes. Also Cola et al., (1997) confirmed that the effect of insulin like growth factor-1 is associated with decreased gluconeogenesis and suppressing free fatty acids release from adipocytes. Sharp et al., (1994) illustrated that hypocholesterolemic effect of colostrum owed to IgG which represent the major colostral immunoglobulin that have a regulatory effect leading to changes in gut microflora which may enhance the excretion of bile acids and leading to increase hepatic conversion of cholesterol into newly synthesized bile acid.

The findings of (Kajikawa et al., 1994: Vassiliou et al., 2001; and Takeuchi et al., 2004). found that lactoferrin interfere with ligand binding to lipoprotein receptor protein (LRP) and inhibit selective uptake of HDL-Cholesteryl ester by 35-50% in human primary adipocytes. LRP may contribute physiologically to HDL-Cholesteryl ester selective uptake in adipocytes, because lactoferrin another LRP ligand that is also a potent inhibit or of Apo-E and an inhibitor of lipoprotein lipase binding to LRP, reporting that lactoferrin reduced the chylomicon into liver in vivo, whereas the liver uptake of β-VLDL is efficiently block. Lactoferrin affect the
micellar solubility of cholesterol, because it apparently suppressed lymphatic triacylglycerols absorption. So it is useful in the control of lipid accumulation.

The hyperglycemia which induced by alloxan injection caused a significant increases in total lipids, cholesterols, free fatty acids, and triacylglycerols contents. This may be attributed to an overproduction of the lipid by the gastrointestinal tract. The increased plasma triacylglycerols (TAG) 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. Our results are in good agreement with the results obtained by (Jae et al., 1991; Venkateswarly et al., 1993; Rai et al., 1997; Gabr, 1998; Johar, 2002; and Barakat, 2006).

Davis et al., (2007) and Kim et al., (2008) reported that bovine colostrum intake can efficiently decrease TAG and total cholesterol levels in type 2 diabetic patients and rats. This is may be due to interaction of various hormones within bovine colostrum such as leptin for fat breakdown. In previous study by Hyogo et al., (2002) confirmed that hepatic triacylglycerol and cholesterol content decrease linearly in mice that were administered leptin.

The increased MDA value in diabetic rats may be attributed to the increased level of oxygen free radicals which could be due to their increased production and/or decreased destruction by non-enzymatic and enzymatic antioxidants. The antioxidative effect of lactoferrin (1.65±0.54 mg/ml) on erythrocytes which was expressed as an enhancement of the reduced glutathione content, a decrease content of products of lipid peroxidation under oxidative stress status, as well as colostral vitamin E functions by donating hydrogen to fatty peroxyl radicals thereby halting lipid peroxidation.

Our result similar to the results of Samiec et al., (1998) and Jain and McVie, (1999) who reported that diabetic patients have lower GSH concentrations in erythrocytes and plasma. In addition Sheng et al., (2005) reported that in diabetic group, GSH contents were generally lower than in the control group, but significant decreases were observed only in liver and kidney. Dincer et al., (2002). illustrated that the maximum decrease was observed in GSH level in the poorly controlled diabetic group. This result indicates that the GSH pathway is susceptible to oxidation and this susceptibility increases in poorly controlled diabetics.

In the present work plasma MDA levels were significantly elevated in diabetic control group, this is in the agreement of results of (Sundaram et al., 1996; Soto et al., 1998; Palmer et al., 1998; El-Missiry and Gindy, 2000; and Johar, 2002; Sailaja Devi and Das, 2005). reported significant increase in the plasma level of MDA, as well as a significant decrease in the activity of SOD in RBCs lysate in alloxan- induced diabetic animals compared to untreated control. Barakat, (2006) illustrated that the decrease in GSH levels in liver during diabetes is probably due to its increased utilization by the hepatic cells. This may be due to an attempt by the hepatocytes to counteract the increased formation of lipid peroxides.

Bounous, (2000) reported that colostrum contain high significant levels of glutathione precursors; glycine, glutamic acid and cysteine.

Kasapovic et al., (2005) reported that colostrum is rich source of nutrients and contain biologically active molecules that are essential for specific antioxidant functions especially copper, zinc superoxide dismutate (Cu-ZnSOD).

Increasing level of IgA may be due to secretory component binds to IgA dimers to form a complex molecule called secretory IgA (sIgA) which protects the IgA from digestion by intestinal proteases. As well as the presence of security molecules as antitrypsin inhibitor in colostrum aid to delay digestive hydrolysis of IgG.

Our results confirmed by the results of (Xanthous et al., 1995; and Uruakpa et al., 2002), who illustrated that colostral IgA is preferentially transferred to the neonatal during the first 3 days postpartum. (Pakkanen and Aalto 1997; and Tripathi and Vashishtha, 2006). confirmed that transforming growth factor-β (TGF-βs) that present in colostrum results in increase production of IgG and IgA. It has been demonstrated that TGF-β enhances expression of secretory component in rat-epithelial cells, which is responsible for the transport of polymeric IgA into intestinal lumen. Moreover, Johnson et al., (2007) showed that serum concentrations of IgG recorded (18.07 mg/ml) in calves received colostrum. Moreover, noted that serum concentrations of IgA about (4.06 mg/ml) in calves received colostrum.

Moreover, Lin et al., (2009), confirmed that immunoglobulin in colostrum are not all hydrolyzed by the digestive proteases but can be absorbed directly into the enterocytes of neonatal pigs in the first few days of life. Therefore, these immunoglobulin proteins in colostrum and perhaps total proteins would have greater digestibility than mature milk.

Our results go hand in hand with the results of (Weiner et al., 1999; Le Rousic et al., 2000; Fetherston et al., 2001; Kelleher and Lonnerdal, 2001; Lilius and Marnila, 2002; and Tenovuo, 2002), who concluded that daily supplementation with bovine colostrum could improve the general healthy conditions of diabetic patients through its pronounced potent hormonal-modulation effects in addition to its offering the protective effects against many of infectious diseases that associated with immunity weakness that could appear in diabetic. In addition of the result of (Mero et al., 2002; and Solomons, 2002). found that bovine colostrum has effective important role in improvement of general immunity of diabetic subjects due to its high contents of nature antibodies and other antimicrobial fractions.
Our results go hand in hand with (Mazzone et al., 1999; and Mansour et al., 2005) reported that serum IgG increase linearly (P<0.03) as colostrum intake increased. In addition to the results of Jensen et al., (2001), confirmed that the IgG concentration in plasma was significantly higher in colostrum fed groups than milk replacer. The percentage of absorbed bovine IgG in the bovine colostrum fed group was 7.0±3.0 % at 3 hours of its intake.

Moreover, Goldsby et al., (2000) confirmed that IgA constitutes only 10%-15% of total immunoglobulins in serum, and it is the predominant class in external secretion of colostrum. In addition Quigley et al., (2002) found that Plasma IgG had increased to 8.0 g/l in calves fed colostrum supplementation. Plasma IgG concentration at 24 h of age was indicative of successful transfer of passive immunity.

Our findings match with the findings of Sparks et al., (2003) reported that the significant positive correlation between serum IgG and total serum protein suggested that IgG derived from ingestion of colostrum contributes significantly to serum protein levels in neonatal calves.

The amelioration of colostrum administration supported of the investigated Ig classes due to biofunctional compound and nutritional aspects accompanied by surcease the acceleration of the oxidative risk. This may reflect the development of tested immunoglobulins against the trigger of diabetes mellitus by natural foodstuff Yousef et al., (2006).

REFERENCES


Absorption and enzyme activities in neonatal pigs is diet dependent. Garlden.

The role of colostrum, milk and involution secretion. 


