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## Review Article

# Camel milk as a potential therapy for controlling diabetes and its complications: A review of *in vivo* studies



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## ABSTRACT

Diabetes is a condition in which there is an elevation of blood glucose. Insulin, which is produced by the pancreas, is an important hormone needed by the body because it enables glucose to be transported into cells. Under the diabetic condition, the cells may not respond properly to insulin or the body does not produce a sufficient amount of insulin, or both. This situation will cause glucose accumulation in the blood that leads to major complications. Oral insulin therapy has been used for many years; however, coagulation in an acidic environment decreases the efficacy of insulin by neutralizing its actions. Several researchers have found that camel milk can be an adjunct to insulin therapy. It appears to be safe and effective in improving long-term glycemic control. Therefore, the aim of this study was to review *in vivo* studies on the effect of camel milk as a potential therapy for controlling diabetes and its complications such as high cholesterol levels, liver and kidney disease, decreased oxidative stress, and delayed wound healing.

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## 1. Introduction

Diabetes mellitus (DM) is a disease characterized by a high level of blood sugar (i.e., glucose) that results from the failure of the body to produce sufficient insulin (type 1 diabetes) or from the inability to respond properly to the insulin that has been produced by the pancreas (type 2 diabetes) [1]. The global prevalence of DM for all age groups was estimated at 2.8% in 2000, and is expected to rise to 4.4% in 2030 [2]. A major part of this increase is expected to occur in Third World countries with the number of diabetics increasing to 35% in 2025 among

those aged 20 years or older. Hyperglycemia is a metabolic disorder (i.e., the circulating blood glucose level is excessive in the blood plasma) that results from defects in insulin secretion, insulin action, or both. The function of insulin is to lower the level of blood glucose, which occurs especially after eating. Chronic hyperglycemia is associated with long-term damage and with the dysfunction and failure of various organs—especially the eyes, heart, nerves, kidneys, and blood vessels; it is linked with hypertension [3]. However, metabolic control can be improved through diet and physical activity with or without antidiabetes drugs, which significantly decrease the risk of complications [4].

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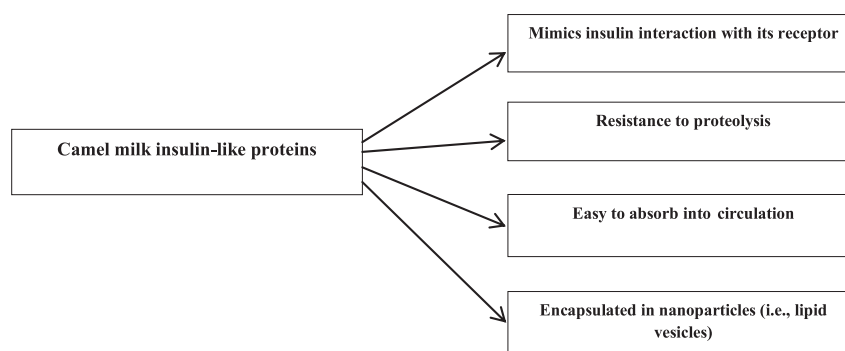
Camel milk achieves the nutritional requirements of the minor population in harsh and arid parts of Africa and Asia. It is common practice in these regions to recommend the consumption of camel milk in its fresh state or its sour state [5] for the general treatment of diabetes [6]. It is different from the milks of other ruminants in that it does not form coagulum in an acidic environment [7]. This is attributed to the low degree of phosphorylation of the caseins in camel milk [5,7]. From a nutritional point of view, camel milk has a low cholesterol content and its fat primarily consists of polyunsaturated fatty acids that are completely homogenized and gives the milk a smooth white appearance [6]. The lactose in camels milk exists in concentrations of 4.8%, but this milk sugar is surprisingly easily metabolized by people who have lactose intolerance [8]. A possible explanation for this is that camel milk produces less casomorphin, which provokes less intestinal motility; this would cause lactose to be more exposed to the action of lactase [9]. Camel milk contains a low amount of  $\beta$ -lactoglobulin [10,11] and  $\beta$ -casein [11]. Because these two protein components are responsible for allergies, camel milk has little or no allergic effects [12]. Furthermore, camel milk has higher antibacterial and antiviral properties than cow milk. This is partially because of the higher concentration of lactoferrin in camel milk (220 mg/L) than in cow milk (110 mg/L) and the higher concentration of lysozyme in camel milk (288  $\mu$ g/100 mL) than in cow milk (13  $\mu$ g/100 mL) [12–14]. In addition, camel milk has a higher level of lactoperoxidase, immunoglobulin G, and secretory immunoglobulin A with antimicrobial activity [12–14], and higher vitamin C content [15,16]. Various research studies have been performed to examine the efficiency of camel milk to treat diabetes. The objective of this research was to review *in vivo* studies on the effect of camel milk as a potential therapy for controlling diabetes (type 1) and its complications such as high cholesterol level, liver and kidney disease, decreased oxidative stress, and delayed wound healing.

## 2. Antihyperglycemic effect of camel milk

Diabetes mellitus is a serious disease with multiple complications that is rising dramatically worldwide. Three-fourths of the world population cannot afford allopathic medicine and thus has to rely on naturopathic medicine, which is basically derived from natural products of animals and plants [17]. Once diabetic patients start insulin therapy, they have to take it permanently and usually insulin dose continue to increase as time progresses. Clinical research on the use of camel milk by patients with type 1 diabetes has indicated that drinking camel milk daily decreases the blood glucose level and reduces insulin requirement by 30% [18]. It appears that camel milk provides an insulin-like protein in a different form than in other mammals and/or delivers some other therapeutic compounds that boosts the health of diabetic patients. However, the mechanism is not yet fully understood. Mucosal surfaces are a common and suitable route for delivering drugs such as peptides and proteins to the body. However, the oral administration of insulin is incapable of overcoming mucosal barriers and is degraded by digestive enzymes before it enters the bloodstream [19]. As a unique feature of camel milk, the

insulin-like protein could be protected in the stomach and absorbed efficiently into blood stream to reach the target. This is because camel milk does not coagulate in an acidic environment and it has a higher buffering capacity than the milk of other ruminants [13]. In addition, since no differences noted in the sequence of camel milk insulin-like protein and its digestion pattern compared to other sources of milk to overcome the mucosal barriers, camel milk insulin-like protein could be protected in the stomach by nanoparticles (e.g., lipid vesicles) to reach the target [20]. Camel milk also contains approximately 52 micro unit/ml of insulin-like protein compared to cow milk (16.32 micro unit/ml) which mimic insulin interaction with its receptor, and it has a higher content of zinc [21] which has a key role in insulin secretory activity in pancreatic beta cells. Beg et al [22] found that the amino acid sequence of some camel milk protein is rich in half cystine, which has a superficial similarity with the insulin family of peptides. In addition, compared to milk from other mammalian species, camel milk possesses a different casein content, a higher amount of polyunsaturated fatty acids (C18:1–C18:3), larger lipid micelles, and a higher amount of vitamin B<sub>3</sub> [23,24]. Furthermore, the small size and weight of camel milk immunoglobulin may offer enormous potential through interaction with the host cell protein and cause an induction of regulatory cells and finally result in a downward regulation of the immune system and  $\beta$ -cell salvage [18,25]. Some researchers suggest that the insulin-like protein in camel milk has the ability to resist proteolytic digestion, which makes its absorption into circulation faster than insulin-like protein from other milk sources (Fig. 1).

A previous study shows that raw camel milk has the ability to reduce blood glucose level by 55% in diabetic rats, compared to raw cattle milk (43%) [15]. Agrawal et al [26] studied the hypoglycemic activity of raw and pasteurized camel milk in streptozotocin (STZ)-induced diabetic rats. Based on the results, the blood glucose levels in diabetic rats treated with raw camel milk decreased from  $169.68 \pm 28.7$  mg/dL to  $81.54 \pm 11.4$  mg/dL ( $p < 0.02$ ) after 4 weeks of treatment, whereas diabetic rats treated with pasteurized camel milk showed a slight decrease from  $135.45 \pm 20.91$  mg/dL to  $113 \pm 29.09$  mg/dL (Table 1) [13,14,26–30]. A new study was conducted by Sbou et al [27] to evaluate the effect of camel milk administered for 5 weeks to alloxan-induced diabetic dogs. A significant reduction in the level of blood glucose from  $10.88 \pm 0.55$  mmol/L to  $5.77 \pm 0.44$  mmol/L occurred in dogs treated with 500 mL of camel milk for 5 weeks (Table 1). The effect of camel milk in comparison with biosynthetic insulin treatment in experimentally induced diabetes in rabbits was investigated by El-Said et al [14]. They found that the mean serum insulin level was significantly higher ( $7.9 \pm 0.9$   $\mu$ IU/mL) for diabetic rabbits treated with camel milk for 4 weeks than for untreated diabetic rabbits and insulin-treated diabetic rabbits ( $2.4 \pm 0.1$   $\mu$ IU/mL and  $5.6 \pm 0.4$   $\mu$ IU/mL, respectively). In diabetic rabbits, treatment with camel milk was able to lower the glucose level more greatly than biosynthetic insulin (Table 1). Al-Numair et al [28] report the antihyperglycemic effect of camel milk on STZ-induced diabetic rats. They found that STZ-diabetic rats that were fed camel milk at the optimum dose of 250 mL/d for 45 days showed a significant



**Fig. 1 – The properties of camel milk insulin-like proteins.**

reduction in plasma glucose level from  $292.38 \pm 19.20$  mg/dL to  $141.57 \pm 12.82$  mg/dL. In addition, a higher plasma level of insulin ( $p < 0.05$ ) was present in STZ-diabetic rats treated with camel milk, compared to untreated diabetic rats (Table 1). A significant reduction ( $p < 0.05$ ) in blood glucose levels (approximately 30%) has been reported in diabetic rats treated with camel milk for 6 weeks [29]. However, the blood glucose levels in diabetic rats treated with cow or buffalo milk showed an improvement of only 12% or 10%, respectively [29]. A similar study was conducted by Khan et al [30] to study the possible antidiabetic effects of camel milk in STZ-induced diabetic rats. They report that the blood glucose levels of diabetic rats that were fed fresh camel milk reduced significantly from 560 mg/dL to 235 mg/dL after 30 days (Table 1). Streptozotocin-induced diabetic mice treated with camel milk whey protein displayed a significant reduction in blood glucose levels from  $411 \pm 37$  mg/dL to  $261 \pm 25.5$  mg/dL after 2 weeks [31]. Throughout the period of study, diabetic mice treated with camel milk whey protein had significantly higher levels of insulin, compared to untreated diabetic mice (Table 1).

Agrawal et al [32] found camel milk had a significant hypoglycemic effect when administered to type 1 diabetic patients as an adjunct therapy for 3 months (Table 2) [18,32,33,35–37]. At the end of 3 months, they observed a significant decrease in insulin doses that were required to achieve glycemic control, and a significant enhancement in hemoglobin A1c level. The mean dose of insulin required before camel milk treatment in the type 1 diabetic patients was  $41.16 \pm 10.32$  units/d. This value gradually reduced to a mean level of  $30 \pm 12.06$  units/d ( $p < 0.002$ ) during 3 months of treatment [32]. In 2005, Agrawal et al [33] determined the long-term efficacy and safety of camel milk as an adjunct to insulin therapy in patients with type 1 diabetes after 1 year. The mean blood glucose level decreased from  $119 \pm 19$  mg/dL to  $95.42 \pm 15.70$  mg/dL ( $p < 0.005$ ) and the mean doses of insulin reduced significantly throughout the study period (Table 2). Another study by Agrawal et al [18] involved 50 newly diagnosed type 1 diabetic patients who were divided in two groups of 25 patients: one group received conventional treatment and the other group consumed 500 mL of fresh camel milk in addition to receiving conventional medical treatment for 12 months. The mean blood sugar level in the camel milk-consuming group reduced from

$115.16 \pm 14.50$  mg/dL to  $100.20 \pm 17.40$  mg/dL, compared to the control group ( $114.40 \pm 17.70$  mg/dL to  $104.00 \pm 15.87$  mg/dL). In addition, the requirement of the daily mean dose of insulin reduced from  $30.40 \pm 11.97$  units/d to  $19.12 \pm 13.39$  units/d in the camel milk-consuming group (Table 2). By contrast, the control group showed no significant difference in the mean dose of insulin required after 1 year. This observation was in agreement with another study conducted by Agrawal et al [34], who reported zero prevalence of DM in the camel milk-consuming Raica community of northwest Rajasthan, India. They stated that people consuming camel milk showed significantly less crude prevalence of DM (0.4%), compared to people who did not consume camel milk (5.5%). Agrawal et al [35] reported a significant reduction ( $p < 0.01$ ) in the mean dose of insulin in type 1 diabetic patients that was required to obtain glycemic control after 6 months of camel milk treatment (from  $41.61 \pm 3.08$  mg/dL to  $28.32 \pm 2.66$  mg/dL). Mohamad et al [36] evaluated the efficacy of camel milk as an adjuvant therapy in young type 1 diabetic patients for 16 weeks. Fifty-four type 1 diabetic patients (average age, 20 years) were divided into two groups of 27 patients in which the first group (i.e., the control) was treated by the usual management (i.e., diet, exercise, and insulin) and the second group was treated with 500 mL camel milk and the usual management. They found a significant difference between the control group and camel milk group after 16 weeks. After 16 weeks of treatment, the fasting blood sugar was decreased from  $227.2 \pm 17.7$  mg/dL to  $98.9 \pm 16.2$  mg/dL, and the required daily insulin dose was reduced from  $48.1 \pm 6.95$  units/d to  $23 \pm 4.05$  units/d. An earlier study reports that camel milk in combination with insulin can be an effective supplementation as an adjunctive therapy in controlling patients with type 1 diabetes, compared to camel milk alone or insulin injection alone [37]. The reduction of fasting blood glucose in type 1 diabetic patients treated with camel milk and insulin was approximately 28% after 3 months, compared to 22% or 11% of patients treated with camel milk alone or insulin alone, respectively (Table 2). Furthermore, the combination of camel milk and insulin reduced the postprandial blood glucose in type 1 diabetic patients by 52%, compared to camel milk alone (30%) or insulin alone (12%) [37]. Some researchers suggest that camel milk can be safely consumed by nondiabetic people or by healthy people [30,38,39].

**Table 1 – Antihyperglycemic effect of camel milk *in vivo* in animal models.**

Refs	Diabetogenic	Model of study	Dosages (daily)	Duration	Blood glucose before	Blood glucose after	Insulin	<i>p</i> *
Agrawal et al [13]	STZ (50 mg/kg body weight by intraperitoneal administration)	Rats (N = 32)	250 mL (raw camel milk)	3 wk	191.33 ± 7.46 mg/dL	86.25 ± 12.77 mg/dL *	ND	< 0.05
Agrawal et al [26]	STZ (50 mg/kg body weight by intraperitoneal administration)	Rats (N = 40)	250 mL (raw cattle milk) 25 mL (raw camel milk) 25 mL (pasteurized camel milk)	4 wk	169.69 ± 28.73 mg/dL 135.45 ± 20.91 mg/dL	110.0 ± 9.97 mg/dL * 81.54 ± 11.43 mg/dL* 113.08 ± 29.09 mg/dL*	ND	< 0.02 < 0.5
Sboui et al [27]	Alloxan (65 mg/kg dissolved in normal saline at a concentration of 100 mg/mL) by intravenous administration)	Dogs (N = 12)	500 mL (raw camel milk)	5 wk	10.88 ± 0.55 mmol/L	5.77 ± 0.44 mmol/L *	ND	< 0.05
El-Said et al [14]	Alloxan (90 mg/kg dissolved in 5 mL of normal saline) via the ear vein	Rabbits (N = 40)	7 mL/kg of raw camel milk	4 wk	528.4 ± 28.2 mg/dL	116.6 ± 11.9 mg/dL *	↑ From 2.4 ± 0.1 to 7.9 ± 0.9 μU/mL*	< 0.05
Al-Numair et al [28]	STZ (40 mg/kg body weight by intraperitoneal administration)	Rats (N = 30)	Biosynthetic human insulin (HuNil) 1.5 IU/kg 250 mL (raw camel milk)	45 d	292.38 ± 19.20 mg/dL	205.7 ± 15 mg/dL *	↑ From 2.4 ± 0.1 to 5.6 ± 0.4 μU/mL*	< 0.05
Hamad et al [29]	STZ (60 mg/kg body weight by intraperitoneal)	Rats (N = 30)	20 mL camel milk + 95 g basal diet 20 mL cow milk+ 95 g basal diet 20 mL buffalo milk+ 95 g basal diet	6 wk	146 ± 9.8 mg/dL 200 ± 11.1 mg/dL 197 ± 10.1 mg/dL	101 ± 9.7 mg/dL * 176 ± 8.9 mg/dL * 177 ± 9.0 mg/dL *	ND	< 0.05
Khan et al [30]	STZ (55 mg/kg body weight by intraperitoneal administration)	Rats (N = 40)	400 mL of raw camel milk	4 wk	520.46 ± 8.90 mg/dL	235.61 ± 7.10 mg/dL *	ND	< 0.05
Badr [31]	STZ (60 mg/kg body weight by intraperitoneal administration)	Mouse (N = 30)	Udenatured camel milk whey protein (100 mg/kg of body weight)	2 wk	411 ± 37 mg/dL	261 ± 25.5 mg/dL *	↑ From 1.7 ± 0.15 to 3.3 ± 0.3 ng/mL*	<0.05

\* = The level of significance at *p* value when compared with data before treatment.

↑ = increase; ND = not detected; STZ = streptozotocin.

**Table 2 – Antihyperglycemic effect of camel milk in type 1 diabetic patients.**

Refs	Dosages (daily)	No. of samples	Duration	Blood glucose before (mg/dL)	Blood glucose after (mg/dL)	Dose of insulin (units/d)	p
Agrawal et al [32]	500 mL raw camel milk	N = 24	3 mo	115.16 ± 7.17	100 ± 16.2 *	↓ From 41.16 ± 10.32 to 30 ± 12.06 *	*p < 0.002
Agrawal et al [33]	500 mL raw camel milk	N = 24	52 wk	119 ± 19	95.42 ± 15.70 *	↓ From 32 ± 12 to 17.83 ± 12.40 *	*p < 0.005
Agrawal et al [18]	500 mL of raw camel milk	N = 24	12 mo	115.16 ± 14.50	100.20 ± 17.40 *	↓ From 30.40 ± 11.97 to 19.12 ± 13.39 *	p < 0.002
Agrawal et al [35]	500 mL of raw camel milk	N = 24	6 mo	128.7 ± 1.17	125.46 ± 1.24 *	↓ From 41.61 ± 3.08 to 28.32 ± 2.66 *	*p < 0.01
Mohamad et al [36]	500 mL raw camel milk	N = 54	4 mo	227.2 ± 17.7	98.9 ± 16.2 *	↓ From 48.1 ± 6.95 to 23 ± 4.05 *	*p < 0.05
El-Sayed et al [37]	500 mL raw camel milk	N = 50	3 mo	199.46 ± 4	155.13 ± 3.5 *	↓ From 55.1 ± 1.4 to 36.2 ± 1.22 *	*p < 0.001
	Insulin treatment			195.6 ± 2.01	173.4 ± 1.66 *	↓ From 50 ± 0.64 to 45.46 ± 0.9 *	
	500 mL camel milk + insulin			205.3 ± 2.16	147.26 ± 1.89 *	↓ From 59.26 ± 0.7 to 20±0.35 *	

\* = The level of significance at p value when compared with data before treatment.  
 ↓ = decrease.

### 3. Antihyperlipidemic effect of camel milk

Diabetes is associated with profound variations in plasma lipids, triglycerides, and lipoprotein profile, and is responsible for vascular complications and an increased risk of heart disease [40,41]. Thus, lowering the cholesterol levels through dietary or drug therapy seems to be associated with a reduced risk of heart disease [42]. Low-density lipoprotein-C (LDL-C) in the human body circulation undergoes reuptake in the liver through particular receptors and is thereby cleared from the circulation [43]. The elevation of LDL levels in the plasma of diabetic patients can be the result of a defect in the LDL-C receptor (i.e., failure in production or function). High-density lipoprotein-C (HDL-C) is protective by reversing cholesterol transport, inhibiting the oxidation of LDL-C, and neutralizing the atherogenic effects of oxidized LDL-C [39]. There is a correlation between the level of very-low-density lipoprotein-C (VLDL-C) and HDL-C. A significant increase in LDL-C and VLDL-C levels may lead to a significant decrease in HDL-C levels. In addition, lower HDL-C levels can also occur because of reduced activity in lecithin-cholesterol acyltransferase (LCAT) [39]. A previous study shows that the administration of camel milk can help decrease the levels of cholesterol in diabetic patients [32,36,37,43].

In one study [27], alloxan-induced diabetic dogs treated with camel milk (Group 1) showed a statistically significant decrease ( $p < 0.05$ ) in the total cholesterol (TC) level from  $6.17 \pm 0.15$  mmol/L to  $4.35 \pm 0.61$  mmol/L after 5 weeks. In this period, diabetic dogs treated with cow milk (Group 2) showed an increase in the TC level from  $5.99 \pm 0.58$  mmol/L to  $7.13 \pm 1.25$  mmol/L (Table 3) [14,27,30,39,44]. However, the diabetic dogs in Group 2 were treated with camel milk instead of cow milk for the next 5 weeks, and showed a 30% improvement in the TC level. Furthermore, diabetic dogs from Group 1 showed an improvement in lipid profile even after 5 weeks of having stopped drinking camel milk [27]. Al-Numair [39] reported that the administration of camel milk is able to reduce hyperlipidemia that is associated with the risk of DM. This study found TC, triacylglycerols (TG), free fatty acid (FFA), phospholipids (PLs), LDL-C, and VLDL-C levels significantly decreased ( $p < 0.05$ ) towards normal levels in plasma and tissues (e.g., liver, kidney, and heart), whereas the plasma HDL-C significantly improved in diabetic rats after treatment with camel milk for 45 days (Table 3). Another study conducted by El-Said et al [14] to evaluate the effect of camel milk on lipid profile in experimentally induced diabetic rabbits was not in agreement with the previous study (Table 3). However, the group of diabetic rabbits treated with camel milk showed a significant ( $p < 0.05$ ) reduction in the TG level from  $603.4 \pm 9.6$  mg/dL to  $524.8 \pm 14.2$  mg/dL after 1 month. To evaluate the protective role of camel milk against dyslipidemia, changes in the lipid profile levels were analyzed in STZ-induced diabetic rats in one study [30]. The results of this study indicated that the levels of TC, TG, and LDL-C were significantly higher ( $p < 0.05$ ) in the control group of diabetic rats and these levels were significantly reduced in the group of rats fed camel milk (Table 3). Other researchers recently studied the hypocholesterolemic effect of Gariss (i.e., fermented camel milk) on the levels of lipid profile of rats [44]. They observed that TG, TC, HDL, and VLDL+LDL were

**Table 3 – Antihyperlipidemic effect of camel milk in *in vivo* animal models.**

Refs	Dosages (daily) & duration	No. of sample	Duration	TG	TC	PLs	HDL-C	LDL-C	VLDL-C	FFA	p *
El-Said et al [14]	7 mL/kg of raw camel milk	Rabbits (N = 40)	4 wk	↓ From 603.4 ± 9.6 to 524.8 ± 14.2 mg/dL	↑ From 274.2 ± 6.6 to 295.9 ± 7.9 mg/dL	↑ From 214.5 ± 41.3 to 364.2 ± 38.4 mg/dL	↓ From 52.1 ± 1.0 to 36.4 ± 3.8 mg/dL	↑ From 119.7 ± 0.4 to 168.8 ± 0.4 mg/dL *	ND	ND	< 0.05*
Sboui et al, [27]	500 mL of raw camel milk 500 mL of raw cow milk	Dogs (N = 12)	5 wk	From 1.03 ± 0.17 to 1.03 ± 0.3 mmol/L ↑ From 1.03 ± 0.17 to 1.14 ± 0.33 mmol/L	↓ From 6.17 ± 0.5 to 4.35 ± 0.61 mmol/L ↑ From 5.99 ± 0.58 to 7.13 ± 1.25 mmol/L	ND	ND	ND	ND	ND	< 0.05*
Al-Numair [39]	250 mL raw camel milk	Rats (N = 30)	45 d	↓ From 157.19 ± 14.14 to 116.40 ± 6.34 mg/dL	↓ From 169.81 ± 10.24 to 98.28 ± 6.36 mg/dL	↓ From 160.99 ± 11.62 to 103.66 ± 9.33 mg/dL	↑ From 34.60 ± 2.57 to 39.03 ± 2.19 mg/dL	↓ From 32.23 ± 2.82 to 24.08 ± 1.26 mg/dL *	↓ From 105.97 ± 7.81 to 38.16 ± 3.25 mg/dL *	↓ From 140.48 ± 10.46 to 80.69 ± 5.63 mg/dL *	< 0.05*
Khan et al [30]	400 mL of raw camel milk	Rats (N = 40)	4 wk	↓ From 167.43 ± 5.8 to 109.23 ± 6.3 mg/dL	↓ From 298.31 ± 12.4 to 196.27 ± 11.9 mg/dL	ND	↓ From 58.43 ± 6.8 to 52.37 ± 5.6 mg/dL	↓ From 191.31 ± 8.4 to 128.34 ± 5.9 mg/dL *	ND	ND	< 0.05*
Ali et al [44]	Fermented camel milk (Gariss) diet formula	Rats (N = 24)	6 wk	↓ From 144.27 ± 4.47 to 68.25 ± 3.30 mg/100 mL	↓ From 135.79 ± 8.74 to 87.93 ± 4.00 mg/100 mL	ND	↑ From 11.66 ± 1.29 to 28.78 ± 1.07 mg/100 mL	ND	ND	ND	< 0.05*

\* = The level of significance at p value when compared with data before treatment.

FFA = free fatty acid; HDL-C = high-density lipoprotein-C; LDL-C = low-density lipoprotein-C; ND = not detected; PLs = phospholipids; TC = total cholesterol; TG = triacylglycerols; VLDL-C = very-low-density lipoprotein-C.

significantly reduced by 52%, 35.3%, 61%, and 53%, respectively, in a group of rats fed a cholesterol-enriched diet supplemented with Gariss for 6 weeks, compared to the control group fed only a cholesterol-enriched diet (Table 3).

An earlier study has shown that no significant changes occurred in the lipid profile after 3 months in diabetic patients (type 1) treated with camel milk [32]. However, Agrawal et al [35] found a significant reduction of LDL-C and TG in type 1 diabetic patients after being treated with camel milk for 6 months (Table 4) [32,35–37]. By contrast, no significant differences in TC, HDL-C, and VLDL levels were shown in diabetic patients after being treated with camel milk (Table 4). Mohamad et al [36] 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, LDL, and VLDL levels after treatment [36]. El-Sayed et al [37] investigated the effect of insulin provided by camel's milk on the lipid profile of type 1 diabetics in comparison with insulin injection alone or camel milk alone. After 3 months, the lipid profile in the type 1 diabetic patients injected with insulin (i.e., the control group) decreased the levels of TG and TC by 9% and LDL-C by 7% (Table 4). The lipid profile conversely decreased significantly ( $p < 0.001$ ) by three-fold for TG and by two-fold for TC and LDL-C in diabetic patients treated with camel milk (Table 4). The diabetic patient group treated with a mixture of insulin and camel milk showed a significant reduction ( $p < 0.001$ ) in TG and TC (approximately 45%) and LDL-C (approximately 30%), compared to control. In addition, the HDL-C level increased significantly ( $p < 0.001$ ) from 41 mg/dL to 49 mg/dL in patients treated with the mixture [37].

#### 4. The effects of camel milk on liver and kidney function

The prevalence of liver disease and increased liver enzyme levels is common in people with DM. Elevation in the levels of liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in diabetic patients reflect the concentration of intracellular hepatic enzymes that have leaked into the circulation and serve as a marker of hepatocyte injury [45]. The beneficial health effects of camel milk were extended to the liver and kidney function. Hamad et al [29] found a significant development in liver function parameters (e.g., ALT and AST activities) appeared within diabetic rat groups treated with camel, cow, and buffalo milk. The greatest improvement was seen in rats fed camel milk: 41% improvement for ALT and 38% improvement for AST. Khan et al [30] evaluated the effects of camel milk on liver function of STZ-induced diabetic rats. The results of their study showed that feeding rats camel milk for 1 month results in a dramatic shift towards a normal level of liver enzymes (ALT and AST) in STZ-induced diabetic rats.

Diabetic nephropathy is originally microvascular in nature and is widely considered an important complication of diabetes. Albuminuria is a well-known predictor of poor renal outcomes [46]. Microalbuminuria (i.e., urine albumin) is defined as levels of albumin ranging 30–300 mg in a 24-hour

**Table 4 – Antihyperlipidemic effect of camel milk in type 1 diabetic patients.**

Refs	Dosages (daily)	No. of samples	Duration	TG (mg/dL)	TC (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)	p
Agrawal et al [32]	500 mL raw camel milk	N = 24	3 mo.	↓ From 66.91 ± 25.6 to 60.16 ± 25.16	↓ From 164.58 ± 20.59 to 158.33 ± 21.55	↑ From 62.58 ± 13.91 to 66.66 ± 11.29	↓ From 92 ± 11.62 to 79.16 ± 17.75*	↓ From 13.5 ± 5 to 12.08 ± 5.08	<0.040*
Agrawal et al [35]	500 mL of raw camel milk	N = 24	6 mo.	↓ From 92.76 ± 0.18 to 31.5 ± 0.17*	↓ From 77.22 ± 0.03 to 76.32 ± 0.04	↓ From 26.82 ± 0.02 to 26.28 ± 0.03	↓ From 65.18 ± 0.14 to 45.54 ± 0.10*	↓ From 6.84 ± 0.02 to 6.3 ± 0.02	< 0.001*
Mohamad et al [36]	500 mL raw camel milk	N = 54	4 mo.	↓ From 170.41 ± 21.68 to 106.91 ± 25.60 *	↓ From 265.33 ± 9.09 to 200.08 ± 11.04*	↓ From 53.00 ± 12.57 to 52.66 ± 10.54	↓ From 102.83 ± 9.6 to 87.08 ± 27.86	↓ From 14.41 ± 4.71 to 13.0 ± 5.44	< 0.05*
El-Sayed et al [37]	500 mL raw camel milk Insulin treatment 500 mL camel milk + insulin	N = 50	3 mo.	↓ From 184 ± 2.1 to 133.6 ± 4.2** ↓ From 193.1 ± 1.7 to 175.7 ± 3.0** ↓ From 182.8 ± 2.15 to 100.8 ± 2.15**	↓ From 251.8 ± 9.3 to 209.2 ± 3.2** ↓ From 271.8 ± 3.35 to 248.6 ± 3.7** ↓ From 283.6 ± 2.56 to 153.3 ± 1.69**	↑ From 44.3 ± 2.0 to 49 ± 1.5* ↑ From 43.1 ± 1.53 to 43.7 ± 1.26 ↑ From 41 ± 1.89 to 48.9 ± 1.22 ( $p < 0.001$ )	↓ From 110 ± 2.9 to 92.4 ± 2.6** ↓ From 109.9 ± 2.45 to 102.6 ± 1.51* ↓ From 103.5 ± 2.91 to 70.6 ± 3.32**	ND ND ND	< 0.001** < 0.01*

\*\*, \* = The level of significance at p value when compared with data before treatment.

HDL-C = high-density lipoprotein-C; LDL-C = low-density lipoprotein-C; ND = not detected; PLs = phospholipids; TC = total cholesterol; TG = triacylglycerols; VLDL-C = very low density lipoprotein-C.

urine collection [47]. Camel milk has potential role in controlling microalbuminuria levels in type 1 diabetic patients [35]. A significant reduction ( $p < 0.001$ ) in microalbuminuria levels has been reported (from  $119.48 \pm 1.68$  mg/dL to  $22.52 \pm 2.68$  mg/dL) in type 1 diabetic patients after adding camel milk to the usual diet for 6 months. Mohamad et al [36] similarly found that the microalbuminuria level decreased from  $92.08 \pm 15.18$  to  $75.75 \pm 3.17$  after 24 hours in type 1 diabetic patients treated with camel milk. Furthermore, kidney function parameters (e.g., levels of uric acid, urea, and creatinine) were enhanced significantly to the normal level in diabetic rats fed camel milk [29,30].

## 5. Effect of camel milk on oxidative stress in diabetes

Oxidative stress and its subsequent damage happen when antioxidant defense mechanisms fail to efficiently counter endogenous or exogenous sources of reactive oxygen species (ROS) [48]. Increased oxidative stress may contribute to DM and to the development of vascular and neurologic complications of the disease [49]. Thus, the control of ROS production is required for physiologic cell function. Reactive oxygen species in cells are neutralized by antioxidant defense mechanisms such as the enzymes superoxide dismutase (SOD), catalase, and glutathione peroxidase. The existence of hyperglycemia may induce the increased production of ROS via nonenzymatic glycation, glucose autoxidation, and alterations in polyol pathway activity with subsequent influence on the whole organism [48]. The most important indicators of oxidative stress are the increased level of lipid peroxidation products and in specific malondialdehyde [50].

Low levels of antioxidant enzymes increase the vulnerability to oxidative stress owing to reduced antioxidant defense mechanisms. This results in the damaging effects of free radicals that could have an essential role in DM. Furthermore, increased oxidative stress in diabetic patients reduces the levels of nonenzymatic antioxidants such as glutathione, vitamin E, and vitamin C [51], which subsequently damages metabolic pathways and may contribute to the development of diabetic complications.

The protective effects of camel milk may be attributed to its antioxidant activity [52–55] and probably has chelating effects on toxicants [24]. It has been reported that camel milk possesses high levels of vitamins (e.g., A, B<sub>2</sub>, C, and E) and is rich in mineral content (e.g., sodium, potassium, copper, magnesium, and zinc) [24,56]. The aforementioned vitamins are antioxidants that are useful in preventing tissue injury associated with toxic agents such as STZ [57]. In addition, the high minerals content in camel milk [56] may act as antioxidant, and thereby remove free radicals [58–60]. Because camels prefer grazing on natural vegetation—in particular, desert bushes, salty plants, and herbs—their diet may provide some of the phytochemicals excreted in camel milk and give additional benefit to diabetic patients treated with camel milk.

El-Said et al [14] evaluated the effect of camel milk on oxidative stress in induced diabetic rabbits. The diabetic rabbits group treated with camel milk showed significant improvements ( $p < 0.05$ ) in the levels of malondialdehyde,

catalase, and glutathione ( $5.6 \pm 0.3$  nmol/mL,  $377.5 \pm 4.2$  U/L, and  $10.1 \pm 0.7$  mg/dL, respectively), compared to untreated diabetic rabbits ( $8.7 \pm 0.2$  nmol/L,  $204.7 \pm 17.9$  U/L, and  $8.6 \pm 0.6$  mg/dL, respectively). Because SOD is decreased in diabetes as a result of its consumption during the conversion of superoxide anions into hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), which prevents the cells from further generating free radicals [61]. Camel milk showed the ability to increase SOD in diabetic rabbits [16], diabetic mice [31], and autistic children [62].

## 6. The effect of camel milk on wound healing process in diabetes

Wound healing is a normal biological process in the human body. This healing process is commonly classified into four phases: hemostasis, inflammation, proliferation, and remodeling. A successful wound healing must pass all four phases in the accurate sequence and time frame. Improper or impaired wound healing can occur by certain factors such as desiccation, infection or abnormal bacterial presence, maceration, necrosis, pressure, trauma, and edema [63].

Delayed wound healing occurs in patients with diabetes and is one of the most serious diabetes-associated complications. The main factors for improper or impaired wound healing in diabetic patients are the presence of replicating organisms such as bacteria within the wound. Milk whey proteins accelerate wound healing in diabetics by enhancing the immune response of wounded tissue cells and by alleviating some diabetic complications [31]. Camel milk contains a varied group of proteins such as serum albumin,  $\alpha$ -lactalbumin, immunoglobulin, lactophorin, and peptidoglycan recognition protein [64]. Recent studies have indicated that camel milk increases the antioxidant activity in the body and showed a therapeutic effect on the treatment of oxidative stress-associated diseases [16,62].

Badr [31] demonstrated that camel milk whey proteins significantly reduced the wound size in treated STZ-induced diabetic mice for 1 month. This result was correlated with various histopathological findings such as increased epithelization activity, angiogenesis, granulation tissue formation, and extracellular matrix remodeling. Hydroxyproline is a primary component in collagen. A significant restoration of hydroxyproline content has been reported after the oral administration of camel milk whey proteins in diabetic mice [31]. The increased level of collagen may strengthen the regenerate tissue in diabetic mice. The previous finding was in agreement with Al-Numair et al [28] who found that treatment with camel milk elevated the levels of hydroxyproline and total collagen content towards normal level in the tail tendon of STZ-diabetic rats.

## 7. Conclusion

Based on evidence-based reviews of research findings on the use of camel milk in diabetes management, it can be concluded that camel milk has a powerful effect in reducing blood glucose levels and insulin requirement, and it limits diabetic complications such as elevated cholesterol levels, liver and kidney diseases; decreased oxidative stress; and delayed wound healing. Camel milk is safe and efficient in



improving long-term glycemic control and can provide a significant reduction in the dose of insulin required by type 1 diabetic patients. Therefore, the daily consumption of camel milk may reduce the risk of diabetes. Camel milk is able to pass through the acidic environment of the stomach and be absorbed into the blood stream. Therefore, it can be included in the preparation of oral insulin to avoid coagulation in the stomach that occurs in milk from other mammalian sources. In addition, further studies are needed to isolate the actual bioactive peptides in camel milk that are similar in producing the insulin effect and responsible for reducing blood glucose in diabetes. Furthermore, fermentation of camel milk in the presence of probiotic bacteria could increase the potential therapy of camel milk to control diabetes. Thus, further *in vitro* and *in vivo* studies are highly recommended.

### Conflicts of interest

The author declares no conflicts of interest.

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