

CAMEL MILK AND IT'S APPLICATIONS IN TREATMENT OF DIABETES: SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Camel (*Camelus dromedarius*) milk has emerged as a plausible alternative treatment for diabetes. This systematic review and meta-analysis is aimed to report on the treatment applications of camel milk in diabetic patients. A comprehensive literature search was performed on PubMed.gov, Google Scholar and Cochrane Central Register of Controlled Trials (CENTRAL) databases to identify all published randomised clinical trials, clinical trials and experimental studies published within the past twenty years. The systematic review was conducted using a PROSPERO protocol prepared following the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Nine studies were included in the systematic review. In a fixed-effects model, we conducted measurements and obtained the following results: the mean difference (MD) for haemoglobin A1c% (HbA1c%) was -0.85% with a 95% confidence interval (CI) of [-1.51, -0.18]; the MD for blood glucose in humans was -5.73 mg/dl with a 95% CI of [-14.92, 3.47]; the standard MD for blood glucose in rats was -5.73 with a 95% CI of [-14.92, 3.47]; the MD for plasma insulin was -5.73 with a 95% CI of [-14.92, 3.47]; and the MD for BMI was -0.22 with a 95% CI of [-1.09, 0.65]. Despite the high level of heterogeneity in the included studies, the findings had overarching evidence with high significance indicating that camel milk improves HbA1c% among patients with diabetes. We recommend that health sectors should properly position foods like camel milk between mainstream treatments and conventional foodstuffs.

Key words: Camel milk, diabetes, meta-analysis, review

In humans, diabetes is one of the most common chronic diseases. The World Health Organisation (WHO) found that between 2000 and 2016, diabetes was a major factor in the increase in premature mortality rates (deaths before the age of 70). Premature deaths in high-income countries due to diabetes fell between 2000 and 2010 but began rising again between 2010 and 2016 (WHO, 2021). During both periods, diabetes-related premature mortality increased in low- and middle-income countries. About 8.5% of the global population aged ≥ 18 had diabetes in 2014. Nearly half (48%) of all people died from diabetes before the age of 70, according to a WHO report in 2019 (WHO, 2021). However, between 2000 to 2016, the risk of death from non-communicable diseases, including diabetes among people aged 30–70 was reduced by 18% (WHO, 2021).

Studying diabetes is crucial for the significance of therapy allocation and informing community health services regarding the disease's dos and don'ts.

Besides, reducing the prevalence of diabetes has been the main focus of most healthcare organisations. As reported by WHO, the prevalence of diabetes is affected low- and middle-income regions. These regions make up more than 80% of the global population living with diabetes (Mendenhall *et al*, 2014).

Type 1 and type 2 diabetes are the most dominant forms of diabetes. Type 1 diabetes is an immune-mediated, specifically autoimmune or idiopathic disease that attacks and damages insulin-producing beta cells of the islets Langerhans in the pancreas. As a result of damaged insulin-producing beta cells, the patient begins to experience a shortage of insulin (Turner and La Gruta, 2022). Type 2 diabetes, also called insulin-independent diabetes, is caused by defects in insulin receptors, diminish insulin release, or both.

Today, there are several treatment options in the form of oral (e.g., metformin, sitagliptin and

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sotagliflozin) and injectable (e.g. insulin, semaglutide and tirzepatide) medications to manage diabetes. Lifestyle and diet adjustments are also widely applied for patients with diabetes.

Before insulin and other advanced medical interventions came by, diabetes was treated using naturally-derived medicines (Boateng and Catanzano, 2015). Fujita *et al* (2003) researched the effects of touchi-extract on type-2 diabetic patients and whether it helped reduce their blood glucose. Touchi-extract is an α -glucosidase inhibitor that indicates a reduced postprandial rise in blood glucose levels (Fujita *et al*, 2003). The study reported that the fasting blood glucose and glycated haemoglobin levels and the triglyceride levels of the touchi-extract groups reduced significantly over four months. In a separate study, Lee *et al* (2003) investigated the usefulness of rice germ oil supplements on diabetes by researching their effect on serum and hepatic lipid levels. Patients who were not dependent on insulin were reported to have responded positively (reduced hyperglycaemic events and relieved symptoms) to sulfonylurea and biguanide preparations.

The primary treatment of type 1 diabetes remains insulin administration through parenteral routes. Camel (*Camelus dromedarius*) milk has emerged as a plausible alternative treatment for diabetes. This interest has come up due to camel milk showing exceptional broad therapeutic qualities on other serious human diseases. Zagorski *et al* (1998) investigated the popularly held belief that camel milk has large insulin concentrations. They studied the effects of camel milk on the blood glucose levels of laboratory rats. Evidence of insulin concentration in camel milk is undisputable and for this reason, camel milk reduces blood glucose levels in diabetic lab rats (Zagorski *et al*, 1998).

In an earlier study, (Agrawal *et al*, 2005a) conducted research aiming to observe the hypoglycaemic activity of camel milk. Diabetes was induced in 32 male albino rats using one intraperitoneal injection of streptozotocin 50mg/kg body weight (Agrawal *et al*, 2005a). Four treatment options based on camel milk were offered to four equal randomised groups. The groups were treated using either raw camel milk, pasteurised camel milk, raw camel milk + lactoferrin, or cattle milk and controlled for four weeks while conducting weekly blood estimations. This experimental study came to three sensible conclusions. Firstly, when diabetic rats were given raw camel milk, their mean blood glucose level dropped significantly. Secondly, adding

lactoferrin to raw camel milk had no additional benefits. Finally, camel milk's hypoglycaemic activity reduces after pasteurisation. These findings confirmed camel milk's therapeutic potential, which can be used as an adjunctive treatment option in humans suffering from diabetes.

Looking at the current body of literature, there is much evidence surrounding the use of camel milk as a treatment option for diabetes. The successful application of camel milk in treating diabetes has also been reported by several investigations reviewed thus far. However, a gap still exists in the consolidation of evidence to inform further applications of camel milk in the treatment process. This systematic review and meta-analysis were carried out to provide credence to the current findings reported by various primary studies. The importance of natural substances in being preventive and therapeutic to major diseases has been the reason for focusing on camel milk. This systematic review and meta-analysis presented findings will give a lot of weight to current and developing applications of camel milk in treating diabetes. This systematic review and meta-analysis have been carried out to report on the treatment applications of camel milk in diabetes patients.

Methods

Protocol

Following the recommendations of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and the Cochrane Handbook for Systematic Reviews of Interventions, we conducted this systematic review and meta-analysis using a PROSPERO protocol. Cumpston *et al* (2019) detailed the PRISMA extension used to compile this review in Chapter 4 of the Cochrane Handbook for Systematic Reviews and Interventions.

Literature Search

We looked through a variety of sources for publications on clinical trials, randomised controlled trials and other forms of experimental experiments. The search took into account research from 2000 to 2022. We searched PubMed.gov, Google Scholar and the Cochrane Central Register of Controlled Trials (CENTRAL) for pertinent papers. We also carefully went through reference lists to back up our findings. We utilised focused filters to narrow down the most recent usage of camel milk for diabetes management. We used a combination of keywords and MeSH headings to discover relevant articles. These MeSH phrases and keywords were used to construct search

queries, which were then extended with Boolean operators (AND, OR), truncation methods (Asterix) and field tags. For diabetes, camel milk and treatment, we also evaluated keyword variations and related search phrases.

Eligibility Criteria

Eligible articles were required to meet the following criteria: (1) They had to be randomised clinical trials, clinical trials, or experimental studies without any quality restrictions to the methodology; (2) The investigation was to either focus on human subjects (primarily adults) diagnosed with type 1 or type 2 diabetes or animal subjects (primarily mice) with streptozotocin-induced diabetes; (3) Randomisation of the included studies must be reporting on the compared clinical outcomes of camel milk when used in treating diabetes to those using placebo modalities; (4) The outcomes of interest reported by the studies must be indicating the therapeutic potentialities of camel milk and the treatment success of the same. Publication formats were not used as restrictions. However, only studies published in the English language would be included. Articles published in non-English languages but had English translations were also included. Assessment for study eligibility was carried out by two independent reviewers participating in the systematic review and meta-analysis.

Data Extraction

Two independent reviewers used an Excel pre-designed data extraction form to extract data. Extracted data included first authors and last names, country, publication year, relevant demographic data (camel milk preparations (raw or pasteurised)), additional medications in the interventions, treatment duration, diabetes type under therapy and outcome improvement). The opinion of a third reviewer resolved any disagreements between the findings of the two data extractors. Extracted data were presented for quality screening and then for statistical analysis.

Statistical Analysis

Statistical analysis was done on Review Manager 5.4 (RevMan 5.4). The results from this phase provided a fixed effects odds ratio for the treatment success of diabetes using camel milk. The meta-analysis tested the effects of treatment using a mean difference (MD) and standard mean of difference (SMD) at a 95% confidence interval for the reduction of diabetic parameters when patients are treated with camel milk. The results of this meta-analysis

were reported on forest plots which represented outcome comparisons of camel milk versus control. Additionally, a funnel plot was generated to represent the publication bias of the included studies. We also used the I^2 statistic to report on the studies' heterogeneity.

Results

Inclusion and Exclusion of Studies

We identified 543 articles from the primary search. In the first step, 430 articles were eliminated by Covidence automation tools for various predefined eligibility reasons, including duplication. We looked at 118 articles that underwent title and abstract screening for the first screening process. Out of these, 93 were eliminated and 25 remained for full-text screening. Eliminated studies were dropped for reasons such as observing camel milk interact with other diseases, missing parameters in the reports, studies focusing only on the antidiabetic composition of camel milk, reviews, book chapters and many more. We selected nine studies (Agrawal *et al*, 2005a; Agrawal *et al*, 2005b; Ejtahed *et al*, 2015; Mohamad *et al*, 2009; El-Sayed *et al*, 2011; Shareha *et al*, 2017; Fallah *et al*, 2020; Korish, 2014; Khan *et al*, 2013) from the 25 submitted for full-text screening. Eliminated 16 studies were dropped for lack of a control study group, missing data, lack of numerical data, studies not reporting on the effects of camel milk on blood glucose and others. Fig 1 below shows a PRISMA 2020 flow diagram for updated systematic reviews, which only searches for databases. The characteristics of the included studies are provided in Table 1.

The effect of camel milk on diabetic humans and rats

In this systematic review and meta-analysis, we looked at nine studies published within the last two decades and found evidence that consuming camel milk improves diabetes and its underpinning factors. In the statistical analysis section, we analysed the effects of camel milk consumed by diabetics on key diabetic indicators such as HbA1c%, fasting blood glucose (in humans and rat subjects) and plasma insulin concentration and body mass index (BMI).

We measured the mean difference in a fixed-effects model and found the mean difference (MD) for HbA1C% was -0.85 [95% CI: -1.51, -0.18] with a significant p-value ($p = 0.01$) (Fig 2). Other outcome measures, including fasting blood glucose in humans (MD -5.73 [95% CI: -14.92, 3.47], $p = 0.22$, Fig 3), plasma insulin in humans (MD -5.73 [95% CI: -14.92, 3.47], $p = 0.69$, Fig 4), BMI in humans (MD -0.22 [95%

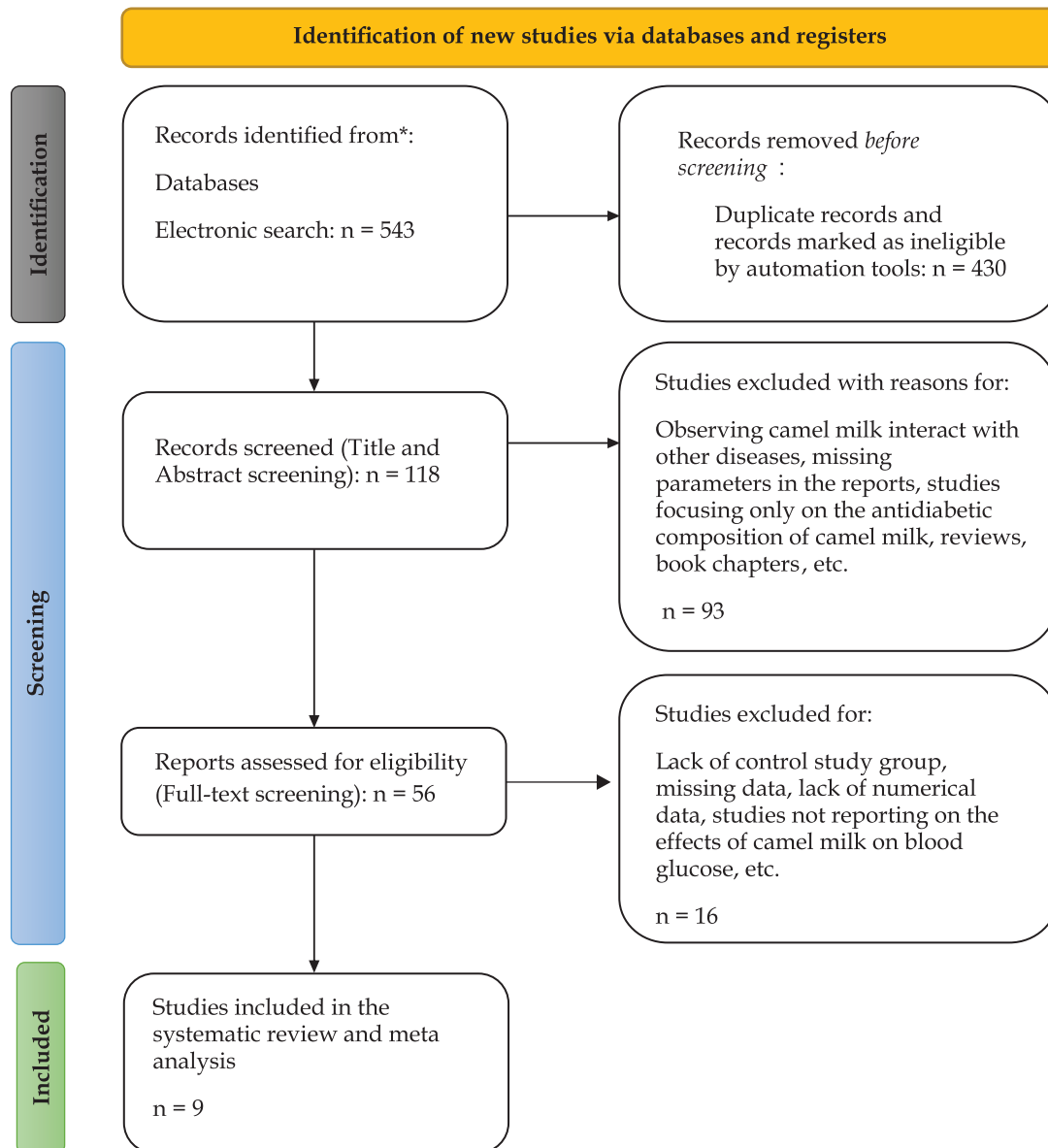


Fig 1. PRISMA flow diagram of studies in systematic review.

CI: -1.09, 0.65], $p = 0.62$, Fig 5) and blood glucose in rats (standard MD -5.73 [95% CI: -14.92, 3.47, $p = 63$, Fig 6]. The level of heterogeneity was considerable for three measures (HbA1C%, fasting blood glucose in humans and blood glucose in rats), while very low heterogeneity was seen for studies evaluating the effect of camel milk on plasma insulin and BMI in humans.

Discussion

In 2004, (Agrawal *et al*, 2004) published an observational study highlighting the prevalence of diabetes in camel milk-consuming Raica rural community of northwest Rajasthan, India. The community of Raica consumed a lot of camel milk

and after observing them, the study found a very low prevalence of impaired glucose tolerance and diabetes (Agrawal *et al*, 2004).

It is widely accepted that camel milk had positive impact on diabetic patients (Sumaira *et al*, 2020). A systematic review had shown that camel milk had beneficial effects on diabetes mellitus by lowering blood sugar levels, reducing insulin resistance and improving lipid profiles (Mirmiran *et al*, 2017). In addition, the extended use of camel milk among patients with diabetes had the potential to serve as a beneficial supplementary therapy when combined with conventional medications. Particularly, it may aid in reducing the necessary insulin dosage and improving HbA1c levels (AlKurd *et al*, 2022).

Table 1. The study characteristics.

| Author | N | Subject | Randomization | Setting | Intervention | | Control | Outcomes measured | Results |
|-----------------|----|------------------|---|---------|---|----------|--|--|---|
| | | | | | Dose | Duration | | | |
| Agrawal (2005a) | 40 | Male albino rats | Group I: (n = 8) on raw camel milk, Group II: (n = 8) on pasteurised milk, Group III: (n = 8) on a standard diet and raw camel milk, Group IV: (n = 6) on a standard diet and cow milk, Group V: (n = 8) on a standard diet | India | Group I - IV: 25 ml of camel milk daily, Group II: 25ml | 4 weeks | Group V: Tap water | Blood glucose | Day 28= Group I: 81.54±11.43, Group II: 113.08±29.09, Group III: 93.24±11.57, Group IV: 203.79±40.66 vs Group V: 77.29±7.42 |
| Agrawal (2005b) | 24 | Humans | Group 1: (n = 12) control group, Group 2: (n = 12) camel milk group | India | of pasteurised camel milk daily, Group III: 1mg of | 1 year | Group 1: usual care | BMI (kg/m ²), Blood sugar, Plasma insulin, HbA1c (%) | Group 1 = BMI: 18.2 ± 3.8, Blood sugar: 105.25 ± 14.50, Plasma Insulin: 19.54 ± 4.3, HbA1c: 7.63 ± 1.03 Group 2= BMI: 19.7 ± 2.97, Blood sugar: 95.42 ± 15.70, Plasma insulin: 18.17 ± 7.12, HbA1c: 6 ± 0.96 |
| Ejtahed (2015) | 20 | Humans | Intervention group (n = 11), Control group (n = 9) | Iran | lactoferrin, Group IV: 25ml of cattle milk | 2 months | Control group: daily 500 mL of cow milk (250 mL morning and evening) | Blood sugar, Plasma insulin | Intervention= Blood sugar: 169.92 ± 45.9, Plasma insulin: 14.01 ± 13.31. Control= Blood sugar: 160.92 ± 57.96, Plasma insulin: 11.69 ± 6.25 |
| Mohamad (2009) | 64 | Humans | Group 1 patients (n = 27), Group 2 patients (n = 27), Control (n = 10) | Egypt | Group 2: 500 ml camel milk in addition to usual care | 16 weeks | Healthy individuals | BMI, fasting blood sugar, HbA1c (%) | Group 1 = BMI: 18.43 ± 3.59, Blood sugar: 227.2 ± 17.7, HbA1c: 09.59 ± 2.05 Group 2= BMI: 24.3 ± 2.95, Blood sugar: 98.9 ± 16.2, HbA1c: 7.16 ± 1.84. Control= BMI: 25.3 ± 7.93, Blood sugar: 81.7 ± 9.16, HbA1c: 6.8 ± 1.08 |
| El-Sayed (2011) | 50 | Humans | Group A (n = 15), Group B (n = 15), Group C (n = 15) | Yemen | Intervention group: daily 500 mL of camel milk (250 mL morning and evening) | 12 weeks | Group A: usual care (diet, exercise and insulin injection) | BMI, fasting blood sugar, HbA1c (%) | Group A = BMI: 17.79±0.27, Blood sugar: 173.4±1.66, HbA1c: 9.27±0.36. Group B= BMI: 17.38±0.18, Blood sugar: 155.13±3.5, HbA1c: 7.28±0.23. Group C = BMI: 20.79± 0.28, Blood sugar: 147.26±1.89, HbA1c: 5.62±0.21 |
| Shareha (2017) | 43 | Humans | Group 1 (n = 22), Group 2 (n = 21) | Libya | Group 1: Usual management for diabetes like diet, exercise and insulin mixtard. Group 2: daily 500 mL of camel milk in addition to the usual management for diabetes. | 3 months | Group 1: Usual care i.e., diet, exercise and insulin dose | HbA1c (%), Fasting blood sugar | Group 1 = HbA1c: 7.72 ± (0.10), Blood sugar: 198.86 ± (3.32). Group 2 = HbA1c: 7.03 ± (0.06), Blood sugar: 187.05 ± (5.29) |

| | | | | | | | | | |
|-----------------------------|----|--------------------|--|--------------|---|----------|--|-------------------------------------|--|
| Fallah <i>et al.</i> (2020) | 40 | Humans | Camel milk group (n = 19), Cow milk group (n = 17) | Iran | Group B: usual care (diet, exercise and insulin injection) + 500 mL/day of camel's milk, Group C: usual care (diet, exercise and insulin injection) + insulin mixed with 500 ml/day of camel's milk | 3 months | Cow milk group: 500 mL of raw cow milk daily | HbA1c (%), Fasting blood sugar | Camel milk group= HbA1c: 9.4±0.3, Blood sugar: 148.4±59.5 Cow milk group= HbA1c: 9.5±0.3, Blood sugar: 152±51.4 |
| Korish (2014) | 80 | Wistar rats | Group C (n=20), Group C-CMK (n=20), Group D (n=15), Group D-CMK (n=20) | Saudi Arabia | Group 2: Usual care + 500 ml of fresh camel milk daily | 8 weeks | Group C: Control normal rats receiving no treatment. Group C-CMK: Control normal rats treated with camel milk. (Approximately 35 ml/rat/day) | Fasting blood sugar, Plasma insulin | Group C= Blood sugar: 76.00 ± 3.88, Plasma insulin: 0.44 ± 0.03. Group C-CMK= Blood sugar: 76.20 ± 6.74, Plasma insulin: 0.43 ± 0.03. Group D= Blood sugar: 459.40 ± 100.04, Plasma insulin: 0.25 ± 0.03. Group D-CMK= Blood sugar: 198.70 ± 135.31, Plasma insulin: 0.38 ± 0.09 |
| Khan <i>et al.</i> (2013) | 40 | Albino wistar rats | Group 1 (n=8), group 2 (n=8), Group 4 (n=8), Group 5 (n=8) | Saudi Arabia | Camel milk group: 500 mL of raw camel milk daily | 30 days | Group 1: Normal control rats, Group 3: Diabetic control group injected with streptozotocin (STZ)-induced diabetes (55 mg kg-1 b.wt.). | Blood sugar | Group 1: 115.64±5.60, Group 2: 121.76±4.30, Group 3: 520.46±8.90, Group 4: 235.61±7.10, Group 5: 135.32±5.20 |
| | | | | | Group D: diabetic rats receiving no treatment. Group D-CMK: Diabetic rats treated with camel milk (Approximately 35 ml/rat/day) | | | | |
| | | | | | Group 2: Normal rats fed with camel milk, Group 4: Diabetic rats fed with camel milk, Group 5: Diabetic rats treated with insulin (6 units kg-1 b.wt./day) | | | | |

There was a long-held notion in the Middle East that drinking camel milk on a regular basis would help prevent and manage diabetes. According to recent investigations, camel milk had characteristics that may substantiate these assertions. Camel milk insulin was thought to have special properties that improved absorption into the bloodstream when compared to insulin from other sources. This could be because insulin was coated in nanoparticles, allowing it to pass through the stomach and into circulation. Furthermore, several components found in camel milk were known to have anti-diabetic properties. The structure of camel insulin and its expected digestion pattern showed no significant alterations that

Human Subjects

Haemoglobin A1c% (HbA1c%)

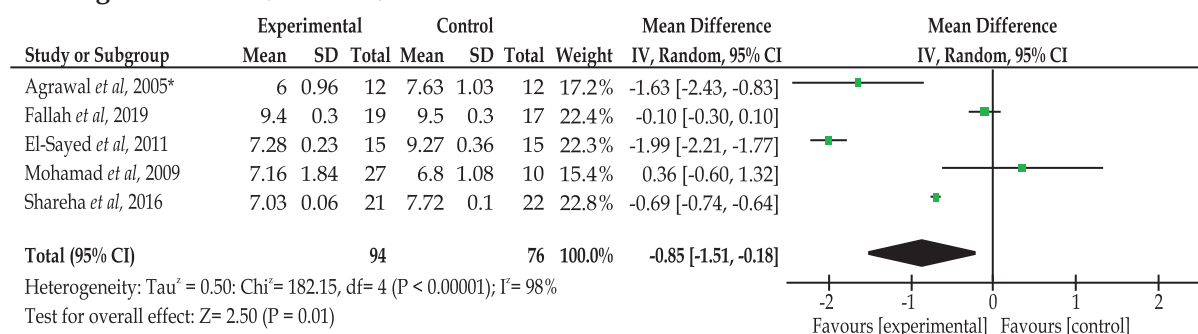


Fig 2. A forest plot of HbA1c in human subjects.

Fasting Blood Glucose

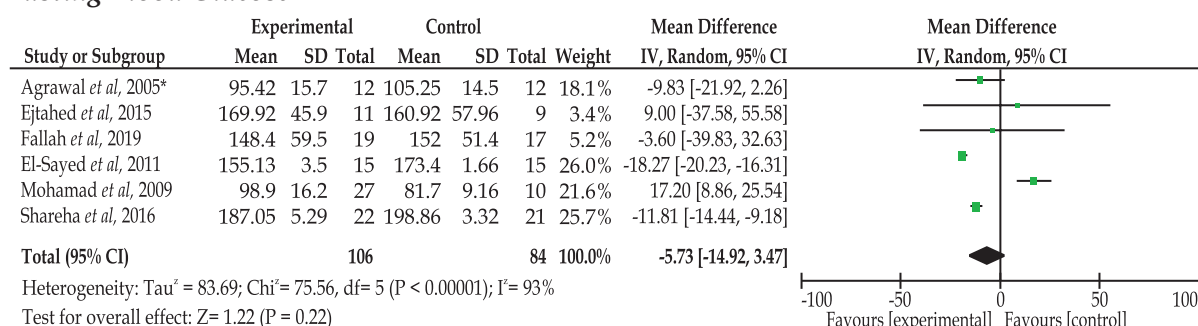


Fig 3. A forest plot of blood glucose in human subjects.

Plasma insulin

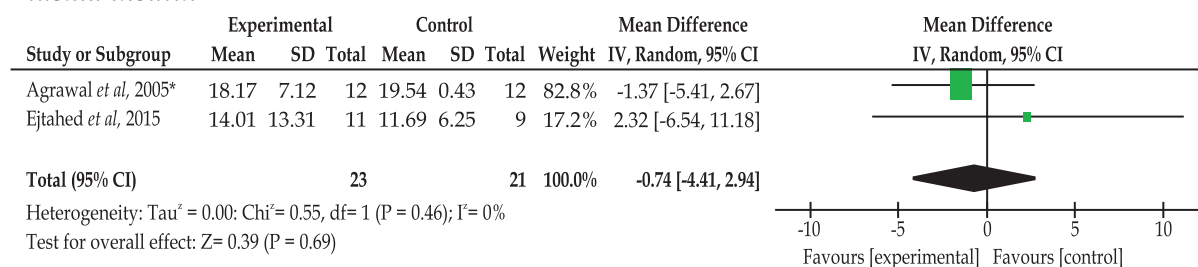


Fig 4. A forest plot of plasma insulin.

would allow it to overcome the digestive system's limitations before (Malik *et al*, 2012).

In a clinical trial, researchers separated 60 patients with Type 2 Diabetes who were already taking oral diabetes medications into two groups. The first group, known as group 1, was given 500 mL of raw camel milk twice a day (in the morning and at night) along with their prescription diabetes medications for three months. The second group, referred to as group 2, only got oral anti-diabetic drugs and did not consume camel milk. The study's findings revealed considerable improvements in a number of metrics. In both groups, fasting blood glucose and postprandial (after-meal) glucose levels decreased significantly. Furthermore, there was a

significant decrease in HbA1c levels, which was a marker used to monitor long-term blood sugar levels. Furthermore, group 1 had a considerable drop in total cholesterol and triglyceride (TG) levels in addition to their prescribed drugs. Throughout the trial, however, there were no statistical differences in urea and creatinine levels, which were indications of kidney function (Sboui *et al*, 2022).

In this comprehensive examination and synthesis of existing research, we examined a collection of nine studies published over the past twenty years. Our investigation revealed compelling evidence suggesting that the consumption of camel milk offers benefits in managing diabetes by reducing HbA1c%, however, there were no significant benefits

BMI

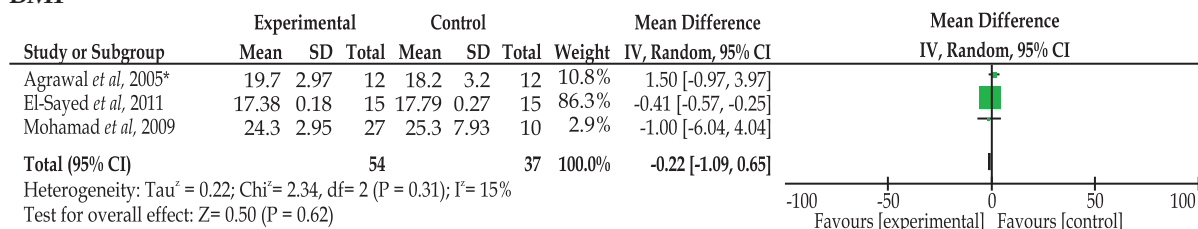


Fig 5. A forest plot of BMI.

Rat Subjects

Blood glucose

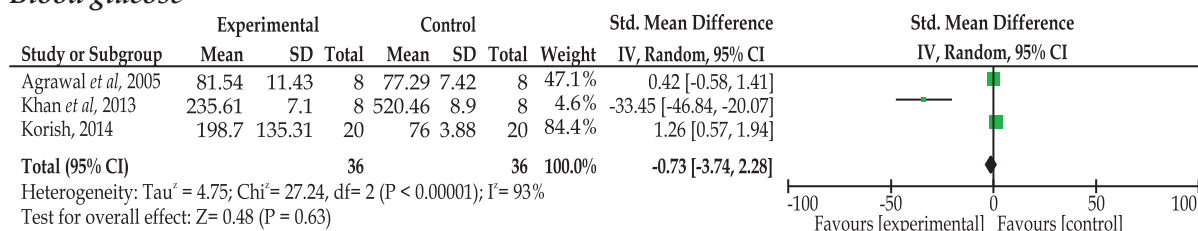


Fig 6. A forest plot of blood glucose in male albino rats.

regarding blood glucose level, plasma insulin level and BMI. These results indicated that camel milk might require consistent use for several months to show antidiabetic efficacy.

Agrawal *et al* (2005a), Korish (2014) and Khan *et al* (2013) present useful results obtained by inducing diabetes into rats and treating them with camel milk. Agrawal *et al* (2005a) pointed to the oxidative potentialities of camel milk due to its high vitamin-C concentration and mineral content (sodium, potassium, iron, zinc, copper and magnesium). As a result of these antioxidants, camel milk insulin receptors in the milk respond favourably to the presence of insulin (Agrawal *et al*, 2005a); (Korish, 2014); (Khan *et al*, 2013). In human subjects, Agrawal *et al* (2005b), Ejtahed *et al* (2015), Mohamad *et al* (2009), El-Sayed *et al* (2011), Shareha *et al* (2017), Fallah *et al*, (2020), Korish (2014) and Khan *et al* (2013) provided more reliable findings. In the study by (Ejtahed *et al*, 2015), the plasma profile contents rose while fasting blood glucose and blood pressure changed. The study demonstrated the success of treatment using camel milk. However, in both interventional and control groups demonstrated positive changes in diabetes risk factors (El-Sayed *et al*, 2011). In another instance, findings of Mohamad *et al* (2009) seemed to contradict those of Agrawal *et al* (2005b) in terms of C-peptide levels. More recent studies (Shareha *et al*, 2017 and Fallah *et al*, 2020) seem to come to a consensus on the reduction of the major diabetic parameter (blood glucose, HbA1c%, plasma insulin,

BMI). As a result, the insulin doses used by diabetic patients are reduced (Agrawal *et al*, 2005b and Fallah *et al*, 2020).

In conclusion, despite the high level of heterogeneity in the included studies, the findings have overarching evidence with high significance indicating that camel milk improves HbA1c% among patients with diabetes. The antidiabetic effects of camel milk can be attributed to the existence of high insulin that has been encapsulated in nanoparticles. The insulin found in camel milk could be absorbed in the intestine as it is not coagulated by stomach acid and may have a role in reducing HbA1c%. (Korish 2014) also reports on insulin-like proteins, polyunsaturated fatty acids, minerals (sodium, potassium, iron, copper, zinc and magnesium), Vitamins C and B3 and immunoglobulins, with low fat and sugar contents. In the present systematic review and meta-analysis, camel milk only qualifies to be used as an adjuvant to other medications for diabetes. We recommend that health sectors properly position foods like camel milk between mainstream treatments and conventional foodstuffs. That way, camel milk will be used much more for therapeutic purposes.

Limitations

The included studies were not specific to one form of diabetes, which may affect the outcomes regarding blood glucose levels in human and animal subjects.

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Disclosure statement

The authors declare no conflict of interest.

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