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Camel milk restores redox balance and reduces inflammation to promote wound healing in diabetic rats

Saleh Albarrak[1], Fahad Alshanbari[2], Abdel Kader Zaki[3], Madeh Sadan[4], Zarroug Ibrahim[2], Yousef Alharbi[2], Tariq Almundarij[2], Saleh Altuwaijri[1], Mohie Haridy[1]*

[1]*Department of Pathology and Laboratory Diagnosis, College of Veterinary Medicine, Qassim University, Buraydah City, Saudi Arabia*
[2]*Department of Medical Biosciences, College of Veterinary Medicine, Qassim University, Buraydah City, Saudi Arabia*
[3]*Department of Physiology, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt*
[4]*Department of Clinical Sciences, College of Veterinary Medicine, Qassim University, Buraydah City, Saudi Arabia*

**Corresponding author: salbarrak@qu.edu.sa*

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Abstract: Diabetes mellitus markedly disrupts wound healing through persistent hyperglycaemia-induced macrophage dysfunction, oxidative stress, and chronic inflammation. This study investigated the therapeutic potential of daily oral camel milk supplementation, rich in insulin-like peptides and antioxidant enzymes, to enhance wound repair in streptozotocin (STZ)-induced diabetic rats. Type 1 diabetes was induced using STZ (55 mg/kg), followed by the creation of standardised 8-mm full-thickness excisional wounds. Animals received camel milk (5 ml/kg/day), and we evaluated systemic and local responses on days 14 and 28. Antioxidant status [catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), lipid peroxidation (malondialdehyde; MDA)], inflammatory biomarkers [C-reactive protein; CRP, amyloid A (AA), tumour necrosis factor-α (TNF-α)], and reparative mediators [transforming growth factor-β (TGF-β), connective tissue growth factor (CTGF)] were assessed alongside histopathological examination. Diabetes significantly reduced antioxidant defences while enhancing oxidative damage and inflammation. Camel milk supplementation restored systemic antioxidant capacity by increasing CAT and GPx activities and reducing MDA levels ($P < 0.05$). It also significantly lowered circulating CRP and AA levels at both time points. Locally, camel milk reduced TNF-α expression and partially restored CAT activity in wound tissues. These findings suggest that camel milk improves diabetic wound healing by strengthening antioxidant defences and suppressing systemic and local inflammation, thereby supporting its potential as a natural therapeutic adjunct.

Keywords: antioxidants; diabetes mellitus; inflammation; oxidative stress; tumour necrosis factor-α; wound healing

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In humans, diabetes mellitus represents a major global health burden, characterised by chronic hyperglycaemia that profoundly disrupts normal tissue repair mechanisms (Burgess et al. 2021). Impaired wound healing is among the most debilitating complications of diabetes, predisposing patients to chronic nonhealing ulcers, recurrent infections, and limb-threatening conditions (Rodriguez-Rodriguez et al. 2022). At the cellular and molecular levels, these outcomes arise from dysregulated macrophage function, excessive oxidative stress, and prolonged inflammation, which collectively compromise the coordinated progression of the wound-healing cascade (Mahmoud et al. 2024). Wound repair in diabetic patients is severely impaired due to the complex interplay of metabolic, vascular, and immunological dysfunctions (Dawi et al. 2025; Xiong et al. 2025). Persistent hyperglycaemia interferes with all stages of wound healing, including haemostasis, inflammation, proliferation, and remodelling, through the induction of oxidative stress, accumulation of advanced glycation end-products (AGEs), and sustained low-grade inflammation. These pathological processes lead to defective angiogenesis, reduced collagen deposition, and impaired fibroblast and keratinocyte activity, ultimately resulting in chronic wounds such as diabetic foot ulcers (DFUs). The condition is further aggravated by peripheral neuropathy and microvascular disease, which diminish sensory perception and blood supply, creating ischaemic and hypoxic environments that hinder tissue regeneration (Porel et al. 2025).

Epidemiological data indicate that approximately 30% of individuals with diabetes develop a DFU during their lifetime, with recurrence rates exceeding 40% within one year and 65% within five years (Armstrong et al. 2023). These ulcers are highly susceptible to polymicrobial infections and frequently progress to gangrene, making DFUs a leading cause of nontraumatic lower-limb amputations worldwide (Idrees et al. 2024). Despite advances in standard care, including glycaemic control, wound debridement, infection management, and advanced dressings, clinical outcomes remain suboptimal, underscoring the urgent need for innovative therapeutic strategies that address the multifactorial pathophysiology of diabetic wound healing (McDermott et al. 2023).

In recent years, attention has increasingly focused on natural bioactive compounds as adjunctive therapies for chronic wounds. Among these, camel milk has emerged as a promising candidate due to its unique biochemical composition, including insulin-like peptides, lactoferrin, antioxidant enzymes, immunoglobulins, and immunomodulatory proteins (Arain et al. 2023). Experimental studies have demonstrated that camel milk–derived peptides enhance macrophage plasticity, promote polarisation toward the pro-healing M2 phenotype, and restore key angiogenic mediators such as vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), thereby accelerating granulation tissue formation and re-epithelialisation in diabetic wound models (Al-Tamimi et al. 2024).

In parallel, camel milk has been shown to attenuate oxidative stress by replenishing endogenous antioxidant defences and suppressing the production of pro-inflammatory cytokine, facilitating the critical transition from the inflammatory to the proliferative phase of wound repair (Ebaid et al. 2015). Emerging biomaterial-based approaches, including hydrogel dressings enriched with camel milk bioactives, have further expanded its therapeutic potential by enabling localised and sustained delivery of bioactive compounds to chronic wounds (Flis et al. 2023). Collectively, these findings position camel milk as a multifunctional, naturally derived intervention with considerable potential to improve wound-healing outcomes in diabetes, warranting further mechanistic investigation and clinical translation.

This study was designed to evaluate the protective and therapeutic potential of camel milk supplementation to promote wound healing in a streptozotocin (STZ)-induced diabetic rat model. We used a randomised, controlled, longitudinal experimental design to systematically examine the effects of diabetes and full-thickness cutaneous wounds on systemic and local oxidative stress, inflammatory responses, and wound-healing dynamics. This investigation comprehensively evaluated the systemic and local effects of camel milk by examining antioxidant status, pro-inflammatory biomarkers, and key mediators of tissue repair, alongside macroscopic wound progression and detailed histopathological changes.

A secondary objective was to determine the therapeutic efficacy of a dietary intervention consisting of 50% camel milk supplementation in mitigating diabetes-associated impairments in wound repair. Through this multifaceted approach, the

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study aimed to elucidate the mechanistic basis by which camel milk may modulate oxidative stress, inflammation, and tissue regeneration during diabetic wound healing.

MATERIAL AND METHODS

Ethical approval

This study followed internationally accepted standards for animal research and was approved by the Animal Ethics Committee of Qassim University (Approval No. 26-06-10). At the conclusion of the study, all animals were humanely euthanised using an overdose of inhaled isoflurane (≥5% in oxygen) delivered in a sealed chamber. Death was subsequently confirmed by cervical dislocation performed by trained personnel and carried out in accordance with established ethical guidelines.

Animal grouping

We transported 96 adult male Sprague–Dawley rats (200–250 g) to the Experimental Animal Unit and housed them under standard hygienic conditions. Following a one-week acclimatisation, animals were assigned to six experimental conditions, each comprising 16 rats, with samples collected on days 14 and 28 as appropriate for serum and tissue analyses. Animals in the healthy condition were neither rendered diabetic nor wounded; however, they underwent all handling and sham procedures. This condition served as the physiological baseline for serum and tissue analyses. The second condition consisted of non-diabetic wounded animals, which received a full-thickness excisional wound without diabetes induction, serving as a model of normal wound healing. The third and fourth conditions involved rats rendered diabetic (third) and then wounded (fourth) to establish an impaired-healing reference model central to the study. The fifth and sixth conditions involved non-wounded and wounded diabetic rats that were given daily camel milk supplementation. This structured, time-resolved grouping strategy separated and evaluated the individual and combined effects of diabetes, wounding, and camel milk treatment on healing outcomes and molecular responses.

Induction of diabetes mellitus

We induced type 1 diabetes mellitus in the designated groups with a single intraperitoneal (i.p.) injection of streptozotocin (STZ; Santa Cruz Biotechnology, Heidelberg, Germany) at 55 mg/kg body weight, freshly dissolved in 100 mmol/l cold citrate buffer (pH 4.5) (Radenkovic et al. 2016). Non-diabetic control rats received an equivalent volume of citrate buffer alone. At 72 h post-injection and at weekly intervals, fasting blood glucose concentrations were measured from the tail vein using a calibrated glucometer (Accu-Chek Performa, Roche Diagnostics). Rats exhibiting persistent hyperglycaemia (≥13.9 mmol/l) were classified as diabetic and included in the study. Diabetic animals were monitored daily for clinical signs of distress, including polyuria, polydipsia, and weight loss, and received supportive care as required. We administered subcutaneous saline when necessary to prevent dehydration and maintain animal welfare.

Excisional wound creation

Prior to surgery, rats were anaesthetised via an intraperitoneal injection of a weight-adjusted combination of ketamine (10%; 1 mg/kg body weight; Dopalen®; Ceva Saúde Animal Ltda., Paulínia, São Paulo, Brazil) and xylazine (2%; 0.25 mg/kg body weight; Xylased; Bioveta, Ivanovice na Hané, Czech Republic). We shaved the dorsal region near the scapular area with an electric clipper (AGC®, blade No. 40; Andis, Sturtevant, WI, USA) and aseptically prepared the site after skin marking. A local anaesthetic (2% lidocaine, 1.0 ml, subcutaneous) was administered prior to incision. A standardised full-thickness excisional wound was created on the right side of the dorsal midline using an 8-mm sterile biopsy punch, ensuring preservation of the underlying musculature. Post-operative analgesia was provided with tramadol hydrochloride (0.5 mg/kg, intramuscular), administered twice daily for three consecutive days. Immediately after wound creation (day 0), wounds were covered with sterile rayon pads (1.0 cm^2) secured with hypoallergenic adhesive tape (Cat No. 1530-0, Micropore 3M®; Riyadh, Saudi Arabia). For subsequent evaluations, dressings were replaced with round adhesive bandages (Band-Aid®; Kenvue Inc., Skillman, NJ, USA). We monitored and documented wound-healing

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progression through morphological assessments on days 0, 7, 14, 21, and 28 post-surgery, following established protocols (Huss et al. 2019; Masson-Meyers et al. 2020; Irwin et al. 2023).

Camel milk supplementation protocol

Fresh raw camel milk was sourced from a certified local farm and stored at 4 °C under hygienic conditions until use. For the intervention groups, camel milk was administered once daily via oral gavage at a dose of 5 ml/kg body weight, commencing on the day of wound creation and continuing until the scheduled euthanasia. We selected this dose based on previous experimental evidence and preliminary studies showing its bioactive efficacy in modulating metabolic and inflammatory pathways. To control for procedural stress, non-supplemented groups (diabetic and non-diabetic controls) received an equivalent volume of distilled water via oral gavage. The supplementation regimen was maintained throughout the experimental period (14 or 28 days), corresponding to the mid-proliferative and late remodelling phases of wound healing.

Serum collection

At the designated time points (days 14 and 28), and at baseline for the negative control group, we used five animals per group. Rats were fasted for 6 h prior to deep anaesthesia. We collected blood samples from the medial canthus using sterile capillary tubes. Samples were allowed to clot at room temperature for 30 min, followed by centrifugation at 3 000 × *g* for 15 min at 4 °C. The clear serum supernatant was carefully transferred to sterile, low-protein-binding microcentrifuge tubes and immediately stored at –20 °C to maintain the integrity of antioxidants and cytokines for subsequent analyses.

Wound bed tissue collection

Immediately after euthanasia, the entire wound bed, including a 2–3 mm margin of adjacent unwounded skin, was aseptically excised on the 3rd, 7th, 14th, 21st, and 28th days following diabetes induction. One half of the excised tissue was briefly rinsed in chilled Dulbecco's Phosphate-Buffered Saline (Cat No. D8537; Sigma-Aldrich, Saint Louis, MO, USA) without calcium or magnesium, supplemented with 10% foetal bovine serum (Cat No. F2442; Sigma-Aldrich, Saint Louis, MO, USA) to minimise proteolytic degradation. We promptly processed each sample to quantify total tissue antioxidants, cytokines, and growth factors according to the protocols described below. The remaining half of the excised wound tissue was used for histopathological evaluation.

Tissue digestion for soluble fraction extraction

Fresh tissue samples (approximately 2–5 mm^3) were finely minced using sterile scalpels in a small volume of chilled DPBS supplemented with 10% FBS. The minced tissue was transferred to a digestion solution containing pre-warmed Collagenase Type I (2 mg/ml; Cat No. C0130; Sigma-Aldrich, Saint Louis, MO, USA) and Dispase II (3 mg/ml; Cat No. D4693; Sigma-Aldrich, Saint Louis, MO, USA) in DPBS.

Enzymatic digestion was performed in a shaking water bath at 37 °C for 90 minutes. To terminate digestion, an equal volume of ice-cold Dulbecco's Modified Eagle Medium (Cat No. 12491023; Thermo Fisher Scientific (Gibco), Waltham, MA, USA) supplemented with 10% FBS and an EDTA-free protease inhibitor cocktail (cOmplete™ Cat No. 04693159001; Roche, Basel, Switzerland) was added. The mixture was centrifuged at 500 × *g* for 5 min at 4 °C.

The resulting supernatant (S1), containing soluble proteins, cytokines, growth factors, and antioxidants released from the extracellular matrix and lysed cells, was carefully aspirated, aliquoted, and stored at –20 °C as the soluble tissue fraction.

The cell pellet was resuspended in cold PBS containing protease inhibitors, filtered through a 70 µm nylon strainer to remove debris, and centrifuged again. The wash supernatant (S2) was combined with S1. The final cell pellet, representing the cellular fraction, was lysed in DMEM supplemented with protease inhibitors. For comprehensive analysis of total tissue content, the processed cellular fraction was recombined with the thawed supernatant prior to biomarker assessment. Protein

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concentrations were determined using a Bradford colourimetric protein assay kit (Bradford Protein Assay Kit, Cat. No. 23200; Thermo Fisher Scientific, Waltham, MA, USA) according to the manufacturer's instructions. We measured biomarkers in the soluble fraction (S1 + S2) and normalised the results to tissue protein content (U/mg protein, pg/mg protein) by correlating analyte concentrations with the total protein content of the corresponding cellular fraction (SPECTRUM – LOT TP 1010; Cairo, Egypt). This approach provided a comprehensive profile of the wound tissue biochemical milieu. We conducted all assays in duplicate using commercial ELISA kits according to the manufacturers' instructions, and measured optical density with a microplate reader (BioTek Synergy HT, Winooski, VT, USA). Each run included appropriate standards and controls.

Antioxidant and oxidative stress markers

Serum and tissue samples were analysed for antioxidant enzymes and a marker of lipid peroxidation using commercially available kits: glutathione peroxidase (GPx; Cat. No. 2524; Biodiagnostic, Giza, Egypt), superoxide dismutase (SOD; Cat. No. 2521; Biodiagnostic, Giza, Egypt), catalase (CAT; Cat. No. 2517; Biodiagnostic, Giza, Egypt), and malondialdehyde (MDA; Cat. No. 2581; Biodiagnostic, Giza, Egypt).

Inflammatory biomarkers

C-reactive protein (CRP), amyloid A (AA), tumour necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β) were quantified using rat-specific ELISA kits (Cat. No. EL0006Ra, SL0625Ra, SL0722Ra, and HS-EL0039Ra, respectively; Sunlong Biotech Ltd., Zhejiang, P.R. China).

Healing and regulatory biomarkers

We measured transforming growth factor-beta (TGF-β), connective tissue growth factor (CTGF), and interleukin-10 (IL-10) using commercially available specific ELISA kits (Sunlong Biotech Ltd., Hangzhou, P.R. China; Cat. No. SL0708Ra, SL0196Ra, and HS-EL0031Ra, respectively).

Morphological scoring system

A standardised morphological scoring system was employed to assess the effects of camel milk on wound healing in rats. Evaluation criteria included: (a) Pain sensitivity: scored as 0 (absent) or 1 (present) based on behavioural responses. (b) Wound colour: graded from 1 to 4, ranging from pinkish to cyanotic. (c) Presence of oedema, hyperaemia, exudate, crust formation, and granulation tissue: each scored as 0 (absent) or 1 (present). (d) Exudate characteristics (when present): scored on a scale of 1 to 3, ranging from serous to purulent.

Histopathological examination

Skin tissue samples collected from the wound site and a 2–3 mm margin of adjacent healthy skin from five animals in each group on days 14 and 28 were immediately fixed in 10% neutral buffered formalin for 48 hours. After fixation, the tissues were dehydrated through a graded ethanol series, cleared in xylene, and embedded in paraffin wax. Sections of 5 µm thickness were cut using a rotary microtome and stained with haematoxylin and eosin (H&E) for general morphological assessment using light microscopy (Suvarna et al. 2018). The sequential histological changes associated with wound healing were evaluated, including: (a) blood clot, necrosis, cellular debris; (b) oedema and inflammatory cells; (c) vasculature (neovascularisation); (d) fibroblastic proliferation; (e) collagen deposition and scar formation; and (f) re-epithelialisation. Lesions were graded according to their severity as follows: – = absent; + = mild (minimal changes); ++ = moderate (moderate but readily apparent changes); and +++ = severe (prominent and abundant changes). We also collected and examined the spleen for histopathological evidence of immunosuppression or immunostimulation potentially induced by diabetes and camel milk supplementation, respectively. We described the histopathological results qualitatively.

Statistical analysis

Data are expressed as mean ± standard error of the mean (SEM), as presented in the tables. We assessed normality using the Shapiro–Wilk test. For comparisons involving multiple groups across two time

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points, we performed a two-way analysis of variance (ANOVA), with experimental condition and time as the main factors. When the overall ANOVA was significant ($P < 0.05$), Tukey's post-hoc test was used for multiple comparisons. Statistical analyses were performed using GraphPad Prism (v9.0; GraphPad Software, Inc., USA). We considered $P < 0.05$ statistically significant for all analyses.

RESULTS

Antioxidant enzymes and MDA

We evaluated the effects of camel milk supplementation on serum antioxidant enzymes and MDA concentrations in diabetic rats with skin wounds (Table 1). Wounded control rats were compared with normal controls to assess the impact of wounding on serum CAT, SOD, GPx, and MDA concentrations. Serum CAT levels were significantly reduced ($P < 0.05$) in wounded controls on day 14 but returned to normal by day 28. No significant differences were observed in serum SOD or GPx levels between wounded and normal controls. In contrast, serum MDA levels were significantly higher ($P < 0.05$) in wounded controls compared with normal controls. Wounded diabetic control rats were compared with wounded non-diabetic controls to evaluate the impact of diabetes on serum CAT, SOD, GPx, and MDA concentrations. Serum CAT levels were lower in wounded diabetic rats, with a significant reduction observed on day 28 ($P < 0.05$). Similarly, serum SOD levels were significantly decreased in wounded diabetic rats compared with their non-diabetic counterparts ($P < 0.05$). No significant differences were detected between the two groups in serum GPx or MDA levels. We compared wounded diabetic rats supplemented with camel milk with untreated counterparts to assess the effects of supplementation on serum CAT, SOD, GPx, and MDA concentrations. Although serum SOD levels did not differ significantly between the two groups, camel milk treatment significantly increased serum CAT and GPx levels ($P < 0.05$) and significantly reduced serum MDA levels ($P < 0.05$). These findings indicate enhanced antioxidant defences and reduced lipid peroxidation in response to camel milk supplementation.

Table 2 presents the effects of camel milk supplementation on tissue antioxidant enzymes and MDA concentrations. Tissue concentrations of CAT, SOD, GPx, and MDA were significantly lower ($P < 0.05$) in the non-diabetic wounded control group compared with healthy controls. By day 28, CAT, GPx, and MDA remained significantly reduced ($P < 0.05$), whereas SOD showed no significant difference, indicating the sustained impact of wounding on antioxidant status. Diabetes further affected antioxidant enzyme activity, with CAT and GPx generally lower

Table 1. Effect of camel milk supplementation on serum antioxidant enzymes and MDA in diabetic rats with skin wounds

Experimental conditions	Sampling day	CAT	SOD	GPx	MDA
1: Healthy control	28	150.9 ± 3.593^{a}	135.0 ± 10.0^{a}	34.04 ± 2.918^{a}	9.705 ± 1.69^{ab}
2: Wounded control	14	103.1 ± 12.85^{a}	151.3 ± 27.03^{b}	25.64 ± 2.2	14.4 ± 2.37^{a}
	28	130.0 ± 4.15^{b}	96.25 ± 21.35	23.35 ± 1.98	16.44 ± 1.26^{b}
3: Diabetic wounded control	14	89.4 ± 8.25^{d}	76.25 ± 11.43^{b}	23.69 ± 1.63^{a}	14.74 ± 1.25^{c}
	28	64.14 ± 1.25^{bc}	82.5 ± 7.5^{a}	20.43 ± 0.97^{b}	17.4 ± 0.82^{d}
4: Diabetic wounded + milk	14	260.2 ± 5.46^{d}	76.25 ± 6.25	37.49 ± 1.55^{a}	7.924 ± 0.82^{c}
	28	280.0 ± 5.73^{c}	80.0 ± 8.89	38.66 ± 2.62^{b}	6.605 ± 0.46^{d}
P-values		0.000 1	0.028 2	0.000 1	0.000 1

[a–d]Within a column and sampling day, mean values sharing the same superscript letter are significantly different ($P < 0.05$) according to the post-hoc test comparisons: Healthy control vs Control wounded; Control wounded vs Control diabetic wounded; and Control diabetic wounded vs Milk + diabetic wounded

Values are presented as mean ± standard error. *P*-values indicate the overall significance among groups for each parameter
CAT = catalase (U/mg protein); GPx = glutathione peroxidase (U/mg protein); MDA = malondialdehyde (nmol/mg protein); SOD = superoxide dismutase (U/mg protein)

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Table 2. Effect of wounding, diabetes, and camel milk supplementation on tissue antioxidant enzymes and MDA in diabetic rats with skin wounds

Experimental conditions	Sampling day	CAT	SOD	GPx	MDA
1: Healthy control	14	24.33 ± 1.167^{a}	2.129 ± 0.254 3^{a}	59.49 ± 2.073^{ac}	12.35 ± 0.546 1^{ac}
	28	27.03 ± 2.316^{bc}	2.161 ± 0.277 4	60.39 ± 3.17^{bd}	13.40 ± 0.572 7^{bd}
2: Wounded control	14	14.12 ± 1.068^{a}	0.940 7 ± 0.082 3^{a}	26.75 ± 1.842^{a}	9.686 ± 0.051 5^{a}
	28	14.84 ± 5.022^{b}	3.708 ± 0.762	8.803 ± 3.295^{b}	29.20 ± 1.515^{b}
3: Diabetic control intact tissue	14	19.31 ± 3.046^{d}	3.916 ± 0.502	26.43 ± 6.275^{c}	22.10 ± 1.594^{ce}
	28	18.50 ± 2.237^{ce}	3.884 ± 0.445 2	22.50 ± 2.339^{d}	22.86 ± 2.36^{df}
4: Diabetic control wounded tissue	14	11.54 ± 0.215^{d}	3.311 ± 0.123	20.42 ± 3.046	30.04 ± 2.157^{e}
	28	11.39 ± 0.173^{e}	3.719 ± 0.309 5	23.19 ± 2.654	33.79 ± 0.962 5^{f}
5: Diabetic + milk intact tissue	14	16.00 ± 3.218	2.028 ± 0.152 5	57.46 ± 4.387^{e}	9.491 ± 0.244 5
	28	14.00 ± 2.395^{a}	2.159 ± 0.044 5	61.55 ± 3.514^{f}	10.61 ± 0.695 6
6: Diabetic + milk wounded tissue	14	19.00 ± 2.534	2.001 ± 0.272 3	34.95 ± 1.176^{e}	12.38 ± 0.547 8
	28	24.67 ± 1.637^{a}	2.058 ± 0.141 3	33.81 ± 2.492^{f}	9.743 ± 0.352 4
P-values		0.000 1	0.000 1	0.000 1	0.000 1

$^{a–f}$Within a column and sampling day, mean values sharing the same superscript letter are significantly different ($P < 0.05$) according to the post-hoc test comparisons: Healthy control vs Non-diabetic wounded control; Groups Healthy control vs Diabetic intact tissue; Diabetic intact tissue vs Diabetic wounded tissue and Milk + diabetic intact tissue vs Milk + diabetic wounded tissue. Values are presented as mean ± standard error. *P*-values indicate the overall significance among groups for each parameter

CAT = catalase (U/mg protein); GPx = glutathione peroxidase (U/mg protein); MDA = malondialdehyde (nmol/mg protein); SOD = superoxide dismutase (U/mg protein)

in intact diabetic tissues compared with healthy controls. These reductions were statistically significant for CAT on day 28 and for GPx on both days 14 and 28 ($P < 0.05$). Comparing wounded and intact tissues in diabetic rats showed that wounding exacerbated oxidative stress: CAT levels decreased significantly ($P < 0.05$), and MDA levels increased significantly ($P < 0.05$) on day 14, with similar trends persisting on day 28. No significant differences were observed for SOD and GPx. Camel milk supplementation partially mitigated these effects, significantly increasing CAT levels ($P < 0.05$) in wounded tissues of diabetic rats on day 28 compared with intact tissues. In contrast, GPx levels were significantly lower ($P < 0.05$) in wounded tissues on day 14, while SOD and MDA remained unchanged between wounded and intact tissues.

Inflammatory biomarkers

The effects of camel milk supplementation on serum concentrations of C-reactive protein (CRP), amyloid A (AA), tumour necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β) in diabetic rats with cutaneous wounds are summarised in Table 3. To assess the effect of wounding on serum inflammatory biomarker levels, we compared wounded control rats with normal control rats. Wounding significantly elevated CRP levels on day 14 ($P < 0.05$), and levels remained elevated through day 28. Similarly, serum AA concentrations were significantly higher in wounded controls compared with normal controls ($P < 0.05$). Although TNF-α and IL-1β levels trended upward in wounded rats, these differences did not reach statistical significance.

To assess the impact of diabetes, we compared serum levels of CRP, AA, TNF-α, and IL-1β between wounded controls and diabetic wounded controls. We observed no significant differences between these groups for any measured parameter. In contrast, diabetic wounded rats receiving camel milk supplementation showed significantly lower CRP and AA concentrations on both day 14 and day 28 than diabetic wounded controls ($P < 0.05$).

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Table 3. Effect of camel milk supplementation on serum inflammatory biomarkers in diabetic rats with skin wounds

Experimental conditions	Sampling day	CRP	Amyloid-A	TNF-α	IL-1β
1: Healthy control	28	136.7 ± 2.5[a]	10.28 ± 0.722[ab]	20.84 ± 1.094	13.97 ± 1.936
2: Wounded control	14	202.1 ± 7.857[a]	20.65 ± 3.053[a]	36.63 ± 6.25	25.74 ± 2.419
	28	157.8 ± 9.286	22.31 ± 0.731 5[b]	26.78 ± 4.219	33.16 ± 8.226
3: Diabetic wounded control	14	187.1 ± 1.428[c]	20.36 ± 0.646 5[d]	32.25 ± 2.813	28.16 ± 0.967 5
	28	181.7 ± 21.07[b]	22.47 ± 0.757[c]	34.13 ± 15.63	25.73 ± 3.726
4: Diabetic wounded + milk	14	104.9 ± 2.142[c]	12.45 ± 0.306[d]	30.53 ± 5.782	21.11 ± 5.113
	28	36.0 ± 2.5[b]	11.09 ± 0.272[c]	37.25 ± 21.88	23.31 ± 1.307
P-values		0.000 1	0.000 6	0.453 2	0.388 3

[a–d]Within a column, mean values sharing the same superscript letter are significantly different ($P < 0.05$) based on post-hoc comparisons: Healthy control vs Control wounded; Control wounded vs Control diabetic wounded; and Control diabetic wounded vs Milk + diabetic wounded

Values are presented as mean ± standard error. *P*-values indicate the overall significance among groups for each parameter

Amyloid-A = serum amyloid A (μg/ml); CRP = C-reactive protein (U/l); IL-1β = interleukin-1 beta (pg/ml); TNF-α = tumour necrosis factor-alpha (pg/ml)

Table 4 summarises the effects of camel milk supplementation on tissue concentrations of CRP, AA, TNF-α, and IL-1β in diabetic rats with cutaneous wounds. To assess the impact of wounding, we compared tissue levels of inflammatory biomarkers in wounded control rats with those in normal controls. On day 14, CRP and IL-1β levels were significantly elevated in wounded controls relative

Table 4. Effect of camel milk supplementation on tissue Inflammatory biomarkers in diabetic rats with skin wounds

Experimental conditions	Sampling day	CRP	Amyloid-A	TNF-α	IL-1β
1: Healthy control	14	14.21 ± 0.62[a]	0.324 ± 0.107 9[b]	15.42 ± 1.569[ac]	10.15 ± 0.730 1[a]
	28	15.92 ± 0.511 2[b]	0.285 3 ± 0.067 68[a]	19.16 ± 0.545[bd]	10.36 ± 0.608 5
2: Wounded control	14	19.17 ± 0.332 6[a]	0.370 5 ± 0.036 06	13.53 ± 0.012 5[a]	33.68 ± 4.144[a]
	28	24.82 ± 2.723[b]	1.127 ± 0.092 63[a]	28.24 ± 2.001[b]	13.33 ± 9.468
3: Diabetic control intact tissue	14	18.27 ± 1.083[c]	0.687 5 ± 0.160 5[bc]	27.01 ± 4.957[ce]	17.43 ± 8.247
	28	18.19 ± 1.001[d]	0.398 ± 0.562 9[d]	25.2 ± 3.144[df]	17.08 ± 7.903
4: Diabetic control wounded tissue	14	36.07 ± 1.961[c]	1.107 ± 0.144[c]	39.49 ± 1.166[e]	25.78 ± 6.565
	28	38.24 ± 3.581[d]	0.843 ± 0.008 485[d]	45.02 ± 2.083[f]	15.04 ± 4.403
5: Diabetic + milk intact tissue	14	18.61 ± 4.356	0.250 7 ± 0.030 86	10.94 ± 1.839	10.11 ± 0.435 7
	28	24.37 ± 2.743	0.266 7 ± 0.041 65	15.35 ± 1.102[g]	12.25 ± 3.591
6: Diabetic + milk wounded tissue	14	26.18 ± 2.148	0.310 7 ± 0.011 5	14.01 ± 1.605	11.59 ± 3.429
	28	24.81 ± 3.032	0.362 5 ± 0.009 192	9.727 ± 1.533[g]	7.531 ± 1.079
P-values		0.000 1	0.000 1	0.000 1	0.056 1

[a–g]Within a column and sampling day, mean values sharing the same superscript letter are significantly different ($P < 0.05$) according to the post-hoc test comparisons: Healthy control vs Non-diabetic wounded control; Groups Healthy control vs Diabetic intact tissue; Diabetic intact tissue vs Diabetic wounded tissue and Milk + diabetic intact tissue vs Milk + diabetic wounded tissue

Values are presented as mean ± standard error

Amyloid-A = amyloid A (μg/ml); CRP = C-reactive protein (U/l); IL-1β = interleukin-1 beta (pg/ml); TNF-α = tumour necrosis factor-alpha (pg/ml)

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to normal controls ($P < 0.05$). Conversely, TNF-α levels were significantly reduced in wounded tissues compared with those in normal tissues, an effect observed only on day 14 ($P < 0.05$). Within the diabetic wounded control group, we compared wounded tissues with intact tissues to assess the effect of wounding on local inflammatory markers. Tissue concentrations of CRP, AA, and TNF-α were significantly higher in wounded tissues than in intact tissues ($P < 0.05$), whereas IL-1β levels did not differ between the two tissue types. In diabetic rats supplemented with camel milk, tissue TNF-α levels were significantly reduced in wounded tissues on day 28 compared with intact tissues ($P < 0.05$).

Healing biomarkers

Table 5 summarises the effects of camel milk supplementation on serum concentrations of TGF-β, CTGF, and IL-10 in diabetic rats with cutaneous wounds. To assess wounding's influence on serum healing biomarkers, we compared wounded control rats with normal controls. Wounding did not significantly alter TGF-β or IL-10 levels at any time point; however, CTGF levels were significantly elevated on day 14 and remained elevated on day 28 ($P < 0.05$). To assess the impact of diabetes, we compared serum concentrations of TGF-β, CTGF, and IL-10 between wounded controls and diabetic wounded controls. Diabetes did not significantly affect TGF-β or IL-10 levels but significantly increased CTGF concentrations ($P < 0.05$). Camel milk supplementation in diabetic wounded rats did not produce significant changes in TGF-β, CTGF, or IL-10 levels on either day 14 or day 28 compared with diabetic wounded controls.

Table 6 shows the effects of camel milk supplementation on tissue concentrations of TGF-β, CTGF, and IL-10 in diabetic rats with cutaneous wounds. To assess the effect of wounding, tissue concentrations of the selected biomarkers in wounded controls were compared with those in normal controls. Wounded controls showed significantly higher levels of TGF-β and CTGF than normal controls ($P < 0.05$), whereas IL-10 levels did not differ significantly. To assess the influence of diabetes on local healing biomarkers, we compared intact tissues from the diabetic wounded control group with tissues from the normal control group. Notably, TGF-β and CTGF levels were significantly elevated in the intact tissues of the diabetic wounded control group on days 14 and 28 ($P < 0.05$).

Within the diabetic wounded control group, we compared wounded tissues with intact tissues to assess how wounding affects local healing biomarkers. CTGF levels were significantly elevated only in wounded tissues on day 14 ($P < 0.05$), whereas TGF-β and IL-10 levels did not differ significantly. In diabetic rats supplemented with camel milk, tissue concentrations of TGF-β and CTGF were significantly higher in wounded tissues than in intact tissues on day 14 ($P < 0.05$).

Table 5. Effect of camel milk supplementation on healing biomarkers in diabetic rats with skin wounds

Experimental conditions	Sampling day	TGF-β	CTGF	IL-10
1: Healthy control	28	2.83 ± 0.29	176.2 ± 4.792[a]	20.21 ± 1.09
2: Wounded control	14	5.05 ± 1.74	383.3 ± 13.13[ab]	19.72 ± 2.15
	28	1.75 ± 0.26	300.9 ± 86.15	45.62 ± 1.51
3: Diabetic wounded control	14	3.15 ± 0.67	514.9 ± 22.92[b]	16.6 ± 3.69
	28	3.67 ± 0.38	306.2 ± 21.46	20.5 ± 3.175
4: Diabetic wounded + milk	14	6.31 ± 0.68	363.9 ± 57.71	45.5 ± 6.83
	28	2.66 ± 0.34	257.1 ± 19.48	24.27 ± 3.43
P-values		0.337 1	0.013 3	0.322 0

[a–b]Within a column, mean values for CTGF sharing the same superscript letter are significantly different ($P < 0.05$). No significant differences were found for TGF-β or IL-10

Values are presented as mean ± standard error. *P*-values indicate the overall significance among groups for each parameter
CTGF = connective tissue growth factor (pg/ml); IL-10 = interleukin-10 (pg/ml); TGF-β = transforming growth factor-beta (pg/ml)

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Table 6. Effect of camel milk supplementation on tissue healing biomarkers in diabetic rats with skin wounds

Experimental conditions	Sampling day	TGF-β	CTGF	IL-10
1: Healthy control	14	136.0 ± 21.36^{ac}	222.2 ± 12.99^{ac}	14.38 ± 5.018
	28	104.6 ± 1.874^{bd}	218.6 ± 9.373^{bd}	6.235 ± 0.058 5
2: Wounded control	14	269.3 ± 2.594^{a}	576.9 ± 3.958^{a}	11.77 ± 3.717
	28	533.8 ± 11.87^{b}	335.3 ± 36.38^{b}	8.018 ± 0.29
3: Diabetic control intact tissue	14	499.6 ± 51.87^{c}	313.1 ± 7.531^{ce}	9.428 ± 1.324
	28	449.0 ± 31.19^{d}	358.9 ± 53.29^{d}	13.54 ± 5.438
4: Diabetic control wounded tissue	14	448.7 ± 53.55	500.4 ± 63.54^{e}	12.27 ± 3.479
	28	384.4 ± 32.8	380.6 ± 60.47	20.39 ± 2.197
5: Diabetic + milk intact tissue	14	95.66 ± 10.09^{e}	197.7 ± 16.64^{f}	22.0 ± 1.097
	28	99.68 ± 11.34	212.7 ± 18.13	15.42 ± 6.032
6: Diabetic + milk wounded tissue	14	222.8 ± 27.57^{e}	308.9 ± 41.62^{f}	16.3 ± 5.578
	28	137.4 ± 4.179	222.2 ± 12.99	14.38 ± 5.018
P-values		<0.000 1	<0.000 1	0.125 8

$^{a–f}$Within a column and sampling day, mean values sharing the same superscript letter are significantly different ($P < 0.05$) according to the post-hoc test comparisons: Healthy control vs Non-diabetic wounded control; Groups Healthy control vs Diabetic intact tissue; Diabetic intact tissue vs Diabetic wounded tissue and Milk + diabetic intact tissue vs Milk + diabetic wounded tissue

Values are presented as mean ± standard error. *P*-values indicate the overall significance among groups for each parameter CTGF = connective tissue growth factor (pg/ml); IL-10 = interleukin-10 (pg/ml); TGF-β = transforming growth factor-beta (pg/ml)

Clinical findings

Macroscopic evaluation of the wounds is summarised in Table 7 and Figure 1. Wound colour, the presence of oedema, hyperaemia, exudate, crust formation, and granulation tissue, the characteristics of exudate (where applicable), and pain sensitivity were evaluated throughout the observation period. Regarding wound colour, lesions in the camel-milk–treated group consistently appeared pinkish, whereas those in the diabetic and non-diabetic control groups exhibited pale and yellow colouration, respectively. Complete wound healing was achieved by day 14 in the camel-milk–treated group, whereas healing was incomplete in the control groups. All groups showed pain sensitivity during the early stages of healing. In the camel-milk-treated diabetic group, pain scores decreased progressively over time and were absent by day 14. In contrast, diabetic wounded control rats exhibited persistent pain responses until day 21, indicating delayed clinical recovery. Similar resolution patterns were observed in the non-diabetic wounded controls. No differences were observed in the presence of oedema or exudate between the

Table 7. Clinical evaluation and follow up of camel milk effect on wound healing in rats

Findings	Wounded control					Diabetic wounded control					Diabetic wounded + milk				
Time per day	3rd	7th	14th	21st	28th	3rd	7th	14th	21st	28th	3rd	7th	14th	21st	28th
A	++	+++	+	+++	+++	++	+++	+	+++	+++	+	++	+	+	+
B	–	–	–	–	–	+	–	–	+	+	–	–	–	–	–
C	–	–	–	–	–	+	–	–	–	–	–	–	–	–	–
D	++	+	+	+	+	++	+	+	+	+	++	+	–	–	–

(–) = absence of lesion; (+) = mild; (++) = moderate; (+++) = severe; A = wound colouring, B = oedema; hyperaemia; exudate; crust and granulation tissue; C = exudate characteristics when applicable; D = pain sensitivity

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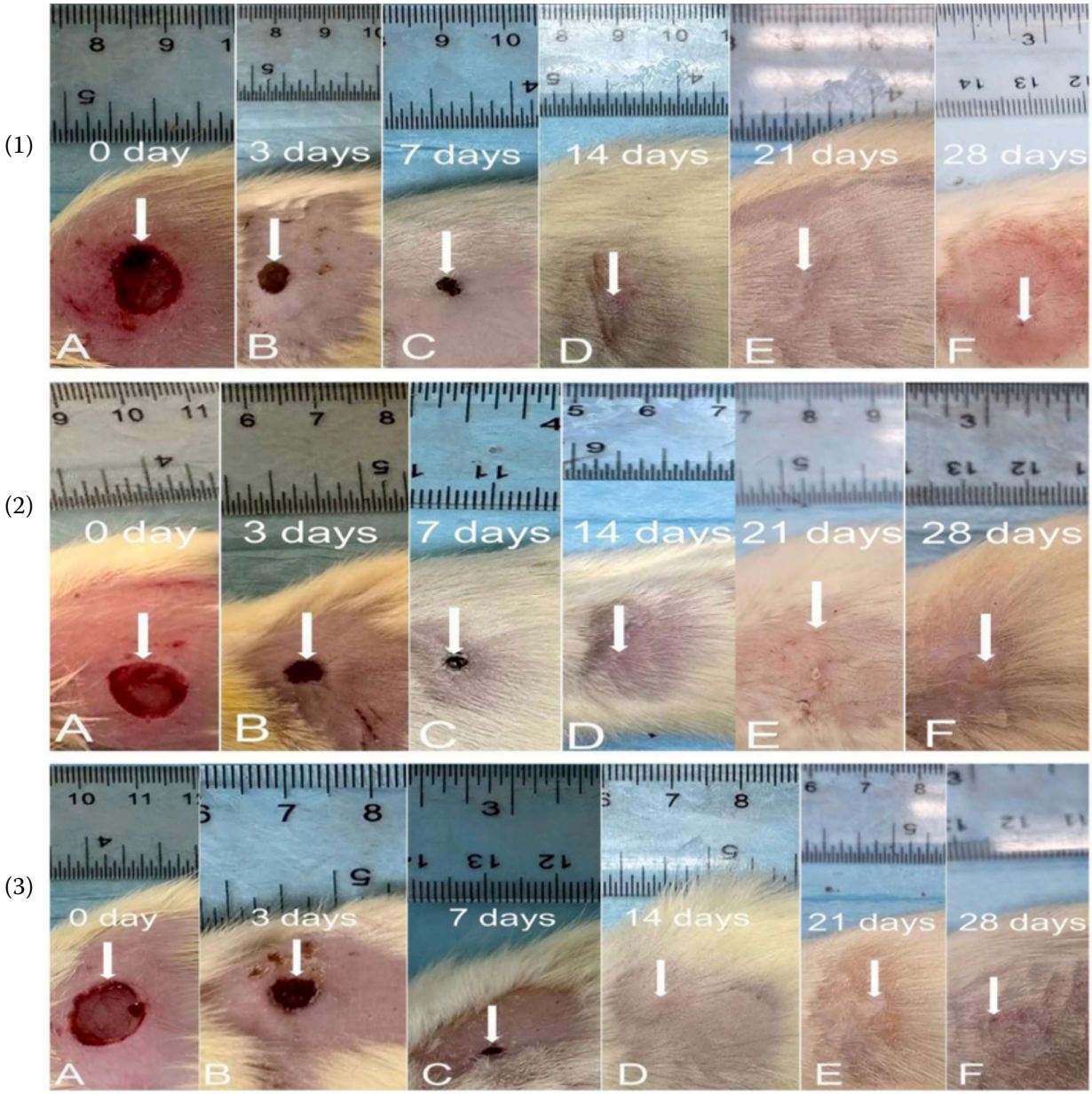


Figure 1. Clinical evaluation and follow up of control non diabetic wound (1); Control diabetic wound and (2) and milk treated diabetic rats (3)

camel-milk–treated group, the diabetic control group, and the non-diabetic control group at any of the six observation time points. In all groups, lesions showed no visible evidence of contamination or necrotic tissue, and neither oedema nor exudate was observed throughout the study period.

Histopathological findings

The control group wound showed a gap filled with a large clot of necrotic material (scab), marked fibroblastic proliferation, and extensive cellular infiltration, primarily by macrophages and neutrophils, along with neovascularisation oriented perpendicular to the wound edge at the 7th dpt (Figure 2A). At the 14th dpt, fibroblastic proliferation and collagenous material filled the wound gap, accompanied by extensive infiltration of inflammatory cells. At the 21st dpt, granulation tissue filled the wound gap and was covered by the epidermis, with underlying inflammatory cell infiltration. At the 28th dpt, inflammation had subsided, and the amount of granulation tissue had decreased.

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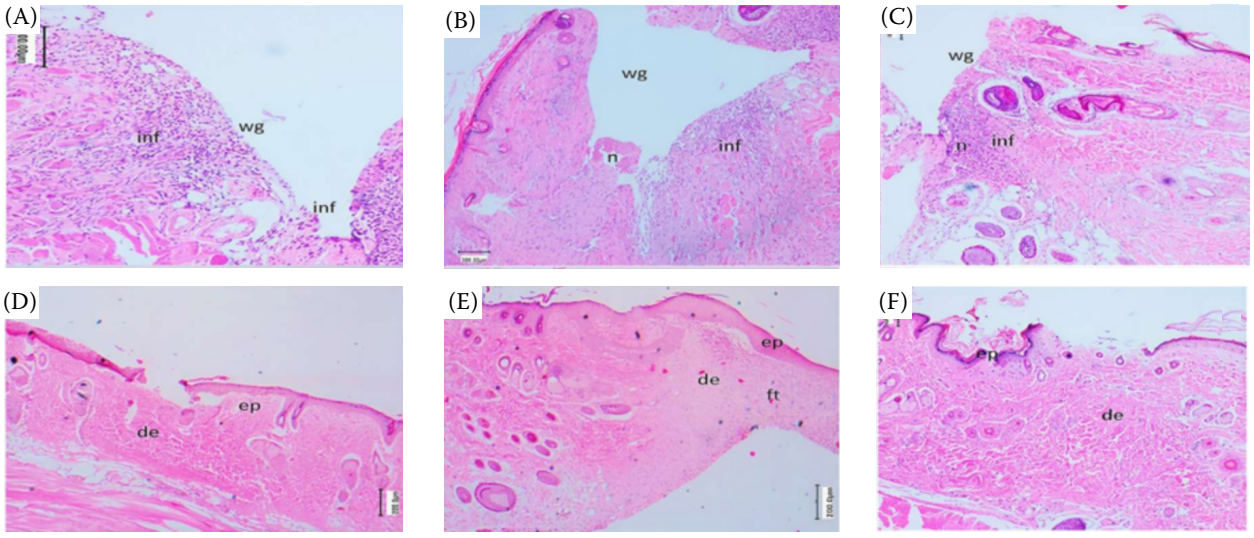


Figure 2. Histopathology of skin wounds in control (A,D), diabetic (B,E) and milk treated diabetic (C,F) groups at the 7th dpt (A–C) and 28th dpt (D–F) revealed delayed healing in diabetic group in comparison to the enhanced wound healing in control and milk treated diabetic group (H&E, bar = 200 µm)

de = dermis devoid of adnexa; ep = epidermis; ft = fibrous connective tissue rich in collagen; inf = inflammation and oedema; n = necrosis; wg = wound gap

The overlying epidermis was intact and filled the gap. The skin had almost returned to normal, except for the incomplete restoration of follicles and adnexal structures (Figure 2D).

The wound gap of the diabetic wound group revealed necrotic tissues with a blood clot, oedema, and heavy infiltration with inflammatory cells, mainly neutrophils at the 3rd dpt. Meanwhile, by the 7th dpt, gaps were filled predominantly with inflammatory cells, mainly neutrophils and macrophages, with limited fibroblast proliferation and delicate blood capillaries (Figure 2B). At the 14th dpt, there was extensive inflammatory cell infiltration, predominantly by macrophages and lymphocytes, along with fibroblastic proliferation, abundant collagen fibre deposition, and the formation of newly developed blood vessels. By 21st dpt, the wounds demonstrated weak re-epithelialisation, increased granulation tissue, reduced inflammatory infiltration, and dense collagen fibre accumulation. By 28th dpt, the wounds exhibited complete re-epithelialisation with a fully intact epidermal layer that appeared hyperplastic and thickened. The subcutaneous tissue showed minimal inflammatory cell infiltration, vascular formation, and extensive development of mature fibrous tissue (Figure 2E).

At the 3rd dpt, the diabetic camel-milk-treated wounds exhibited inflammatory features including haemorrhagic red blood cell extravasation, tissue oedema, and marked neutrophil accumulation. By the 7th dpt, granulation tissue formed within the wound gap, with pronounced infiltration of neutrophils and eosinophils (Figure 2C). At the 14th dpt, the wound gap was markedly reduced in size and showed complete re-epithelialisation, accompanied by pronounced fibroblast proliferation and collagen fibre deposition, with a decreased number of inflammatory cells. By the 21st dpt, marked re-epithelialisation was evident, together with substantial deposition of densely packed collagen fibres, while fibroblasts and infiltrating neutrophils and macrophages were minimal. By the 28th dpt, inflammation had subsided, and the amount of granulation tissue had decreased. The overlying epidermis had become intact and filled the wound gap (Figure 2F).

Wound-healing scores, including re-epithelialisation, vascularisation, necrosis, connective tissue formation, and collagen synthesis, were assessed in all animals, as presented in Table 8. Re-epithelialisation did not differ at the 3rd, 7th, and 14th dpt in the diabetic groups (2 and 3) compared with the control group; however, it showed a marked increase at the 21st and 28th dpt. Notably, necrosis resolution, vascular development, connective tissue formation, and collagen synthesis remained markedly delayed at the 3rd, 7th, 14th, 21st, and 28th dpt in the diabetic group relative to both the control and camel-milk-treated diabetic groups.

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Table 8. Histopathological scoring of wound healing in control, diabetic wound and milk treated diabetic rats

Findings	Wounded control					Diabetic wounded control					Diabetic wounded + milk				
Time per day	3rd	7th	14th	21st	28th	3rd	7th	14th	21st	28th	3rd	7th	14th	21st	28th
A	+++	++	+	–	–	+++	+++	++	+	–	+++	++	++	–	–
B	+++	++	+	–	–	++	++	++	+	–	+++	++	+	–	–
C	–	++	+++	+	–	–	++	++	++	++	–	++	+++	+	–
D	–	++	+++	+	–	–	++	++	++	+++	–	++	+++	+	–
E	–	++	+++	+	–	–	++	++	++	+++	–	++	+++	+	–
F	–	–	++	+++	+++	–	–	+	++	++	–	–	++	+++	+++

(–) = absence of lesion; (+) = mild; (++) = moderate; (+++) = severe; A = blood clot, necrosis, cellular debris; B = oedema and inflammatory cells; C = vasculature (neovascularisation); D = fibroblastic proliferation; E = collagen synthesis and scar formation; F = re-epithelialisation

The spleen at the 7th dpt revealed a reactive parafollicular zone surrounding the white pulp in the control group (Figure 3A), mild perifollicular lymphoid depletion in diabetic rats (Figure 3B), and repopulation of the white pulp with basophilic lymphocytes and the formation of small germinal centres in camel-milk-treated diabetic rats (Figure 3C). At 28th dpt, the spleen of the control group exhibited prominent normal white pulp (Figure 3D), whereas the diabetic group showed marked lymphoid depletion (Figure 3E). In contrast, the camel-milk-treated diabetic group exhibited prominent germinal centres and marked lymphoid repopulation (Figure 3F).

DISCUSSION

This study provides compelling evidence that daily oral camel milk supplementation markedly accelerates wound healing in STZ-induced diabetic rats through a multifaceted mechanism. This enhancement appears to result from the restoration of antioxidant defences, suppression of pro-inflammatory mediators, modulation of critical tissue-repair biomarkers, and improved histopathological tissue remodelling. Collectively, these outcomes are consistent with, and substantially extend, the growing literature identifying camel milk as a bioactive

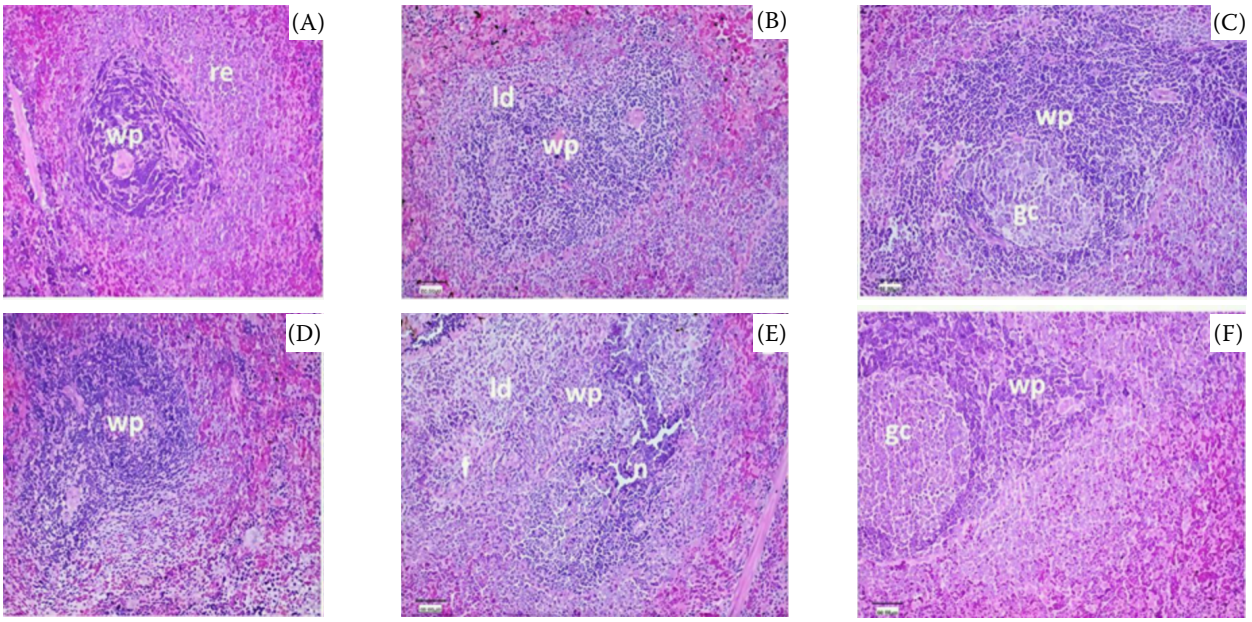


Figure 3. Histopathology of spleen of control (A,D), diabetic (B,E) and milk treated diabetic (C,F) groups at the 7th dpt (A–C) and 28th dpt (D–F) revealed intact reactive white pulp in control group, lymphoid depletion in diabetic group and repopulation and germinal centre formation in camel milk-treated diabetic group (H&E, bar = 50 µm)
gc = germinal centre; f = fibrosis; n = necrosis; ld = lymphoid depletion; re = reactive zone; wp = white pulp

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functional food with therapeutic value in diabetic complications, particularly those involving impaired wound repair (Arain et al. 2023; Al-Tamimi et al. 2024).

Diabetes-induced hyperglycaemia is known to trigger excessive generation of reactive oxygen species (ROS) through several interrelated mechanisms, including mitochondrial dysfunction, glucose autoxidation, and the accumulation of advanced glycation end-products (Gonzalez et al. 2023). Together, these processes culminate in pronounced oxidative stress that disrupts all phases of the wound-healing cascade (Mahmoud et al. 2024). In the present study, the marked reduction in both serum and tissue antioxidant enzymes, particularly CAT and SOD, in diabetic wounded rats aligns with previous reports demonstrating impaired antioxidant capacity in diabetic wounds (Ebaid et al. 2015). Notably, serum CAT levels in the diabetic wounded control group declined progressively from day 14 to day 28, indicating a sustained and worsening oxidative burden. Tissue antioxidant analyses further confirmed persistent suppression of CAT and GPx in both intact and wounded diabetic tissues, with injury imposing an additional insult that further exacerbated these deficits. The significant elevation in MDA, a well-established marker of lipid peroxidation, in diabetic wounded rats reinforces the conclusion that uncontrolled oxidative stress drives membrane damage and cellular dysfunction in this diabetic wound model.

Camel milk supplementation markedly improved both systemic and local antioxidant status. Treated wounded diabetic rats showed significant increases in serum CAT and GPx activities, along with a substantial reduction in MDA levels, bringing them close to healthy controls. These results align with previous reports indicating that camel milk constituents, particularly lactoferrin and intrinsic antioxidant enzymes such as CAT and SOD, can directly scavenge reactive oxygen species while enhancing endogenous antioxidant gene expression (Arain et al. 2023). The pronounced restoration of tissue CAT levels by day 28 in wounded diabetic rats treated with camel milk is especially noteworthy, suggesting that sustained supplementation may be necessary to fully replenish tissue-specific antioxidant reserves. Moreover, preserved GPx activity in treated animals indicates maintenance of selenium-dependent glutathione detoxification pathways, which diabetes commonly impairs (Zhao et al. 2022). Collectively, these findings highlight camel milk as a potent antioxidant intervention that can mitigate the oxidative microenvironment characteristic of diabetic wounds.

Chronic, non-resolving inflammation is a defining feature of diabetic wound pathology, driven by the persistent recruitment of pro-inflammatory macrophages, dysregulated cytokine signalling, and defective efferocytosis (Rodriguez-Rodriguez et al. 2021; Mahmoud et al. 2024). In the present study, wounding alone significantly elevated serum CRP and AA levels in non-diabetic controls, reflecting an appropriate, self-limiting systemic inflammatory response to tissue injury. In contrast, diabetic wounded rats showed prolonged, persistent elevations of these acute-phase reactants, consistent with the sustained inflammatory milieu characteristic of diabetes (Elajaili et al. 2025). At the tissue level, this dysregulation was even more pronounced: diabetic wounded tissues demonstrated markedly higher concentrations of CRP, AA, and TNF-α compared with intact diabetic tissues, indicating that the superimposition of wound injury on the diabetic state further amplifies local pro-inflammatory signalling. These findings suggest that diabetes not only prolongs the systemic inflammatory response but also intensifies local inflammatory activity within the wound microenvironment, thereby impairing the normal progression of wound healing.

The striking reduction in serum and tissue CRP and AA concentrations after camel milk supplementation is one of this study's most compelling findings. By day 28, serum CRP in treated wounded diabetic rats was approximately 80% lower than that in untreated wounded diabetic controls, a magnitude of effect rarely observed with single dietary interventions. This profound anti-inflammatory action likely reflects the combined activities of multiple camel milk bioactives. Immunoglobulins present in camel milk may neutralise damage-associated molecular patterns released from necrotic wound tissue, while lactoferrin suppresses NF-κB activation and subsequent transcription of pro-inflammatory cytokines (Arab et al. 2021; Albarrak and Al-Sobayil 2024). Additionally, camel-milk-derived peptides have been shown to promote macrophage polarisation from the pro-inflammatory M1 phenotype to the pro-reparative M2 phenotype, facilitating the critical transition from the inflammatory to the proliferative phase of healing (Ebaid et al.

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2015). The significant reduction in tissue TNF-α observed in camel-milk-treated diabetic wounded rats on day 28 supports this interpretation, as TNF-α is a master regulator of sustained inflammation and is typically overexpressed in diabetic wounds (Qin and Deng 2025). While serum TNF-α and IL-1β did not reach statistical significance in this study, likely due to inter-animal variability and the relatively short half-lives of these cytokines in circulation, the clear trends toward reduction suggest that larger sample sizes or more frequent sampling could reveal additional significant effects.

Effective wound healing depends on the tightly coordinated activity of growth factors and matricellular proteins that regulate fibroblast proliferation, angiogenesis, collagen synthesis, and re-epithelialisation (Chandra et al. 2026). Among these mediators, TGF-β serves as a central orchestrator, driving myofibroblast differentiation and extracellular matrix deposition while exerting immunosuppressive effects that promote inflammatory resolution (Porel et al. 2025). CTGF, a key downstream effector of TGF-β, further amplifies fibrogenesis and angiogenesis during tissue repair (Sheibani 2022). In the present study, serum CTGF levels were significantly elevated in both wounded non-diabetic and diabetic rats, a pattern consistent with active tissue remodelling. Notably, diabetes induced an even greater rise in CTGF concentrations compared with wounded non-diabetic controls, an observation that may appear paradoxical given the impaired healing characteristic of diabetic wounds. However, this finding aligns with emerging evidence that CTGF-related pathways become dysregulated in the diabetic milieu, wherein compensatory overexpression fails to translate into effective tissue repair due to disruptions in downstream signalling, altered receptor availability, or impaired matrix integration (Furlong et al. 2007; Xiong et al. 2025).

Tissue-level analysis highlighted the compartment-specific impact of diabetes and camel milk on key healing mediators. In wounded non-diabetic controls, TGF-β and CTGF rose appropriately within wound tissue, reflecting normal reparative activation. Diabetic intact tissues, however, showed elevated levels of both factors even without injury, indicating a baseline pro-fibrotic state previously noted in other diabetic complications (Dawi et al. 2025). Camel milk supplementation effectively normalised these elevations: treated diabetic tissues, both intact and wounded, displayed TGF-β and CTGF concentrations closer to healthy controls. This suggests restoration of physiological regulation, as excessive TGF-β activity can drive fibrosis, whereas properly timed signalling supports healing (McDermott et al. 2023). Importantly, treated diabetic wounds healed better despite lower absolute growth factor levels, indicating improved temporal coordination. The transient rise in TGF-β and CTGF on day 14, followed by attenuation by day 28, further suggests that camel milk enabled an appropriately localised and time-limited growth factor response.

IL-10 is a key anti-inflammatory cytokine that promotes macrophage efferocytosis and limits antigen presentation (Mittal et al. 2015; Proto et al. 2018). Although IL-10 levels did not differ significantly between groups, the modest increase observed on day 14 in camel-milk-treated wounded diabetic rats remains noteworthy, given the essential role of IL-10 in minimising collateral tissue damage and facilitating progression to the proliferative phase (Jackson et al. 2012). The absence of a pronounced IL-10 response suggests that camel milk's anti-inflammatory benefits likely arise more from suppressing pro-inflammatory mediators than from directly stimulating IL-10 production.

The histopathological findings strongly confirm the biochemical improvements observed. Untreated diabetic wounds exhibited hallmark features of impaired healing, including delayed re-epithelialisation, persistent inflammatory infiltrates, poor neovascularisation, and disorganised collagen architecture, with incomplete epidermal continuity and immature fibrous tissue still evident at day 28. In contrast, camel milk-treated diabetic wounds showed markedly accelerated repair. By day 14, treated wounds showed complete re-epithelialisation, well-organised granulation tissue, and substantially reduced inflammation, milestones untreated diabetic wounds typically reach only by day 21 or later. Additionally, the preservation of skin appendages and more orderly collagen deposition in treated animals indicate that camel milk not only accelerated wound closure but also improved overall tissue regeneration.

Macroscopic assessment reinforced the histological findings. Camel milk-treated wounds consistently exhibited healthy pink colour, whereas diabetic control wounds appeared pale or yellow, reflecting ischaemia and fibrinous exudate. The

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treated group achieved complete wound closure on day 14, whereas both diabetic and non-diabetic controls showed delayed closure. Treated wounds also lacked oedema, exudate, and crust formation, indicating a smooth and uncomplicated healing trajectory. These macroscopic improvements have important translational relevance, as clinical wound assessment relies heavily on visual indicators such as colour, exudate, and degree of epithelialisation.

The present findings are consistent with and extend previous studies on camel milk–mediated wound repair. Ebaid et al. (2015) reported improved wound closure with topical camel milk in diabetic mice, while Al-Tamimi et al. (2024) demonstrated immunoregulatory and proangiogenic effects of camel milk peptides *in vitro*. This study advances the field by demonstrating efficacy following oral administration, indicating systemic bioavailability and coordinated local and systemic actions. Strengths include integrated serum and tissue biomarker profiling, evaluation of splenic immune modulation, assessment of growth-factor dynamics, and a rigorous comparative design. Importantly, daily oral camel milk (5 ml/kg) produced biochemical and histological improvements comparable to those reported for pharmacological interventions, supporting its potential as an adjunctive therapy.

Several limitations merit consideration. First, the camel milk used in this study was not subjected to detailed compositional analysis. Because camel milk composition varies with factors such as breed, diet, health status, stage of lactation, and environmental conditions, some degree of biological variability cannot be excluded. Although previous studies from our group have identified bioactive constituents with immunoprotective, antioxidant, and metabolic properties (Albarrak 2023; Albarrak and Al-Sobayil 2024), future studies should include standardised compositional profiling and quantification of major bioactive molecules to facilitate comparisons across studies and clarify underlying mechanisms. Second, although diabetes was confirmed 72 h after streptozotocin administration and only rats with fasting blood glucose levels ≥13.9 mmol/l were included, the study did not obtain serial measurements of blood glucose and body weight during treatment. Consequently, we could not determine the relative contributions of improved metabolic status and the direct wound-healing effects of camel milk. Future studies should incorporate longitudinal monitoring of these parameters. Finally, although we administered distilled water as a vehicle control in equivalent volumes to account for gavage-related stress, repeated long-term gavage may have exerted minor physiological effects. However, because all corresponding control groups underwent identical procedures, any such influence is unlikely to have confounded the observed differences between groups.

The STZ-induced type 1 diabetes model does not fully reflect the pathophysiology of type 2 diabetes that underlies most diabetic foot ulcers; alternative dietary or genetic models would enhance clinical relevance. Another limitation was the absence of quantitative wound-healing measurements, such as wound area, wound diameter, and percentage wound contraction. As a result, the authors evaluated wound healing mainly through clinical, histopathological, and biochemical assessments. Future studies should incorporate standardised planimetric measurements to provide a more objective evaluation of wound closure and further validate the therapeutic potential of camel milk in diabetic wound healing. The 28-day duration captured the early phases of healing but did not permit assessment of late remodelling or scar maturation, which require longer follow-up. Although multiple biomarkers were examined, the specific camel milk–derived peptides and molecular pathways involved remain undefined, highlighting the need for mechanistic and proteomic studies. Dose–response relationships were not evaluated, and functional immune assays are needed to confirm systemic immunomodulation. Finally, comparisons with established wound-care therapies would help contextualise therapeutic efficacy.

Despite these limitations, the findings position camel milk as a practical and well-tolerated adjunct for diabetic wound care. Its established safety, widespread use in regions with high diabetes prevalence, and lack of cold-chain requirements support its feasibility, while oral supplementation avoids the limitations of topical administration. Notably, improved wound healing was accompanied by enhanced systemic antioxidant and immune status. These findings provide a strong rationale for pilot clinical trials in patients with diabetic foot ulcers, where low-cost adjunctive therapies could make a meaningful contribution to reducing disease burden.

In conclusion, this study shows that daily oral camel milk supplementation markedly accelerates

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diabetic wound healing in rats through a multifaceted mechanism involving restored antioxidant defences, attenuated systemic and local inflammation, normalised growth factor signalling, and improved histopathological remodelling. These benefits were evident across systemic indices, including serum biomarkers, splenic histology, and local wound parameters, spanning tissue biochemistry, structural organisation, and macroscopic healing. By simultaneously targeting oxidative stress, chronic inflammation, and impaired reparative signalling, the three principal pathological drivers of diabetic wound chronicity, camel milk exerts broader therapeutic effects than interventions directed at single pathways. Collectively, these findings provide a compelling preclinical rationale for clinical evaluation of camel milk in diabetic foot ulcer management and offer a mechanistic basis for future optimisation of dosing, formulation, and potential combination strategies in treating human diabetic patients.

Conflict of interest

The authors declare no conflict of interest.

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