

Camel Milk; A Superfood as a Treatment for Diabetes

Tahereh Mohammadabadi*

Associate Professor, Department of Animal Science, Faculty of Animal Science and Food Technology, Agricultural Sciences and Natural Resources University of Khuzestan, Mollasani, Ahvaz, Iran

***Corresponding Author:** Tahereh Mohammadabadi, Associate Professor, Department of Animal Science, Faculty of Animal Science and Food Technology, Agricultural Sciences and Natural Resources University of Khuzestan, Mollasani, Ahvaz, Iran.

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Abstract

Under the diabetic condition or hyperglycemia, the cells may not respond properly to insulin or defects in insulin secretion by the pancreas, therefore glucose level of blood is excessive. Chronic hyperglycemia is linked with the dysfunction and failure of various organs especially the eyes, heart, nerves, kidneys, liver and blood vessels; and make hypertension. However, hyperglycemia can be improved with or without ant diabetes drugs, which significantly decrease the risk of complications. Oral insulin therapy has been used for many years; however, coagulation in an acidic environment, neutralize its actions and decreases the efficacy of insulin. Therefore, insulin injection is used. Controlling diabetes, as a worldwide metabolic disease, by effective alternative treatments is currently a topic of great interest. Several researchers have found that camel milk can be used for insulin therapy. It appears to be safe and effective in improving long-term glycemic control. Camel milk is believed to be a suitable hypoglycemic agent in experimental animals and patients with diabetes. It is revealed the camel milk containing insulin like proteins that influence insulin secretion and insulin receptors activity. Also it can improve diabetes dysfunction like kidney and liver failure and wound healing. All animal studies showed significant reductions in the diabetes parameters such as blood glucose, insulin resistance and improving lipid profiles. In most of the clinical trials, the favorable effects of raw camel milk on diabetes mellitus observed by the recommended dose 500 mL/day for 3 months which also improve risk factors in diabetic patients.

Keywords: *Insulin; Diabetic; Camel Milk; Liver Failure*

Introduction

Diabetes mellitus is the most common metabolic disease that consequently caused to cardiovascular diseases, kidney and liver failure. Diabetes treatment includes various antidiabetic drugs which regulate blood glucose but they have several negative effects on patient health. In addition to, oral administration of insulin destroys insulin in the acidic medium of stomach. Therefore, proper treatment of diabetes includes insulin injections as continuously to maintain blood glucose level [65].

Nowadays, the researchers following other suitable alternative treatments for insulin. Camel milk contains insulin like proteins, which does not form coagulum in the acidic media of stomach that can be an effective alternative for insulin [57]. It is concluded, in India the incidence risk of diabetes in people who consume camel milk regularly, is much lower compared to others who don't consume camel milk. Camel milk improves the glycemic control and decreasing insulin resistance in diabetes condition [68]. It is detected a high amount (about 52 U/L) of insulin in camel milk; also, camel milk contains large value of immunoglobulin, lactoferrin, lactoperoxidase, peptidoglycan recognition proteins and vitamin C, which have antimicrobial and pharmacological properties [69].

Duo to properties of anti-bacterial, anti-carcinogenic, anti-oxidant, anti-hypertensive and anti-diabetic of camel milk, it has important benefits on health [22]. Using of camel milk in diabetes patients causes to reduce blood sugar and required insulin dose [3]. Camel milk improves other aspects related to diabetes such as obesity, inflammation, wound healing and oxidative stress damages [8].

Therefore, camel milk and some its effective components influence insulin secretion by effect on the pancreatic beta cells and insulin receptor function in the insulin-sensitive tissues [21].

Effective components and properties of camel milk

Camel milk as desert white gold is very same to human milk than other milks and very different with other ruminant milk [73]. Camel milk is a superfood containing high amounts of minerals, vitamins and immune modulatory components [17]. The age, area, pregnancy, nutrition, seasonal changes, health and genetics influence camel milk composition [19].

The chemical composition of camel milk including 3.4% protein, 3.5% fat, 4.4% lactose, 0.79% ash and 87% water [17]. Higher amount of vitamin C, unsaturated fatty acids, low cholesterol and lack of beta-lactoglobulin are the most unique properties of camel milk in comparison with other milks [47]. The lactose of camel milk easily metabolized in lactose intolerance people [75], due to less production of casomorphin in camel milk that increase intestinal motility; therefore lactose expose more to lactase enzyme and digest quickly [22].

The insulin like protein in camel milk due to the low phosphorylation of the caseins is different from the other milks does not destroy in stomach [70]. Camel milk has little or no allergic potents due to lack of b-lactoglobulin and low amount of b-casein as protein responsible for allergies [11]. The higher concentration of lactoferrin and lysozyme in camel milk than in cow milk and high amount of lactoperoxidase, immunoglobulin G, A and vitamin C resulted in higher antibacterial and antiviral properties than cow milk [4].

Camel milk proteins are effective on diabetes, autism, diarrhea and tumors [34] and it can prevent cardiovascular, nephropathy and retinopathy in diabetic patients [12]. The camel milk has traditionally been used to treat tuberculosis, psoriasis, intestinal disorders and food allergies but scientific researches regarding the camel milk benefits are rare [2].

The unique characteristics of camel milk in treatment of diabetes

The chronic hyperglycemia and diabetes mellitus increases angiotensin II of tissue that induces oxidative stress, endothelial damage, thrombosis, inflammation and insulin resistance and consequently caused to retinopathy, neuropathy, nephropathy, cardiovascular diseases and delay in wound healing [18].

Camel milk has globally been used as antidiabetic in patients and experimental models [9,49]. It is revealed, that camel milk contains insulin like protein and amino acids sequence is enriched with half-cysteine same with insulin, can be absorbed from intestine without being destroyed in the stomach different with other insulin foods sources [70]. The reason is presence of fat micelles in camel milk that protect or cover insulin in acidic environment of stomach and transfer insulin to circulatory system in the diabetic patients [69]. Therefore, it is as a potential therapy for controlling diabetes mellitus 1, high cholesterol level, liver and kidney disease, decrease oxidative stress and improve wound healing. Daily drinking of camel milk may meet about 60% of the insulin in diabetic patients [70,74].

Studies have reported reduction of insulin doses up to 30–35% in type 1 diabetic patients who use camel milk, due to inhibition of high levels of diabetes-inhibitory secretary hormones like TNF- α and TGF- β 1 that stimulate insulin and insulin like receptors [46].

Insulin concentrations in camel milk have significantly depended on the lactation stages as well as temperature and storage conditions [2,63]. Camel milk has immune- modulatory effects on beta-cells of the pancreas and reduces insulin doses required in diabetes 1 patients [2].

How camel milk has the anti-diabetic properties?

Obviously, camel milk effects including; effect on insulin receptor function and glucose transport in the insulin-sensitive tissues; effect on insulin secretion by the pancreatic β -cells, via the survival, growth and activity of the pancreatic cells [21].

Raw camel milk contains insulin and/or insulin-like proteins (52 units' insulin /liter) that are 3 times more insulin like proteins than cow milk absorbed in intestine. These proteins act directly on the insulin sensitive tissues, directly act on the insulin receptors and thereby potentiate its activity and signaling [2].

It is certificated, the specific proteins and bioactive peptides of camel milk that act directly or indirectly on specific cellular pathways and control insulin synthesis and secretion by the pancreatic β -cells [21]. Also, camel milk immunoglobulins have the anti-inflammatory, the anti-apoptotic and the anti-oxidative effects that influence the secretory activity and function of the pancreatic β -cells [44] that these can explain the hypoglycemia effects of camel milk.

Also it is concluded that lactoferrin can be effective on insulin and insulin receptor signaling. On base of studies, lactoferrin has negatively effect on hyperglycemia and positively affect insulin sensitivity and anti-inflammatory responses and activate insulin receptor [60], therefore can be involved in the transport and the glucose uptake by the insulin-sensitive tissues through the membrane glucose transporter 4 and or direct positive modulation of this transporter activity [35].

On base of studies, camel milk may have a hypoglycemic action by negative modulation on the glucagon receptor and glucagon secretion by the α -cells pancreas or inhibiting glucose release from liver [21].

Camel milk, camel milk whey proteins hydrolysates and bioactive peptides inhibit the key enzymes that indirectly control the secretion of insulin such as the dipeptidyl peptidase IV [61]. The identified bioactive peptides and whey proteins of camel milk have the potential for their binding to modulation of GIP and GLP-1 receptors similar with the insulin receptor [21].

It is evident that defects in redox and the immune systems caused to destruction of the β -cells pancreatic resulting in diabetes mellitus. Many studies reported the beneficial effects of camel milk and its proteins on the redox and the immune systems and anti-inflammatory and the anti-oxidative actions of camel milk and positive impact on the function of the pancreatic β -cells and insulin secretion and prevent diabetes mellitus [52]. Other studies also reported the beneficial effects of camel milk and whey proteins on B and T cell proliferation and modulate immunity [48] led to decrease in the pathological and histological alterations of the pancreas with an improvement in insulin secretion and glycaemia [53].

Moreover, camel milk decrease β -cell damages because of immunoglobulins and protective proteins (lactoferrin and lactoperoxidase that resistant to digestion by pepsin in the stomach) and antioxidant agents; like zinc and vitamin C and B₃ [7]. High levels of antioxidant factors such as zinc, selenium and other trace elements in camel milk prevent lipid peroxidation, via enhancing the anti-oxidant system or by glutathione peroxidase activation [56].

As high production of oxidative stress factors in diabetes can lead to deleterious effects including damage to polyunsaturated fatty acids in membrane lipids, proteins, DNA and eventually cell death [39], can reduce of free radical and have anti-inflammatory effects and immune modulatory functions on the β -cells of the pancreas [29,46]. Micro minerals such as zinc in the camel milk have a key role in insulin secretion activity from β -cells of pancreas [70].

Overall, most of the beneficial effects of camel milk on type 1 diabetes through reduction of fasting blood glucose, hemoglobin A1c (HbA1c) and the doses of insulin injection [56]. Metabolic diseases such as hyperglycemia, hyperlipidemia and insulin intolerance can be prevented by the antioxidant properties of camel milk [9,12].

One of the main causes of β -cell dysfunction in type 2 diabetes mellitus is the effect of oxidative stress that camel milk is helpful to reduce reactive oxygen by higher contents of vitamin C [67].

Camel milk and wound healing in diabetic patients

Delay in wound healing is one of the most serious diabetes issues due to low level of neutrophils. But, in the diabetic condition, these cells can't reach to their maximum level within six hours [23]. Reduction of oxidative stability and immune response in diabetic patients is another big issue [25]. Many recent studies using camel milk whey proteins or derived peptide fractions showed they improved wound healing potential in diabetic animals. The anti-oxidative activity of camel milk whey proteins enhances the proliferation of immune cells and accelerates the wound healing process during diabetes [25].

It is revealed that camel milk and whey supplementation improves wound healing by increasing GSH synthesis and improving the function of the cellular antioxidant defense system or antioxidant protection [19].

Maybe the reason is the reduction of the pro-inflammatory cytokines like TNF- α and IL-6 and the restoration of the anti-inflammatory IL-10 [23]. Also the effect of camel milk components in promoting wound healing due to their anti-microbial properties and their stimulatory effects on wound repair and immune cells such as neutrophils and macrophages [23].

Many key cell surface receptors such as chemokine and toll-like receptors may be the targets for camel milk proteins/peptides of camel milk. Therefore, camel milk proteins may be promising food for the immune-modulation in chronic diabetic wounds [21].

It is reported whey protein in camel milk, serum albumin, immunoglobulin, lactoferrin, α -lactalbumin and peptidoglycan due to anti-oxidant functions help in healing process [40].

Camel milk and liver, kidney failures and cardiovascular parameters of diabetic patients

The camel milk can normalize renal and liver failures in diabetic patients. In these patients, the alanine aminotransferase (ALT) and aspartate aminotransferase (AST) may recover 41 and 48%, respectively [16]. Decrease in triglycerides, total cholesterol and LDL (Low density lipoproteins) and increase in HDL (high density lipoproteins) have been observed by consumption of camel milk [26]. The researcher concluded that using raw camel milk led to improvements in liver functions and ALT and AST enzymes activity by 47.3 and 19.2%, respectively, as compared to diabetic rats [51].

Hamad, *et al.* [36] reported using of camel milk in diabetes rats for 6 month improved activity of ALT and AST enzymes by 41 and 38%, respectively, also decreasing of urea, uric acid and creatinine observed. Hypoglycemia effects of camel milk improved kidney and liver function in compared to cow and buffalo milks.

Full fat camel milk inhibits lipolysis as a potential risk factor for diabetes mellitus. Higher concentrations of linoleic acid and polyunsaturated fatty acids along with vitamins as antioxidants remove free radicals and keep the tissues specifically β -cells of pancreas safe from injuries [19]. Nephropathy, proteinuria and cardiovascular challenge appear to be major complications in type 1 and 2 diabetes mellitus [59].

Significant decrease in microalbuminuria has been reported in type 1 diabetes mellitus patients (119 - 22.52 mg/dL) due to six month's continuous use of camel milk in diet [9]. Similarly, consumption of camel milk just for 24h reduces microalbuminuria in diabetes mellitus patients [57]. There are also solid evidences of normalization of uric acid, creatinine and urea as renal function parameters [16]. Casein and peptides of camel milk have ACE inhibitory activity that is proved as antihypertensive agents to reduce urinary albumin excretion [16].

In study of Agrawal [9], using of camel milk (500 ml/day) by type 1 diabetes patients for six months, showed camel milk improve microalbuminuria levels (119.48 ± 1.68 to 22.52 ± 2.68) in diabetic patients, but the mechanism behind this effect is still unknown.

It is concluded that treatments with raw camel milk, pasteurized, stored at 4°C for two and four days, freeze-dried at -20°C and reconstituted freeze-dried decreased the levels of HbA1C, urea and creatinine as compared with diabetic group [51].

The researchers used 500 mL raw camel milk for 16-week in type 1 diabetic patients (average age 20 years). Results declared HbA1c, lipid profile, creatinine clearance and albumin excretion in 24-hour urine decreased, that camel milk can control metabolic function of type 1 diabetics, by elevating endogenous insulin secretion [57]. It is revealed high amount of vitamin C in camel milk has important role especially in controlling micro vascular and nephropathy in type 1 diabetic patients [67].

Camel milk processing and diabetes

Raw camel milk consumption is more common and beneficial, and heat may destroy its therapeutic efficacy [24,71], But without acid fermentation or heat, storage at high temperature with low hygiene conditions may increase foodborne diseases and spoil camel milk [30]. Therefore, heat treatment should be used, but destroying vitamins, casein and whey proteins by heating reduce the nutritional value of camel milk [58]. Camel's α -lactalbumin and peptidoglycan recognition protein is also affected by heat treatment. Cleavage of disulphide bridges can denature α -lactalbumin in several ways [33]. Vitamin C can be quickly destroyed by heating. The anti-diabetic properties of camel milk may be destroyed due to heating [54].

Other hygienic and simple cooling methods increase the maximum shelf life of camel milk. Selected starter cultures or enzymes and nanofiltration or encapsulation methods can be used to enrich or release bioactive peptides of camel milk [62].

Unpasteurized camel milk decreased diabetic whereas in the case of pasteurized milk, a minimum change was observed during 4 weeks in induced rats [28].

Heat treatments, cooled, freeze-dried and drying of camel milk may be leads to decrease the insulin concentration of camel milk, which resulted in decrease the efficiency of camel milk to lower blood glucose level [51].

Elagamy [27] indicated that heating camel milk at 100°C decreased α -lactalbumin, IgG, lysozyme and lactoferrin. Also the biological activity of these protective proteins of camel milk at 75°C for 30 minutes was higher than 100°C. Attia, *et al.* [20] demonstrated that heat treatment of camel milk caused to demineralization of the caseins micelle and increase of soluble Ca amount. Treatment with raw camel milk, pasteurized, stored at 4°C for two and four days and freeze-dried at -20°C were increased significantly glutathione levels in diabetic group as compare with without camel milk group [51]. Diabetic rats treated with boiled camel milk did not show any significant effect on liver and kidney functions [51].

Agrawal, *et al.* [10] reported that insulin/insulin like protein activity decreases by boiled camel milk. The highest reduction in glucose level of diabetic rats is for raw camel milk and therapeutic activity of camel milk destroyed after heating and boiling at 100°C [51].

Raw camel milk by 500 mL reduces the blood glucose level of diabetic rats by 55% compared to raw bovine milk which was 43% [28].

Consuming of raw camel milk led to significant decrease in insulin intake from 32.5 units/day to 17.5 units/day [12]. Feeding 500 mL camel milk in type 1 diabetes patients for 6 months had no significant changes in mean insulin and plasma glucose, but decreased mean of required insulin dose (from 41.6 to 28.3 U/day) [56].

Agrawal, *et al.* [13] observed decrease of risk factors incidence, blood glucose, fasting blood glucose and HbA1c and 30% reduction in required insulin in type 1 diabetes patients by 500 mL raw camel milk, regularly.

Using of 500 ml/day camel milk for six months in diabetes patient's decreased daily insulin that before treatment with camel milk was 93.50 unit/kg and after camel milk supplementation was 60.64 unit/kg [9].

The researchers used 500 mL raw camel milk for 16-week in type 1 diabetic patients and observed serum insulin increased and consequently diabetes decreased [57].

Some researches on using camel milk in diabetes patients

Researches showed the levels of total cholesterol and triglyceride of liver tissue significantly decreased for diabetic rats treated with raw camel milk and camel milk stored in 4°C for two days within 8 week as compared to the diabetic group. But therapeutic efficiency of camel milk after heating at 100°C (boiled camel milk) will be removed [51].

Feeding raw camel milk increased insulin levels ($10.00 \pm 2.61 \mu\text{U/ml}$) in the diabetic rats compared to the untreated group ($5.51 \pm 2.69 \mu\text{U/ml}$) [51].

The researcher reported 500 mL raw camel milk for 16 week in type 1 diabetic patients (average age 20 years) decreased daily insulin dose and fasting blood sugar that camel milk can improve metabolic control of young type 1 diabetics, by boosting endogenous insulin secretion [57].

Diabetic rats were fed with raw camel milk, decreased blood glucose, triglycerides, total cholesterol, LDL and VLDL and increased HDL cholesterol as compared with untreated diabetic rats [42]. Consumption of raw camel milk for 3 weeks in induced diabetic rats showed mean blood glucose levels were higher than control and cow milk groups [5].

Diabetic rats was received raw camel milk for four weeks, significantly increased insulin hormone, insulin growth factor 1(IGF-1) and glutathione peroxidase (GPx) as compared to the untreated rats [5].

Raw camel milk for 60 days in induced diabetes rats reduced blood glucose and hematological parameters and improved degenerative changes in uterus, liver and kidneys [72].

Researchers used raw camel or pasteurized camel milk for 4 weeks in diabetic rats that results showed significant decrease in mean blood sugar in diabetic rats by using raw camel milk was more than pasteurized camel milk. This study proved hypoglycemic activity of camel milk decreases after pasteurization [5].

Alloxan-induced diabetic rats treated with raw camel milk significantly decreased blood glucose, total cholesterol, triglyceride, LDL, VLDL, cholesterol and increased HDL as compared with diabetic untreated group [37].

Study on raw camel milk consumption by 500mL to type 1 diabetic for 52 week showed in the group receiving camel milk, there was a significant reduction in HbA1c, mean blood glucose and required insulin dose [10].

In one study in Rajasthan, it is proved the prevalence of type 2 diabetes was 5.2% among tribal population and 0.7% in non-tribal consumed camel milk. Prevalence of pre-hypertension and hypertension was 36.4% and 19.7% among tribals and 23.5% and 17.5% in non-tribal population [66].

To evaluate effects of 500 mL raw camel's milk in type 1 diabetes patient for 3 month, significant reduction in insulin requirements showed camel milk is as a therapy in management of type 1 diabetes [29].

Induced diabetic rats treated with camel milk peptides for a week, increased antioxidant enzymes like glutathione peroxidase and improved wound healing in diabetic conditions [25].

Type 1 diabetes patients received 500 ml camel milk for 3 months. After 3 months there was significant improvement in fasting blood sugar and HbA1c levels and significant reduction in insulin requirement by 30% reduction [3].

Type 2 diabetes consumed 500 mL either pasteurized camel milk or cow milk for two months. Mean insulin concentration was significantly increased from 64.59 to 84.03 pmol/L by the camel milk, but no significant differences were shown in fasting blood sugar, lipid profile, blood pressure and insulin resistance between the two groups [25]. These results suggest that camel milk might control insulin level in patients with type 2 diabetes [25].

Supplementation of camel milk for 4 weeks in diabetic animals significantly decreased blood glucose and improved microalbuminuria compared to diabetic control animals. Camel milk may control diabetic nephropathy and improvement of kidney function [32].

In separate clinical trials for 3 months, 6 months and 1 year, consuming camel milk showed significant hypoglycemic effect and reduced insulin requirement at the end of 2 years in patients in comparison with control group [12,14].

The using of camel milk compared with cow milk in patients with type 2 diabetes after 2 months, showed significant increase in serum insulin concentration, blood glucose and the dose of required insulin in the camel milk group than the cow milk group [55].

Agrawal, *et al.* [12] reported reducing FPG, HbA1c and daily insulin dose required in type 2 diabetic patients by camel milk.

The results showed that daily drinking 500 mL raw camel milk leads to improve blood glucose levels and reduce insulin doses [41]. Another study in Yemen on 50 type 1 diabetic patients clearly showed that camel milk mixed with insulin was an effective supplementation, as adjunctive therapy in management of type 1 diabetes and the daily doses of insulin can be reduced up to 66% (20 units/day) after 12 week of treatment [29]. The new studies have also shown that camel milk improves the liver and the kidney functions in diabetic rats [36,70].

Camel milk contains higher concentrations of insulin (58.67 ± 2.01 UL) compared to cow's milk (17.01 ± 0.96 UL) and insulin-like growth factor-I [36].

Shori [70] concluded that camel milk has a powerful effect in reducing blood glucose levels and insulin requirement and it decrease cholesterol levels, liver and kidney diseases and oxidative stress and improve wound healing.

Fermented camel milk significantly reduced fasting blood sugar, postprandial glucose, HbA1c and HOMA-IR in type 2 diabetes patients but no hypoglycemic effect on glucose tolerant was detected [31]. No significant elevation of fasting serum insulin by fermented camel milk consumption observed [31].

Elevation of serum insulin is reported in Meena, *et al.* [53] study on type 1 diabetic rats receiving camel milk, also Manaer, *et al.* [50] reported C peptide levels in type 2 diabetic rats fed with Shubat (traditional fermented camel milk) significantly increased.

In study of Agrawal, *et al.* [8], prevalence of diabetes in Raica community consuming camel milk was 0%; Raica community not consuming camel milk was 0.7%; non-Raica community consuming milk was 0.4% and non-Raica community not consuming camel milk was 5.5%. Therefore consumption of camel milk was highly significant as protective factor for diabetes [8].

The efficacy of Sudanese Camel dromedary's raw milk on insulin doses in type 1 diabetic patients for 12 months have been evaluated. On base of result 0.5 L/day of raw dromedary's camel milk has caused significant reduction in insulin dosages and fasting blood sugar was reduced by 67%, postprandial blood sugar was reduced by 65% and HbA1c was reduced by 37% [1].

Conclusion

Camel milk administration can have positive effects on glycemic control, by reducing fasting blood sugar, insulin resistance and improving lipid profiles in diabetes patients. In most studies, the recommended dose of camel milk was 500 mL/day which led to improvement of diabetes markers after 3 months in diabetes patients. Also camel milk can prevent liver and kidney failures derived from diabetes mellitus and improve wound healing. Although the high amount of digestion resistant insulin and high level of antioxidants as anti-inflammatory factors are the possible explanation for anti-diabetic effect of camel milk. Maybe the variation in camel milk composition and clinical characteristics of patients, short duration of intervention and low sample size could be the reasons of inconsistent results in different studies.

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