

Effect of Camel Milk Whey Fraction on Streptozotocin-Induced Diabetic Rats

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Abstract

This research examines the evaluation of camel milk whey fraction anti-diabetic effects in streptozotocin (STZ)-induced diabetic rats, which was done to measure weekly glucose level and lipid profiles. After 16 hours of fasting, streptozotocin was administered intraperitoneally (IP) in a single dose at a dosage of 65 mg/kg body weight. 24 hours later, glucose levels were checked. Diabetic rats are those whose blood glucose levels are greater than 200 mg/dl. For six weeks, camel milk whey fraction was given to the rats daily via feeding tubes. Rats in the normal control, diabetic control, metformin, and experimental groups had their serum lipid profiles levels were analysed to look into the impact on blood glucose levels. When camel milk whey fraction was supplied to diabetic rats, blood glucose and lipid profiles were significantly decreased to values that were close to control with the exception of HDL. Due to its high vitamin and mineral content, camel milk whey fraction is thought to offer medicinal benefits that can help in the treatment of a variety of illnesses. The camels' preference for staring at natural plants has been linked to the anti-diabetic properties of camel milk whey fraction. Other advantages of camel milk's whey fraction include prevention of ulcers and blood sugar regulation. In summary, this study demonstrated that giving camel milk whey fraction supplements to diabetic rats possess hypo glycaemic effects and guards against the liver and kidney damage caused by streptozotocin.

Keywords: Streptozotocin, whey fraction lipid profiles, diabetic.

Introduction

Diabetes mellitus more commonly referred to as "diabetes" is a chronic disease associated with abnormally high levels of inadequate production of insulin (which is made by the pancreas and lowers blood glucose), or inadequate sensitivity of cells to the action of insulin (Yuen *et al.*, 2021). Insulin resistance also called IR is a resistance to the hormone insulin, resulting in increasing blood sugar. Treatment can help, but this condition can't be cured. It requires a medical diagnosis. Lab tests or imaging always required. Chronic can last for years or be lifelong. The hormone insulin helps control the amount of sugar (glucose) in the blood with insulin resistance, the body's cells don't respond normally to insulin. Glucose can't enter the cells as easily, so it builds up in the blood. This can eventually lead to type 2 diabetes (Mitchell *et al.*, 2019).

The global prevalence in 2019 was estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9 % (700 million) by 2045. The prevalence is higher in urban (10.8%) than rural (7.2 %) areas and high income (10.4%) than low-income countries (4%) (Cho *et al.*, 2018). Diabetes is associated with reduced life expectancy, significant morbidity

due to specific diabetes related microvascular complications, increased risk of macrovascular complications (ischemic heart disease, stroke and peripheral) vascular disease) and diminished quality of life. There are important differences between defining diabetes to identify an individual with diabetes and the consequent clinical and social implication of this diagnosis and defining diabetes for epidemiological purposes. In the former the diagnosis requires careful substantiation with retesting on another day unless the person is symptomatic and the plasma glucose is unequivocally elevated, whereas in epidemiological study repeat testing is rarely performed. When repeat testing is performed, approximately 75% of people with diabetes mellitus detected in epidemiological studies are confirmed to have clinical diabetes (Chen *et al.*, 2019).

The total population of camel in the world is believe to be 20.89 million, of which 89% are non-humped dromedary camels (*camelusbactrianus*) and the remaining 11% are the 2-humped (*camelusbactrianus*) that are generally found in the cold deserts of Asia while more than 60% of the dromedary camel population is concentrated in the arid areas of North East African countries like Somalia, Sudan, Ethiopia and Kenya. Ethiopia ranks third, in the world by the number of camel herds after Somalia and Sudan (Ahmadi *et al.*, 2019). For desert people in Asia and Africa, Camel is vital to daily life as a source of food and a means of transportation, and just as importantly, its milk has been used as medicines for diverse ailments since ancient times. Camel can produce more milk for a longer period of time in arid zones and harshly environment than any other domestic livestock species. The daily yield of camel ranges from 3 to 10kg in a lactation period of 12 to 18 months. Camel milk so called white gold of desert is more similar to human milk than any other milk and differs from other ruminant milk because it contains low cholesterol, low sugar, high mineral (Sodium, potassium, Iron, copper, zinc and magnesium), high vitamin C, protective proteins like lactoferrin, lactoperoxidase, immunoglobulins, lysozyme (Al-Haj, 2020). Camel milk has been acknowledged for a long time to provide a potential treatment for a series of diseases such as dropsy, jaundice, anti-hypertensive, asthma and leishmaniasis or kalaazar. It has been reported that camel milk contains the low quality of B-casein and the lack of B-lactoglobulin which cause allergic reaction in lactose intolerant person. Nevertheless, it contains insulin like and protective protein used for the treatment of many ailments like autism and diarrhea and possess anti tumors properties (Wang *et al.*, 2018). Moreover, camel milk is endowed with very strong immune system and remedy for peptic ulcers, anti-malignant, anti-platelet and anti-thrombotic properties. More recently, studies confirmed that camel milk is unique in terms of antioxidative factors, antiviral, ant fungal, antihepatitis, treatment for para tuberculosis, anti-cancer, preventives and aging, remedy for autoimmune diseases, cosmetics and detergent (Wang *et al.*, 2018).

Statement of the Problems

Diabetes mellitus is a complicated health condition with multiple causes and many treatment options. Various myths may influence diabetics health seeking behavior, and

they may use traditional medicine, which include normal foods and herbs, for primary health care. Some people believed that combining conventional and traditional medicines improved the effectiveness of treatment. Reasons for using traditional medicines include the high cost of conventional treatment and the availability and accessibility of the traditional medicines.

Objective of the Research

To determine the effect of camel milk whey fraction in weekly glucose level of streptozotocin induced diabetic rats, lipid profile and compare the effect of camel milk whey fraction and metformin.

Materials and Method

Experimental Animals

Adult Wistar albino rats weighing between 80-110g were obtained from the National Research Institute, Vom. They were kept in a cage at room temperature with 12-hour light dark cycle for one week to acclimatize and were allowed access to food and water *ad libitum*. Principles of laboratory animal care guideline were followed (NIH publication No. 85-23, revised 1985).

Isolation of whey fraction

The freshly procured camel milk sample were de-fatted (100ml) by centrifugation at 2500 rpm for 30 min at 4°C. Casein was removed by precipitating skimmed milk with 1N HCl adjusting pH to 4.6; It was recentrifuged again for 15 min. Whey were filtered through Millipore filter (0.45µm) to completely remove casein precipitates; the filtrates (whey samples) were frozen at -2°C to avoid microbial spoilage during the experimental period and prior to proceeding for further analysis (Moradian *et al.*, 2014).

Induction of diabetes with streptozotocin

Collection of samples of blood

After 30 days, the animals were sacrificed by decapitation and the blood samples were collected. Blood samples were collected in tubes containing anti-coagulants for the estimation of blood glucose. The serum was submitted for centrifugation at 1000 rpm to be separated within 15 min at 4°C and was saved in aliquots, stored at -2°C for further analysis. However, the liver, kidney and pancreas were rapidly removed and washed with cold normal saline, after cut were preserved in 10% of neutral formalin for microscopic pathological studies.

Biochemical study of the serum

Blood glucose, Total cholesterol, LDC, HDC and TG) by using the diagnostic kits as aforementioned.

Statistical analysis

Results were noted as means and standard deviation of three replicates. The significant of differences was calculated by using student t-test. $p < 0.05$ was considered statistically significant.

Result

Mean blood glucose of normal rats was 82.26 ± 4.09 mg/dl at zero week whereas in case of metformin, diabetic controls 250ml, 500ml, 500ml, 750ml and 1000ml were 482.49 ± 7.21 , 422.49 ± 7.21 , 463.37 ± 5.76 , 469.23 ± 7.07 , 463.37 ± 9.39 , and 462.83 ± 8.4 mg/dl respectively. In Group 250ml, 500ml, 500ml, 750ml, 1000ml, Metformin after 1st, 2nd, 3rd, 4th, 5th and 6th week of trial, the mean blood glucose levels markedly dropped to, whereas in group of diabetic control rats it keeps rising up to 610.11 ± 1.82 mg/dl (Table 1).

Table 1. Effect of camel milk whey fraction treatment of blood glucose level of normal control, diabetic control, metformin control and experimental streptozotocin induced diabetic rats.

Wee ks	Normal Control	Diabetic Control	Metformin Control	250 mL/kgbw	500 mL/kgbw	750 mL/kgbw	1000 mL/kgbw
Wee k 0	82.2 ± 4.09^a	422.49 ± 7.21^b	482.49 ± 7.21^c	463.37 ± 5.76^c	469.23 ± 7.07^c	463.37 ± 9.39^c	462.83 ± 8.41^c
Wee k 1	82.54 ± 3.88^a	501.41 ± 4.98^e	459.28 ± 8.75^d	419.55 ± 5.11^c	412.82 ± 6.28^{bc}	395.23 ± 7.94^b	390.59 ± 7.87^c
Wee k 2	81.00 ± 3.40^a	560.05 ± 5.73^e	435.54 ± 8.36^d	393.42 ± 4.88^c	386.22 ± 6.87^{bc}	370.02 ± 7.77^b	362.35 ± 7.62^{bc}
Wee k 3	81.65 ± 2.17^a	565.80 ± 1.86^e	409.88 ± 8.32^d	347.46 ± 4.13^c	337.37 ± 5.17^{bc}	324.20 ± 6.87^b	314.54 ± 6.29^{bc}
Wee k 4	81.25 ± 2.52^a	577.80 ± 6.11^f	386.74 ± 7.32^e	323.74 ± 3.96^d	305.48 ± 4.33^c	276.88 ± 5.85^b	265.57 ± 8.77^b
Wee k 5	84.60 ± 2.11^a	598.00 ± 3.67^e	347.82 ± 17.37^d	299.57 ± 3.83^c	281.85 ± 4.21^c	236.48 ± 3.95^b	230.20 ± 4.84^b
Wee k 6	87.17 ± 1.87^a	610.11 ± 1.82^f	329.40 ± 6.07^e	277.45 ± 3.52^d	257.91 ± 3.86^c	185.14 ± 3.73^b	171.31 ± 3.67^b

Results are given as means $\pm$ SD for groups of seven animals, values are statistically significant, means in the same raw with different superscript are significantly different ($p < 0.05$).

Table 2. Effect of camel milk treatment on lipid profile on of normal control, diabetic control, metformin control and experimental streptozotocin induced diabetic rats.

Parameters	Normal Control	Diabetic Control	Metformin Control	250 mL/kgbw	500 mL/kgbw	750 mL/kgbw	1000 mL/kgbw
TC (mg/dL)	75.03±1.3 5 ^a	296.91±3 .27 ^e	267.91±1. 65 ^b	260.49±1. 82 ^d	257.23±2. 51 ^c	250.86±1 .33 ^b	245.86±1. 33 ^b
HDL (mg/dL)	54.91±1. 65 ^e	16.69±0. 47 ^a	23.26±0.7 4 ^c	24.57±0.9 5 ^b	27.31±0.5 1 ^c	30.25±0. 61 ^d	34.51±0.6 4 ^d
LDL (mg/dL)	78.03±3. 44 ^a	196.14±0 .61 ^c	181.29±1. 74 ^c	178.60±0. 96 ^d	174.26±2. 13 ^c	171.57±3. 81 ^b	163.11±3. 10 ^b
TG (mg/dL)	119.54±1 .38 ^a	330.63±2. 54 ^b	225.31±1. 15 ^{ab}	217.91±0. 75 ^{ab}	210.34±1. 07 ^{ab}	205.63±7. 66 ^b	200.88±0. 75 ^{ab}

Results are given as means ±SD for groups of seven animals, values are statistically significant, means in the same row with different superscript are significantly different ($p < 0.05$), TC: Total cholesterol, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, TG: Triglycerides.

Discussion

Effect of camel milk whey fraction on serum glucose level of normal control, diabetic control, metformin control and experimental streptozotocin induced diabetic rats.

The anti-diabetic properties of camel milk are very complex involving many cellular and molecular mechanisms and aspects of metabolism and transport of glucose as well as the synthesis and secretion of insulin (El-Sayed *et al.*, 2022). Data presented in (Table 1) showed the effect of six weeks of daily ingestion of camel milk whey fraction on serum glucose levels of streptozotocin induced diabetic rats. Results indicated that highest serum glucose level (drug control) was observed in week 0 with the streptozotocin induced diabetic rat group. Mean blood glucose of normal rats was 82.26 ± 4.09 mg/dl at zero week whereas in case of 250ml, 500ml, 500ml, 750ml, 1000ml, Metformin and diabetic controls they were 463.37 ± 5.76 , 469.23 ± 7.07 , 463.37 ± 9.39 , 482.83 ± 8.4 , 422.49 ± 7.21 , and 422.49 ± 7.21 mg/dl respectively. In Group 250ml, 500ml, 500ml, 750ml, 1000ml, Metformin after 1st, 2nd, 3rd, 4th, 5th and 6th week of trial, the mean blood glucose levels markedly dropped towards normal level. Mean blood glucose level in normal group was within the normal range (70 to 90 mg/dl). The overall mean of six weeks trial showed significant decreases in mean blood glucose level of Group 250ml, 500ml, 500ml, 750ml, 1000ml, Metformin rats getting camel milk whey fraction, as compared to diabetic control rats getting no treatment. During six weeks trial overall drop in blood glucose level in diabetic rats was observed to be 40%, 45%, 60%, 63% and 32% in rats getting camel milk whey fraction respectively. On the other hand, the oral intake of camel milk whey fraction significantly ($P < 0.05$) decreased the serum glucose level in diabetic rats, while the normal rat was not affected. In this present study, the camel milk whey fraction is more potent than metformin drug as shown above.

Hamad *et al.* (2011) investigated the antidiabetic effects of camel milk compared with cow and buffalo milk on diabetic Sprague-Dawley rats proved that camel milk had higher hypoglycemic effects (49%) compared with cow and buffalo milk (11%).

Effect of camel milk whey fraction on serum lipid profile of normal control, diabetic control, metformin control and experimental streptozotocin induced diabetic rats.

Diabetes is associated with profound variations in serum lipids, T.CHOL, HDL, TG, and LDL, are responsible for vascular complications and an increased risk of heart disease (Shiro, 2015). Thus, lowering the cholesterol levels through dietary or drug therapy seems to be associated with a reduced risk of heart disease (Shiro, 2015).

Data in table 3 showed a decrease in serum total triglyceride (TG) and total cholesterol (TC) compared with diabetic control treated with camel milk whey fraction. The results showed that the oral administration of camel milk whey fraction significantly decreased TC, TG and LDL in diabetic rat groups compared to diabetic control. The results cleared that the oral administration of camel milk whey fraction caused a significant increase in high-density lipoprotein (HDL) compared to diabetic control. The higher increase in HDL values was found with 250ml, 500ml, 750ml, 100ml and Metformin groups compared to diabetic control. From these results, it could be concluded that the oral administration of camel milk whey fraction improved the lipid profile of diabetic rats.

Studies by El-Said *et al* (2010) who evaluated the effect of camel milk on lipid profile in experimentally induced diabetic rabbits revealed the potential of camel milk as hypo lipidaemic agent. However, the group of diabetic rabbits treated with camel milk showed a significant ($p < 0.05$) reduction in the TG level from 603.4 ± 9.6 mg/dL to 524.8 ± 14.2 mg/dL after 1 month. To evaluate the protective role of camel milk against dyslipidemia, changes in the lipid profile levels were analyzed in streptozotocin induced diabetic rats in one study. The results of this study indicated that the levels of TC, TG, and LDL-C were significantly higher ($p < 0.05$) in the diabetic control rats group and these levels were significantly reduced in the group of rats fed with camel milk whey fraction. Mohamad *et al.*, (2009) showed the efficiency of camel milk as an adjuvant therapy on the lipid profile of young type 1 diabetic patients. The TC and TG level in type 1 diabetics decreased by 25% and 37%, respectively, after treatment with camel milk for 16 weeks; however, there were no significant differences in HDL and LDL.

Conclusion

In the current investigation, the camel milk whey fraction was revealed to have therapeutic efficacy in streptozotocin-induced diabetic rats. Due to the presence of insulin/insulin-like proteins, camel milk whey fraction exhibits a notable therapeutic benefit in the treatment of metabolic problems brought on by diabetes. This finding might have an impact on how persons with diabetes mellitus are clinically managed. So, the whey portion of camel milk would be useful for making healthful beverages.

Recommendations

- There is need to isolate the most active compound present in the chromatograph as an anti-diabetic compound required.
- To determine the pharmacological study in order to produce a new drug with broad spectrum activity.
- Camel milk should be given to people with lactose intolerance and diabetic patients as an adjunct to insulin therapy.

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