International Journal of Pharmacology

Int. J. Pharmacol. **2026**; 22(4): 53160
https://doi.org/10.31083/IJP53160

Research Article

Protective Effects of Frankincense Supplementation Against Oxidative Stress and Inflammatory Imbalance in Diabetic Rats

Fahad Alshanbari[1], Abdelkader Zaki[1], Yousef Alharbi[1], Tariq Almundarij[1], Saleh Altuwaijri[2], Mohie Haridy[2], Saleh Albarrak[2,*]

[1]Department of Medical Biosciences, College of Veterinary Medicine, Qassim University, 52571 Buraydah, Saudi Arabia
[2]Department of Pathology and Laboratory Diagnosis, College of Veterinary Medicine, Qassim University, 52571 Buraydah, Saudi Arabia
*Correspondence: salbarrak@qu.edu.sa (Saleh Albarrak)
Academic Editor: Mehmet Ozaslan
Submitted: 21 April 2026 Revised: 10 June 2026 Accepted: 18 June 2026 Published: 26 August 2026

Abstract

Background: Persistent oxidative stress and chronic low-grade inflammation are hallmarks of diabetes mellitus, and both are important factors in the onset and course of diabetic complications. Although frankincense (*Boswellia sacra*) is widely known for its anti-inflammatory and antioxidant properties, its coordinated effects on pro- and anti-inflammatory mediators in the context of diabetes remain poorly understood. **Methods:** Three groups of adult male Sprague-Dawley rats were randomly assigned: 10 healthy control rats, 15 diabetic control rats, and 15 diabetic rats administered oral frankincense extract (500 mg/kg/day) for 28 days. Type 2 diabetes mellitus was induced in the designated groups by a single intraperitoneal injection of streptozotocin (STZ; 55 mg/kg). On days 14 and 28, serum samples were collected to measure antioxidant indicators, including glutathione peroxidase (GPx), catalase (CAT), superoxide dismutase (SOD), and malondialdehyde (MDA). Tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), transforming growth factor-β (TGF-β), connective tissue growth factor (CTGF), serum amyloid A (SAA), C-reactive protein (CRP), and interleukin-10 (IL-10) were among the inflammatory and regulatory biomarkers evaluated. Histopathological samples were collected from the liver, kidneys, and pancreas on day 28 of the experiment. **Results:** Diabetic controls exhibited significant reductions in CAT, SOD, and GPx activities compared with healthy controls ($p < 0.05$), alongside elevated MDA, CRP, SAA, TNF-α, and IL-1β ($p < 0.05$). Frankincense supplementation for 28 days significantly increased CAT (101.3 ± 19.11 U/L) and GPx (39.39 ± 0.93 mU/mL) compared with diabetic controls (64.14 ± 1.25 U/L and 20.43 ± 0.97 mU/mL; $p < 0.05$ and 0.001, respectively). MDA levels were reduced from 17.4 ± 0.82 to 9.44 ± 0.29 nmol/mL ($p < 0.001$). CRP and SAA decreased markedly to 50.4 ± 2.08 U/L and 9.65 ± 0.40 ng/mL, respectively ($p < 0.01$ vs. diabetic controls). TNF-α was significantly reduced to 14.11 ± 0.98 pg/mL on day 14 ($p < 0.001$), but returned to levels comparable to untreated diabetic rats by day 28. At the end of the experiment, Frankincense supplementation significantly elevated TGF-β levels ($p < 0.01$) but did not significantly alter CTGF levels, while IL-10 levels decreased significantly ($p < 0.001$). Frankincense ameliorated and partially restored the adverse histopathological findings of diabetes in rats, including hepatocyte swelling and fatty degeneration, glomerular hemorrhage and inflammation, and pancreatic injury. **Conclusions:** Frankincense supplementation at 500 mg/kg for 28 days effectively attenuates diabetes-induced oxidative stress by restoring antioxidant activities and reducing lipid peroxidation, while suppressing key proinflammatory mediators. These findings support the further investigation of frankincense as an adjunctive strategy for managing the oxidative and inflammatory burden associated with diabetes.

Keywords: *Boswellia sacra*; diabetes mellitus; oxidative stress; antioxidants; inflammation; tumor necrosis factor-α

1. Introduction

Diabetes mellitus represents one of the most important worldwide health concerns of the twenty-first century. The International Diabetes Federation projects that 537 million adults worldwide received a diabetes diagnosis in 2021, and that number is predicted to increase to nearly 783 million by 2045 [1]. Several chronic consequences, including cardiovascular disease, nephropathy, retinopathy, and neuropathy, are associated with this metabolic condition, which is typified by persistent hyperglycemia brought on by abnormalities in insulin secretion, action, or both [2]. In addition to the traditional disturbances in glucose regulation, growing evidence points to two interconnected pathological processes, oxidative stress and chronic low-grade inflammation, as major contributors to the onset and advancement of complications associated with diabetes.

The hyperglycemic environment that characterizes diabetes disrupts cellular redox homeostasis through several interrelated mechanisms. These include enhanced generation of reactive oxygen species (ROS) arising from mitochondrial electron transport chain impairment, glucose autoxidation, and increased flux through the polyol and hexosamine pathways. Persistent ROS overproduction exceeds the capacity of intrinsic antioxidant defenses, particularly key enzymatic systems such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), resulting in extensive damage to cellular macromolecules. A prominent consequence of this oxidative stress is lipid

peroxidation, typically indicated by elevated malondialdehyde (MDA) levels, thereby compromising membrane integrity and disrupting cellular function.

Concurrent with these redox disturbances, prolonged hyperglycemia stimulates proinflammatory signaling pathways, notably through activation of nuclear factor-κB (NF-κB), which upregulates the production of inflammatory mediators including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and acute-phase proteins such as C-reactive protein (CRP) and serum amyloid A (SAA) [3]. This chronic inflammatory state is further intensified by alterations in regulatory cytokines and repair-associated factors, including transforming growth factor-β (TGF-β), connective tissue growth factor (CTGF), and interleukin-10 (IL-10), all of which are essential for maintaining immune balance, facilitating tissue repair, and ensuring the resolution of inflammation.

The constraints and potential adverse effects associated with conventional antidiabetic therapies have prompted growing interest in complementary and alternative treatment approaches [4]. While metformin continues to serve as a first-line therapy, its use is often limited by gastrointestinal side effects and, albeit rarely, the risk of lactic acidosis. Likewise, sulfonylureas are commonly associated with weight gain and an elevated risk of hypoglycemia, whereas thiazolidinediones have been implicated in fluid retention, weight gain, and unfavorable cardiovascular outcomes [5]. In this context, plant-derived natural products have emerged as promising candidates for developing multi-target antidiabetic interventions with potentially improved safety profiles [6]. Among these, frankincense, the oleo-gum resin obtained from *Boswellia* species, has garnered significant scientific interest due to its broad spectrum of pharmacological activities, particularly its anti-inflammatory and antioxidant properties [7].

A growing body of preclinical evidence underscores the therapeutic potential of frankincense in metabolic disease contexts. A systematic review by Mahdian et al. [8] indicated that *Boswellia* species ameliorate hyperglycemia, improve lipid profiles, and mitigate diabetic complications through mechanisms including enhanced insulin sensitivity, preservation of pancreatic β-cell function, and attenuation of oxidative stress. In streptozotocin (STZ)-induced diabetic rats, administration of *Boswellia sacra* ethanol extract (200 mg/kg/day) produced significant reductions in blood glucose, increased circulating insulin levels, strengthened antioxidant defense systems, suppressed pro-inflammatory cytokine production, and maintained pancreatic and hepatic histoarchitecture, demonstrating efficacy comparable to metformin [9]. Consistent findings have been reported for *Boswellia serrata*, whose gum resin has been shown to alleviate oxidative stress and reduce markers of hepatic and pancreatic injury in diabetic models [10]. At the molecular level, boswellic acids, particularly 11-keto-β-boswellic acid (KBA) and acetyl-11-keto-β-boswellic acid (AKBA), appear to exert antidiabetic and cardioprotective effects through modulation of adenosine monophosphate-activated protein kinase (AMPK) signaling pathways and interactions with key enzymes involved in metabolic regulation [11,12].

Although evidence supporting the antidiabetic activity of frankincense is steadily increasing, several important mechanistic aspects remain insufficiently defined. Most available studies have focused primarily on its glucose-lowering and broad antioxidant properties, with comparatively limited attention to its integrated effects on inflammatory regulatory networks. In particular, the impact of frankincense on key modulatory biomarkers, such as CTGF, and on the dynamic balance between proinflammatory cytokines (TNF-α, IL-1β) and anti-inflammatory mediators (IL-10) has not been comprehensively elucidated. Moreover, uncertainties persist regarding optimal dosing regimens and treatment duration. To address these gaps, the present study evaluates the effects of *Boswellia sacra* supplementation on oxidative stress indices, lipid peroxidation, proinflammatory biomarkers (CRP, SAA, TNF-α, IL-1β), and anti-inflammatory mediators (TGF-β, CTGF, IL-10) in a STZ-induced diabetic rat model. A 28-day supplementation protocol (500 mg/kg body weight), as described by Al-Edany and Alhelfi [13], was employed. This comprehensive approach is intended to clarify the multi-target actions of frankincense and to further substantiate its potential as an adjunctive therapeutic strategy for alleviating oxidative stress and inflammatory dysregulation in diabetes mellitus (Fig. 1).

2. Materials and Methods

2.1 Animals

A total of 40 adult male Sprague–Dawley rats (8–10 weeks old, weighing 200–250 g) wereused in this study. The animals were originally obtained from the animal facility of the College of Pharmacy, King Saud University, Riyadh, Saudi Arabia, and subsequently maintained in the College experimental animal unit under standard husbandry conditions (22 ± 2 °C, 50–60% relative humidity, and a 12 h light/12 h dark cycle) with free access to a standard pellet diet and water ad libitum. After a one-week acclimatization period, the animals were randomly allocated into three main groups. The first group (n = 10) consisted of healthy control rats that underwent all handling and experimental procedures and served as the physiological baseline for serum measurements. The second group (n = 15) consisted of diabetic control rats. The third group (n = 15) comprised diabetic rats that received daily frankincense supplementation for 28 days. Sample size was based on previous similar studies and a target statistical power. Animals showing infection, >20% weight loss, abnormal behavior, or unrelieved severe distress were excluded and managed according to humane endpoint criteria. All animals were humanely euthanized at study completion using an over-

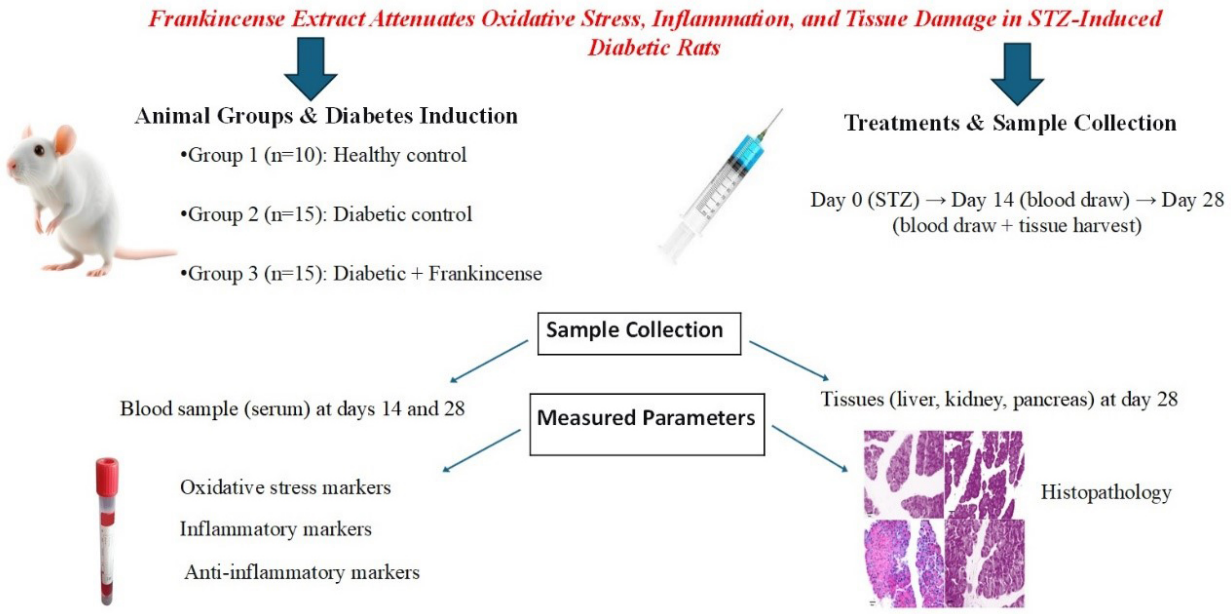

Fig. 1. A detailed flowchart of the design process employed in the current study.

dose of inhaled isoflurane (≥5% in oxygen) administered in a sealed chamber, followed by confirmation of death through cervical dislocation performed by trained personnel, in accordance with ethical guidelines.

2.2 Induction of Diabetes Mellitus

Type 2 diabetes mellitus was induced in the designated groups by a single intraperitoneal (i.p.) injection of STZ (Santa Cruz Biotechnology, Germany) at a dose of 55 mg/kg body weight, freshly prepared in cold 0.1 M citrate buffer (pH 4.5). After 15 min, the animals were given nicotinamide (55 mg/kg) intraperitoneally [14]. Non-diabetic controls received an equal volume of citrate buffer. Fasting blood glucose was measured 72 h post-injection and subsequently at weekly intervals using tail vein blood samples and a calibrated glucometer (Accu-Chek Performa, Roche Diagnostics). Rats with fasting blood glucose ≥250 mg/dL were deemed diabetic and included in the experiment. Diabetic animals were monitored daily for clinical signs of distress, including polyuria, polydipsia, and body weight loss, and were provided supportive care as required. Subcutaneous saline was administered as needed to prevent dehydration and ensure animal welfare.

2.3 Frankincense Supplementation Protocol

Frankincense (*Boswellia sacra*) gum resin granules were finely crushed and ground into a powder. A total of 50 grams of powder were macerated in 500 mL distilled water at room temperature for 24 h. The mixture was centrifuged at 1000 rpm for 10 min, and the supernatant was vacuum-filtered through Whatman No. 1 filter paper. The aqueous extract was stored at 4 °C until use. The intervention group received oral frankincense extract (500 mg/kg) once daily for 28 days, as per Al-Edany and Alhelfi [13]. This dose was selected based on prior experimental evidence demonstrating its bioactive efficacy in modulating metabolic and inflammatory pathways. To control for gavage-related stress, non-supplemented groups (diabetic and non-diabetic controls) received an equivalent volume of distilled water via oral gavage. The supplementation regimen was maintained consistently throughout the experimental period.

2.4 Serum Collection

At the designated time points (days 14 and 28), as well as at baseline for the healthy control group, rats were fasted for 6 h before blood collection. Animals were anesthetized with 3-5% isoflurane for induction and maintained at 1.5-3% isoflurane in oxygen during blood collection. Blood samples were collected from the medial canthus using sterile capillary tubes, left to clot at room temperature for 30 minutes, then centrifuged at 3000 ×g and 4 °C for 15 minutes. The resulting clear serum was carefully aliquoted into sterile, low protein-binding microcentrifuge tubes and stored immediately at –20 °C to preserve the stability of antioxidants and cytokines for subsequent biochemical analyses.

2.5 Antioxidant and Oxidative Stress Markers

Serum samples were analyzed for antioxidant enzyme activities and lipid peroxidation using commercially available assay kits, including GPx (Biodiagnostic, Cat. No. 2524), SOD (Biodiagnostic, Cat. No. 2521), CAT (Biodiagnostic, Cat. No. 2517), and MDA (Biodiagnostic, Cat. No. 2581), according to the manufacturers' instructions.

2.6 Inflammatory and Regulatory Biomarkers

Serum concentrations of inflammatory biomarkers, including CRP, SAA, TNF-α, and IL-1β, were quantified using rat-specific enzyme-linked immunosorbent assay (ELISA) kits (Sunlong Biotech Ltd., China; Cat. Nos. EL0006Ra, SL0625Ra, SL0722Ra, and HS-EL0039Ra, respectively). Anti-inflammatory and regulatory mediators, such as TGF-β, CTGF, and IL-10, were measured using commercially available rat-specific ELISA kits from the same manufacturer (Sunlong Biotech Ltd., China; Cat. Nos. SL0708Ra, SL0196Ra, and HS-EL0031Ra, respectively), in accordance with the manufacturers' protocols.

2.7 Histopathology

Parts of the liver, kidneys, and pancreas of all groups were sampled at the end of the experiment and immersed in 10% neutral buffered formalin. The fixed tissue samples, about 1 cm^3 in size, were trimmed to 5 mm and processed as follows: dehydrated through a series of ascending grades of alcohol, cleared in three changes of xylene, impregnated with paraffin wax, and finally embedded in melted paraffin (60 °C). The tissues were then sectioned at 5 µm and routinely stained with hematoxylin and eosin (H&E) for microscopic examination.

2.8 Statistical Analysis

Data are expressed as the mean ± standard error of the mean (SEM). Normality was assessed using the Shapiro–Wilk test, and group comparisons over two time points were analyzed by two-way analysis of variance (ANOVA) (treatment and time factors). When the overall ANOVA indicated significance ($p < 0.05$), Tukey's post hoc test was applied for multiple comparisons. All statistical analyses were conducted using GraphPad Prism software (version 9.0; GraphPad Software, Inc., Boston, MA, USA), with $p < 0.05$ considered statistically significant.

3. Results

3.1 Effect of Frankincense Supplementation on Oxidative Stress in Diabetic Rats

Diabetic control rats exhibited significantly reduced serum antioxidant enzyme activities compared with healthy controls ($p < 0.01$; Table 1). Serum CAT activity was markedly decreased in diabetic rats (64.14 ± 1.25 U/L) relative to healthy controls (150.9 ± 3.59 U/L). Following 28 days of frankincense supplementation (500 mg/kg), CAT activity increased significantly to 101.3 ± 19.11 U/L ($p < 0.05$ vs. diabetic controls), approaching normal physiological levels. Similarly, SOD activity was significantly suppressed in diabetic control rats (82.5 ± 7.5 U/mL) compared with healthy controls (135.0 ± 10.5 U/mL; $p < 0.01$). Frankincense supplementation for 28 days restored SOD activity to 78.75 ± 9.43 U/mL in treated diabetic rats; however, this change represented only a modest improvement. GPx activity also declined significantly following diabetes induction (20.43 ± 0.97 mU/mL) compared with healthy rats (34.04 ± 2.91 mU/mL; $p < 0.01$). Treatment with frankincense significantly increased GPx levels to 39.39 ± 0.93 mU/mL after 28 days ($p < 0.001$ vs. diabetic controls), restoring values to levels close to those observed in the healthy group. Overall, frankincense supplementation markedly ameliorated diabetes-induced oxidative stress by restoring key antioxidant enzymes toward normal levels.

3.2 Effect of Frankincense Supplementation on Lipid Peroxidation in Diabetic Rats

Diabetic control rats exhibited a significant increase in serum MDA levels (17.4 ± 0.82 nmol/mL) compared with healthy controls (9.7 ± 1.69 nmol/mL, $p < 0.01$ on day 28; Table 1), reflecting increased lipid peroxidation. Following 28 days of frankincense supplementation (500 mg/kg), MDA concentrations were significantly reduced relative to untreated diabetic rats (9.44 ± 0.29 vs. 17.4 ± 0.82 nmol/mL; $p < 0.001$). Notably, MDA levels in frankincense-treated diabetic rats approached those observed in healthy controls, indicating effective attenuation of diabetes-induced oxidative damage to membranes.

3.3 Effect of Frankincense Supplementation on Inflammatory Biomarkers in Diabetic Rats

Serum levels of CRP, SAA, TNF-α, and IL-1β were quantified (Table 2). Diabetic control rats exhibited a marked increase in systemic inflammatory biomarkers compared with healthy control animals ($p < 0.05$). Specifically, serum CRP levels were significantly elevated in untreated diabetic rats (187.1 ± 1.42 and 181.7 ± 21.07 U/L) relative to healthy controls (136.7 ± 2.5 U/L; $p < 0.05$). Following 28 days of frankincense supplementation (500 mg/kg), CRP concentrations were significantly reduced to 50.40 ± 2.08 U/L ($p < 0.001$ vs. diabetic controls), indicating a pronounced anti-inflammatory effect. Similarly, serum SAA levels were significantly higher in diabetic control rats compared with healthy animals (22.47 ± 0.76 vs. 10.28 ± 0.72 ng/mL; $p < 0.01$). Frankincense treatment for 28 days resulted in a significant reduction in SAA levels (9.65 ± 0.40 ng/mL; $p < 0.01$ vs. diabetic controls), with values approaching those observed in the healthy group.

Proinflammatory cytokines were also markedly elevated in diabetic rats. TNF-α levels increased significantly in diabetic controls (34.13 ± 5.63 pg/mL) compared with healthy rats (20.84 ± 0.94 pg/mL; $p < 0.01$). Frankincense supplementation significantly reduced TNF-α concentrations on day 14 ($p < 0.001$ vs. diabetic controls); however, by day 28, TNF-α levels in frankincense-treated rats were elevated and comparable to those observed in untreated diabetic rats, indicating a transient anti-inflammatory effect that diminished with prolonged supplementation. Likewise, serum IL-1β levels were significantly elevated in diabetic control animals (25.73 ± 3.73 pg/mL) compared with healthy controls (13.97 ± 1.94 pg/mL; $p < 0.01$). Treatment with frankincense resulted in a modest reduction in IL-1β

Table 1. Serum levels of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and malondialdehyde (MDA).

Group	CAT (U/L)	SOD (U/mL)	GPx (mU/mL)	MDA (nmol/mL)
Healthy control group	150.9 ± 3.59	135.0 ± 10.5	34.04 ± 2.91	9.7 ± 1.69
Diabetic control group (day 14)	89.4 ± 8.25*	76.25 ±11.43**	23.69 ± 1.63*	14.74 ± 1.25*
Diabetic control group (day 28)	64.14 ± 1.25**	82.5 ± 7.5**	20.43 ± 0.97**	17.4 ± 0.82**
Diabetic + frank. group (day 14)	121.8 ± 19.05[a]	100.25 ± 7.44[a]	32.58 ± 2.55[b]	10.55 ± 1.09[b]
Diabetic + frank. group (day 28)	101.3 ± 19.11[a]	78.75 ± 9.43	39.39 ± 0.93[c]	9.44 ± 0.29[c]

Data are presented as the mean ± standard error of the mean (SEM). * and ** denote significant differences in the diabetic control group versus the healthy control ($p < 0.05$ and $p < 0.01$, respectively). Different superscript letters (a, b, c) indicate significant differences versus the diabetic control within the same day ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively).

Table 2. Serum levels of C-reactive protein (CRP), serum amyloid A (SAA), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β).

Group	CRP (U/L)	SAA (ng/mL)	TNF-α (pg/mL)	IL-1β (pg/mL)
Healthy control group	136.7 ± 2.5	10.28 ± 0.72	20.84 ± 0.94	13.97 ± 1.94
Diabetic control group (day 14)	187.1 ± 1.42*	20.36 ± 0.64*	32.25 ± 2.81*	28.16 ± 0.96**
Diabetic control group (day 28)	181.7 ± 21.07*	22.47 ± 0.76**	34.13 ± 5.63**	25.73 ± 3.73**
Diabetic + frank. group (day 14)	31.71 ± 18.93[c]	14.14 ± 2.54[a]	14.11 ± 0.98[c]	26.23 ± 7.09
Diabetic + frank. group (day 28)	50.4 ± 2.08[c]	9.65 ± 0.40[b]	39.23 ± 7.18	21.71 ± 2.55

Data are presented as the mean ± SEM. * and ** denote significant differences in the diabetic control group versus the healthy control ($p < 0.05$ and $p < 0.01$, respectively). Different superscript letters (a, b, c) indicate significant differences versus the diabetic control within the same day ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively).

levels to 21.71 ± 2.55 pg/mL; however, this decrease did not reach statistical significance versus the diabetic control group, indicating a limited or partial effect of frankincense on IL-1β-mediated inflammatory signaling.

Collectively, these findings suggest that frankincense supplementation attenuates diabetes-induced systemic inflammation, as evidenced by reductions in acute-phase reactants and key proinflammatory cytokines.

3.4 Effect of Frankincense Supplementation on Anti-inflammatory Biomarkers in Diabetic Rats

The effects of frankincense supplementation on serum levels of anti-inflammatory biomarkers, including TGF-β, CTGF, and IL-10, were evaluated (Table 3). Diabetic control rats showed no significant difference in serum TGF-β levels compared with healthy control rats. In contrast, frankincense supplementation in diabetic rats significantly increased serum TGF-β concentrations on days 14 and 28 relative to the diabetic control group ($p < 0.001$ and $p < 0.01$, respectively). CTGF levels were markedly elevated in diabetic control rats compared with healthy controls (514.9 ± 22.92 and 306.2 ± 21.46 vs. 176.2 ± 4.79 pg/mL; $p < 0.001$ and $p < 0.05$ on days 14 and 28, respectively). Frankincense administration exhibited a significant reduction in serum CTGF levels only on day 14 ($p < 0.01$), indicating that frankincense supplementation exerted a transient modulatory effect on CTGF expression that was not sustained with prolonged treatment.

In contrast, serum levels of the anti-inflammatory cytokine IL-10 showed no significant differences between healthy and diabetic control rats ($p > 0.05$), suggesting that diabetes did not significantly affect systemic IL-10 levels during the experimental period. Notably, IL-10 levels decreased significantly on days 14 and 28 following frankincense supplementation ($p < 0.05$ vs. diabetic controls), indicating that frankincense may have altered immune homeostasis by diminishing the need for elevated IL-10-mediated anti-inflammatory activity.

3.5 Histopathological Findings

In the control group, the general structure of the hepatic parenchyma was preserved. The hepatic lobules were composed of normal hepatocytes, surrounded by sinusoids, and arranged radially towards the centrilobular veins, with Kupffer cells and red blood cells in the capillary lumen. Portal areas were also normal, with no observed inflammatory infiltration, fatty degeneration, or abnormal distribution of fibroblasts or collagen in rats (Fig. 2A). In STZ-treated rats, hepatocytes were enlarged and contained abundant glycogen with obscured narrow sinusoids; in some fields, hepatocytes also contained focal fatty vacuoles (Fig. 2B). Dilated central veins as well as sinusoids were also observed (Fig. 2C). In frankincense diabetic rats, hepatic tissue showed near-restoration of normal hepatic architecture closely resembling the control group (Fig. 2D).

Table 3. Serum levels of transforming growth factor-β (TGF-β), connective tissue growth factor (CTGF), and interleukin-10 (IL-10).

Group	TGF-β (pg/mL)	CTGF (pg/mL)	IL-10 (pg/mL)
Healthy control group	2.83 ± 0.29	176.2 ± 4.79	20.21 ± 1.09
Diabetic control group (day 14)	3.15 ± 0.67	514.9 ± 22.92***	16.6 ± 3.69
Diabetic control group (day 28)	3.67 ± 0.38	306.2 ± 21.46*	20.5 ± 3.17
Diabetic + frank. group (day 14)	11.00 ± 1.93^{c}	327.8 ± 68.23^{b}	14.27 ± 3.43^{a}
Diabetic + frank. group (day 28)	5.53 ± 0.20^{b}	230.3 ± 7.08	8.45 ± 2.51^{c}

Data are presented as the mean ± SEM. * and *** denote significant differences in the diabetic control group versus the healthy control ($p < 0.05$ and $p < 0.001$, respectively). Different superscript letters (a, b, c) indicate significant differences versus the diabetic control within the same day ($p < 0.05$, $p < 0.01$, and $p < 0.001$, respectively).

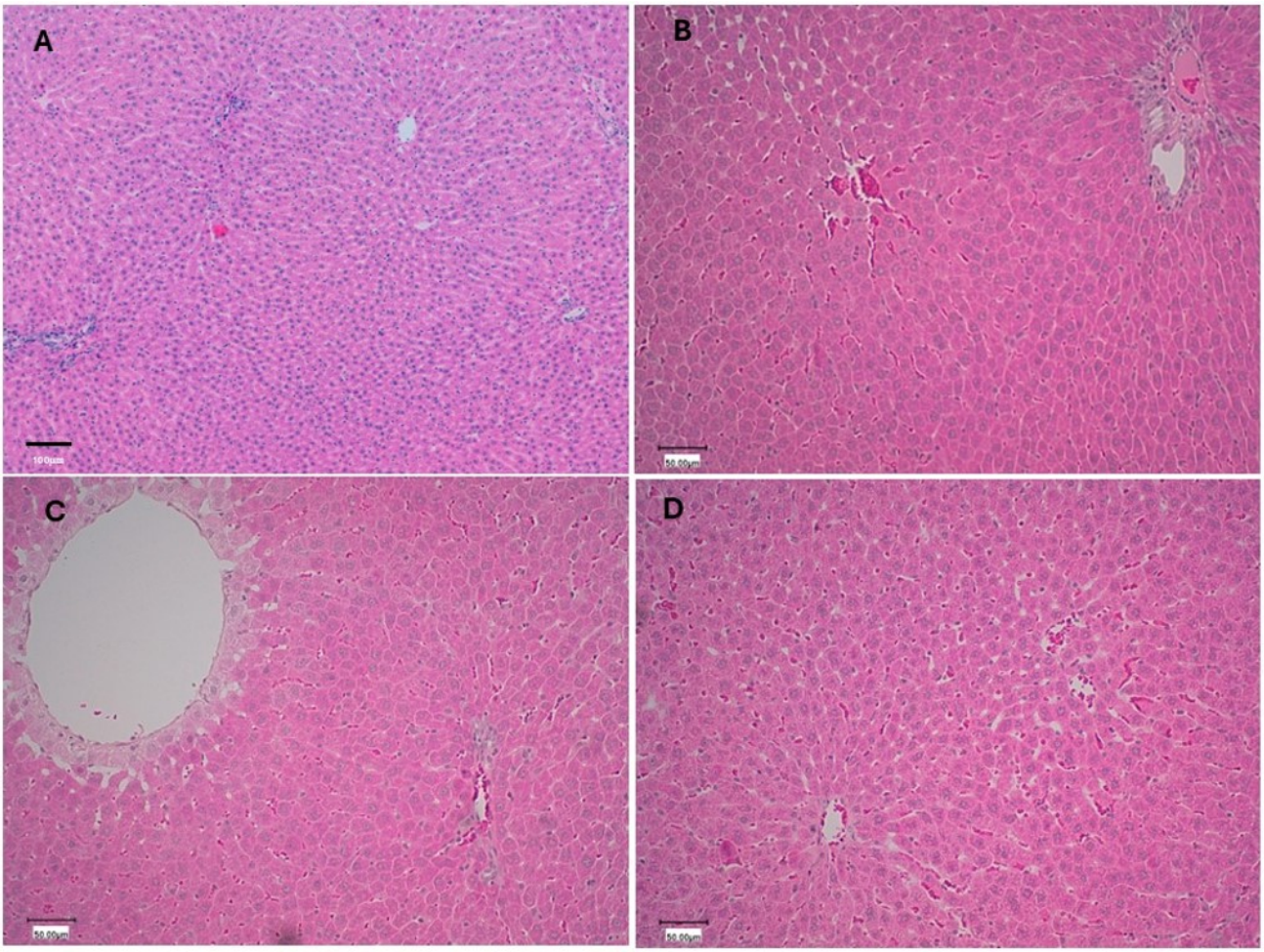

Fig. 2. Histopathological evaluation of hepatic tissue in control, STZ-induced diabetic, and Frankincense-treated diabetic rats. (A) Liver of a control rat with preserved hepatic parenchyma architecture (hematoxylin and eosin (H&E), scale bar = 100 µm). (B) Liver of a streptozotocin (STZ)-treated rat with enlarged glycogen-rich hepatocytes with obscured narrow sinusoids (H&E, scale bar = 50 µm). (C) Liver of an STZ-treated rat with dilated central veins as well as sinusoids (H&E, scale bar = 50 µm). (D) Liver of a frankincense-treated diabetic rat with near-restoration of normal hepatic architecture (H&E, scale bar = 50 µm).

Control rats displayed healthy renal tissue with normal glomeruli and tubules (Fig. 3A). In contrast, STZ-diabetic rats exhibited thickened glomerular basement membrane, glomerular hemorrhage, and severe glomerular injury (Fig. 3B,C). Renal tubules were swollen, and lumens were narrow or absent. Tubular epithelial denudation and desquamation were also observed (Fig. 3B,C). In frankincense diabetic rats, there was a marked improvement in renal histology, with restoration of glomerular and tubular structures (Fig. 3D).

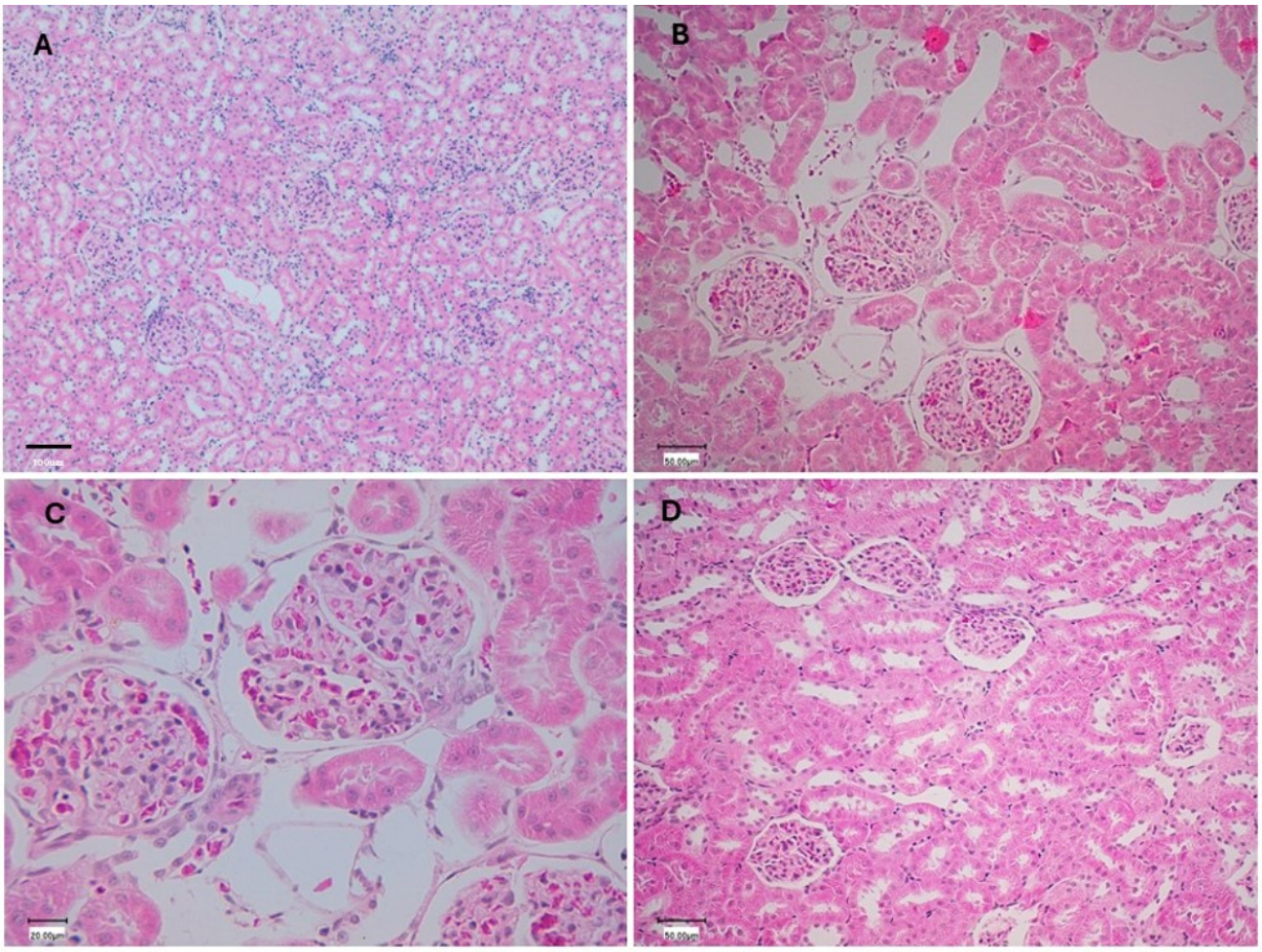

Fig. 3. Histopathological evaluation of renal tissue in control, STZ-induced diabetic, and Frankincense-treated diabetic rats. (A) Renal tissue of a control rat with normal glomeruli and tubules (H&E, scale bar = 100 µm). (B) Renal tissue of an STZ-treated rat with thickened glomerular basement membrane, glomerular hemorrhage, and severe glomerular and tubular injury (H&E, scale bar = 50 µm). (C) Higher magnification of panel B (H&E, scale bar = 20 µm). (D) Renal tissue from frankincense-treated diabetic rats with improved renal histology to control levels (H&E; scale bar = 50 µm).

In the control group, the exocrine and endocrine tissues were normal (Fig. 4A). In the STZ-diabetic group, shrinkage in islet size and reduced numbers of α- and β-cells were observed. Moreover, there was progressive exocrine pancreatic damage, including acinar cell atrophy (Fig. 4B), architectural distortion, nuclear pyknosis, and cytoplasmic changes (Fig. 4C). In frankincense-diabetic rats, restoration of the pancreatic endocrine and exocrine tissues to near-normal architecture was observed (Fig. 4D).

4. Discussion

The present study provides comprehensive evidence that frankincense (*Boswellia sacra*) supplementation exerts significant antioxidative and anti-inflammatory effects in a STZ-induced diabetic rat model. Following 28 days of oral administration at a dose of 500 mg/kg body weight, frankincense effectively restored the activity of key endogenous antioxidant enzymes, including CAT, SOD, and GPx, while concomitantly reducing MDA levels, a reliable biomarker of lipid peroxidation. These findings indicate a robust protective effect against diabetes-induced oxidative stress.

In parallel, frankincense treatment markedly attenuated the diabetes-associated elevation of systemic proinflammatory mediators, including CRP, SAA, TNF-α, and IL-1β, underscoring its potent anti-inflammatory potential. Notably, the intervention exerted differential and time-dependent effects on anti-inflammatory and regulatory cytokines, including TGF-β, CTGF, and IL-10. This pattern suggests a nuanced immunomodulatory action, characterized by selective regulation of inflammatory pathways rather than indiscriminate immunosuppression.

4.1 Restoration of Antioxidant Defense Mechanisms

The observed restoration of antioxidant enzyme activities in the present study is consistent with a growing body of evidence supporting the redox-modulating properties of

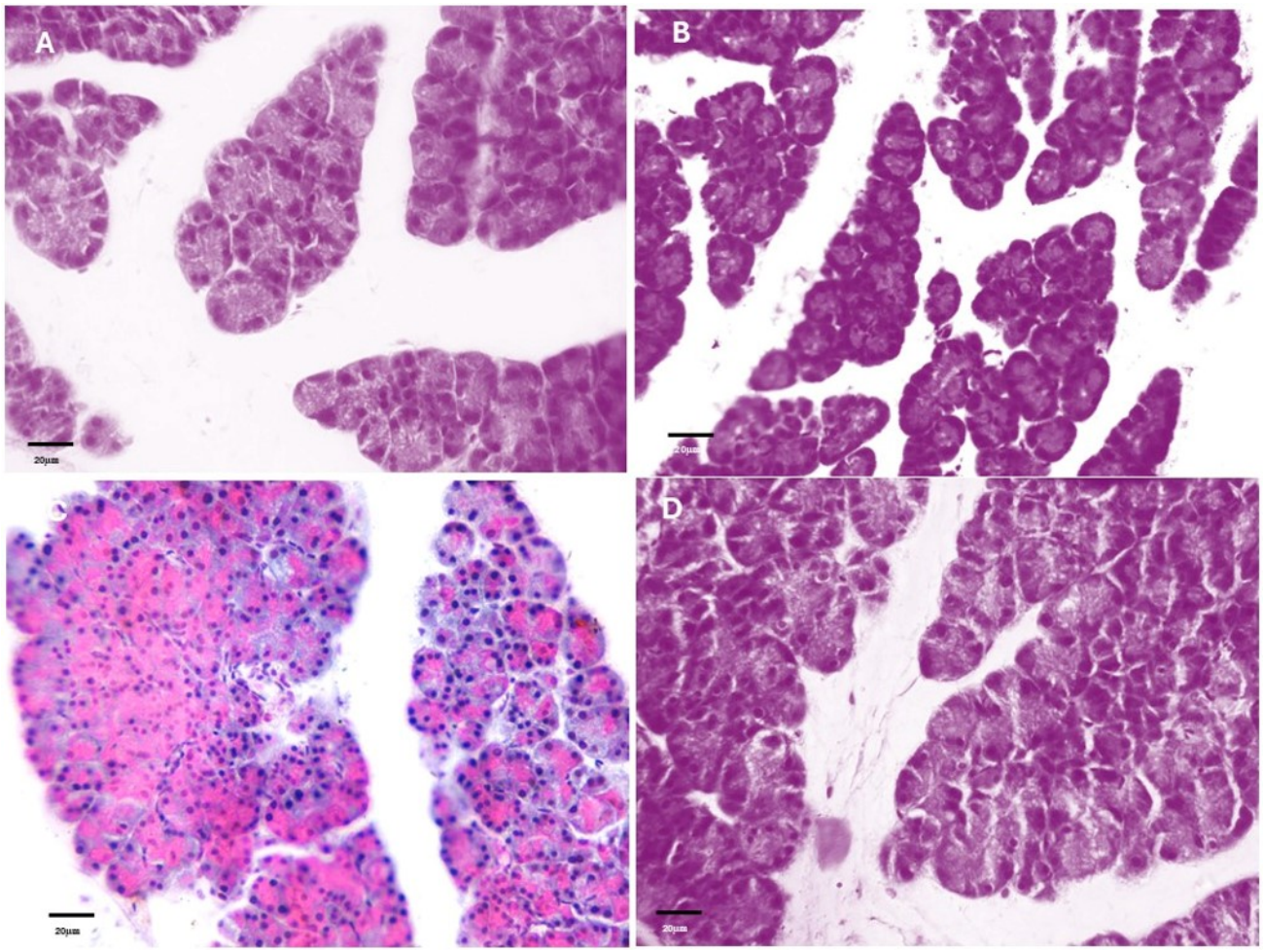

Fig. 4. Histopathological evaluation of pancreatic tissue in control, STZ-induced diabetic, and Frankincense-treated diabetic rats. (A) Pancreatic tissue of a control rat with acini with cuboidal cell lining and central lumen (H&E, scale bar = 20 µm). (B) Pancreatic tissue of an STZ-treated rat with acinar cell atrophy (H&E, scale bar = 20 µm). (C) architectural distortion, nuclear pyknosis, and cytoplasmic change (H&E, scale bar = 20 µm). (D) Pancreatic tissue of a frankincense-treated diabetic rat with restoration of the pancreatic endocrine and exocrine tissues to almost normal architecture (H&E, scale bar = 20 µm).

frankincense (Boswellia spp.) [6]. Al-Matubsi et al. [9] reported that administration of *Boswellia sacra* ethanol extract (200 mg/kg/day) significantly increased SOD and reduced GPx levels in STZ-induced diabetic rats, accompanied by preservation of pancreatic β-cell architecture and improved hepatic histology. Similarly, Kherouf et al. [10] demonstrated that *Boswellia serrata* gum resin markedly reduced oxidative damage markers and ameliorated hepatic and pancreatic injury in diabetic models, with efficacy comparable to that of conventional antioxidant therapies.

Notably, the present finding that GPx activity exceeded that of healthy control levels following frankincense supplementation suggests the induction of a robust adaptive antioxidant response. This effect may be attributed to the pentacyclic triterpenic acid (PTA) constituents of *Boswellia* resin, particularly AKBA, which has been implicated in regulating redox homeostasis [15]. Abo-Zalam et al. [16] highlighted the potent antioxidant and cytoprotective properties of AKBA, emphasizing its role in mitigating oxidative stress under pathological conditions.

Mechanistically, boswellic acids have been shown to suppress ROS generation through multiple pathways, including direct radical scavenging, chelation of transition metal ions, and modulation of NF-κB signaling, there by attenuating oxidative stress at the transcriptional level [17]. In support of these mechanisms, a systematic review and meta-analysis by Mahdian et al. [8] concluded that *Boswellia* species exert antidiabetic effects by improving glycemic control and lipid metabolism, preserving pancreatic β-cell integrity, enhancing insulin sensitivity, and reducing oxidative stress across a range of experimental diabetic models.

4.2 Attenuation of Lipid Peroxidation

The significant reduction in serum MDA levels following frankincense supplementation underscores the ca-

pacity of *Boswellia* extract to mitigate diabetes-induced membrane lipid peroxidation. This observation is particularly relevant, as MDA is not merely a passive biomarker of oxidative injury but actively contributes to cellular dysfunction through the formation of protein adducts and DNA crosslinks, thereby exacerbating tissue damage and metabolic dysregulation [18]. The near normalization of MDA concentrations observed in the treated diabetic rats, approaching those of healthy controls, suggests effective preservation of membrane integrity and stabilization of cellular redox homeostasis.

These findings are consistent with the well-documented antioxidant properties of boswellic acids, which act as non-redox inhibitors of the lipoxygenase (LOX) and cyclooxygenase (COX) pathways, thereby interrupting oxidative and inflammatory cascades at their enzymatic sources [8,19]. Indeed, by attenuating lipid peroxidation and downstream propagative damage, these compounds confer protection against the amplification of oxidative stress commonly observed in diabetic states. In support of this mechanism, Al-Tamimi et al. [11] demonstrated that boswellic acids exert cardioprotective effects by modulating AMPK signaling and interacting with key metabolic enzymes, highlighting broader systemic benefits beyond direct radical scavenging. Furthermore, a recent meta-analysis of clinical trials reported that *Boswellia* supplementation significantly improves glycemic indices, including glycated hemoglobin (HbA1c), while reducing total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels in patients with type 2 diabetes mellitus [20]. These clinically meaningful metabolic improvements further support the translational relevance of the present findings and suggest that attenuation of oxidative stress represents a central mechanism underlying the multifaceted antidiabetic effects of *Boswellia species*.

4.3 Anti-Inflammatory Effects and Cytokine Modulation

With respect to inflammatory biomarkers, the present findings demonstrate a pronounced anti-inflammatory effect of frankincense supplementation. Serum CRP levels were markedly reduced from 181.7 ± 21.07 to 50.40 ± 2.08 U/L, while SAA concentrations decreased from 22.47 ± 0.76 to 9.65 ± 0.40 ng/mL following 28 days of treatment, approaching values observed in healthy controls. These marked reductions underscore the efficacy of frankincense in attenuating systemic inflammation associated with diabetes.

These observations are supported by a comprehensive systematic review of human studies conducted by Al-Yasiry and Kiczorowska [7], which concluded that *Boswellia* species possess potent anti-inflammatory, antioxidant, and immunomodulatory properties. Notably, 91.8% of randomized controlled trials included in the review reported superior therapeutic outcomes with *Boswellia* preparations across a range of inflammatory disorders, including osteoarthritis, asthma, and inflammatory bowel disease. This strong clinical evidence reinforces the translational relevance of the anti-inflammatory effects observed in the present experimental model.

Boswellic acidsare the principal bioactive constituents of frankincense and belong to the class of pentacyclic triterpenic acids (PTAs) [21]. The major boswellic acids identified in frankincense include β-boswellic acid (BA), acetyl-β-boswellic acid (ABA), KBA, and AKBA, all of which have been shown to inhibit proinflammatory enzymes and contribute to the resin's pharmacological activity [22]. At the cellular level, AKBA, a major bioactive constituent of *Boswellia* resin, has been shown to suppress the gene expression of proinflammatory cytokines, including IL-1β, interleukin-6 (IL-6), and TNF-α, in advanced glycation end-product (AGE)-stimulated human monocytic cells, while concurrently enhancing the expression of anti-inflammatory cytokines such as IL-10 and IL-4 [15]. The partial reduction in IL-1β levels observed in the current study is consistent with these mechanistic insights. However, the magnitude of suppression was less pronounced than that observed for CRP and SAA. This differential responsiveness may reflect distinct regulatory mechanisms, as acute-phase reactants are more directly regulated by NF-κB signaling, whereas IL-1β production is tightly controlled by inflammasome-dependent pathways [23]. Although the extract used in the present study was not subjected to detailed chemical characterization, the boswellic acid composition and content of *Boswellia sacra* have been reported in recent work by Javed et al. [24], providing supporting evidence for the presence of these active constituents. Nonetheless, the lack of direct quantification of boswellic acids in the current samples is acknowledged as a limitation, and incorporating such analyses in future investigations would further strengthen the reliability of the findings.

4.4 Differential Effects on Anti-Inflammatory Mediators

The differential effects of frankincense supplementation on TGF-β and CTGF warrant careful consideration. While frankincense significantly elevated TGF-β levels, potentially indicative of enhanced tissue repair, regeneration, and remodeling, it did not produce sustained modulation of CTGF, a key profibrotic mediator downstream of TGF-β signaling. This dissociation suggests that the administered dose and treatment duration (500 mg/kg for 28 days) may preferentially activate anti-inflammatory and regenerative pathways without triggering the fibrotic responses typically associated with chronic or excessive TGF-β activation. Such selective engagement of protective signaling pathways may represent a favorable therapeutic profile, particularly in the context of diabetic complications where aberrant fibrosis is a major concern [25].

In line with this interpretation, Chen et al. [26] reported that *Boswellia* extracts modulate the TGF-β/Smad signaling cascade in a context-dependent manner, promot-

ing tissue repair and the resolution of injury in acute settings while suppressing pathological fibrosis in chronic disease models. These findings support the notion that frankincense-derived constituents can fine-tune TGF-β signaling outcomes rather than indiscriminately amplifying downstream fibrogenic responses. Furthermore, the observed reduction in IL-10 levels following frankincense treatment may reflect a diminished requirement for compensatory anti-inflammatory signaling as systemic inflammation is attenuated, rather than a direct immunosuppressive effect. In states of uncontrolled diabetes, elevated IL-10 levels may paradoxically signify a counter-regulatory response to excessive proinflammatory activity [27]. Consequently, the the marked reduction in IL-10 concentrations to levels below those of both diabetic and healthy controls following frankincense treatment likely indicates treatment-related modulation of this anti-inflammatory cytokine rather than normalization of its levels and may reflect a reduced requirement for sustained endogenous anti-inflammatory responses.

Consistent with these patterns, our data suggest that frankincense may exert a transient, time-dependent immunomodulatory effect, influencing both pro- and anti-inflammatory cytokines rather than producing uniform, sustained suppression.

4.5 Histopathological Study

The histopathological findings in the liver, kidney, and pancreas corroborate the biochemical data, demonstrating that frankincense supplementation markedly attenuates STZ-induced structural injury. Moreover, frankincense restored the hepatic architecture of diabetic rats by inhibiting the production/action of cytokines involved in the induction of islet inflammation [28]. The lesions in the liver following STZ treatment included enlarged glycogen-rich hepatocytes, fatty degeneration, and vascular dilatation [29]. The renal lesions in STZ-treated rats included thickened glomerular basement membranes, glomerular hemorrhage, and severe glomerular and tubular injury [30]. Topical frankincense treatment for relieving high-risk diabetic foot in rats by reducing inflammation and improving microcirculation was approved [31]. Additionally, frankincense reduced renal stone formation in rats by attenuating tubular necrosis and alleviating inflammatory changes [32]. In the STZ diabetic group, islet shrinkage, acinar cell atrophy, architectural distortion, nuclear pyknosis, and cytoplasmic changes were observed [33]. In frankincense-treated diabetic rats, restoration of the pancreatic endocrine and exocrine tissues to near-normal architecture was observed. Nawar et al. [34] reported an alleviative role for aqueous extract of frankincense against diabetes in rats. Furthermore, Nawar et al. [34] reported that frankincense can lower blood sugar levels and oxidative stress, improve lipid profile, reduce hepatic enzymes, and reduce inflammatory cytokines induced by diabetes.

4.6 Study Limitations and Future Directions

Several limitations of the present study should be acknowledged. First, the use of a single frankincense dose (500 mg/kg body weight) precludes assessment of dose–response relationships and limits identification of an optimal therapeutic window. Second, although the 28-day intervention period was sufficient to elicit significant biochemical and inflammatory changes, this period may not adequately capture long-term effects on chronic diabetic complications such as nephropathy, neuropathy, or cardiovascular dysfunction. Third, the absence of a positive control group treated with a standard antidiabetic agent (*e.g.*, metformin) limits a direct comparative evaluation of the efficacy of frankincense relative to established pharmacotherapies.

Therefore, future investigations should incorporate multiple dosing regimens, longer treatment durations, and comparisons with conventional antidiabetic medications to improve the definition of therapeutic potential, safety, and translational applicability. Such studies will be essential for advancing *Boswellia*-derived compounds from experimental models toward clinical use.

5. Conclusion

Collectively, these findings position frankincense as a promising multi-target adjunctive therapeutic candidate for managing diabetes-induced oxidative stress and inflammation. The coordinated restoration of endogenous antioxidant enzyme activities, attenuation of lipid peroxidation, together with the differential effects on inflammatory and regulatorycytokines, underscore the capacity of *Boswellia sacra* to favorably influence both metabolic and inflammatory pathways. This integrated protective profile highlights the therapeutic potential of frankincense in mitigating the complex oxidative and inflammatory burdens associated with diabetes mellitus and supports its further evaluation as a complementary strategy in diabetic disease management. However, since these results derive from a preclinical model that lacks a positive control and does not assess long-term diabetic complications, these findings should be interpreted with caution. Thus, studies with dose–response analyses, appropriate controls, and long-term outcomes are needed to establish the therapeutic potential of frankincense for clinical application.

Abbreviations

STZ, streptozotocin; CAT, catalase; SOD, superoxide dismutase; GPx, glutathione peroxidase; MDA, malondialdehyde; CRP, C-reactive protein; SAA, serum amyloid A; TNF-α, tumor necrosis factor-α; IL-1β, interleukin-1β; TGF-β, transforming growth factor-β; CTGF, connective tissue growth factor; IL-10, interleukin-10.

Availability of Data and Materials

The datasets obtained and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

SAlb, FA, and AZ conceived and designed the study. SAlb, FA, AZ, YA, TA, and SAlt conducted measurements of antioxidant levels and inflammatory/regulatory parameters. AZ performed the data analysis. MH performed the histopathological evaluations. SAlb and AZ drafted the manuscript and contributed to writing, revision, and final approval of the article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the ARRIVE guidelines and was approved by the Animal Ethics Committee of Qassim University (Approval No. 26-06-10). All procedures followed the NIH guidelines for the care and use of laboratory animals, with efforts made to minimize animal discomfort and to use the minimum number of animals necessary for valid results.

Acknowledgment

The researchers would like to thank the Deanship of Graduate Studies and Scientific Research at Qassim University for financial support (QU-APC-2026).

Funding

This research was financially supported by the Deanship of Graduate Studies and Scientific Research at Qassim University (QU-APC-2026).

Conflicts of Interest

The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

The authors report using AI-assisted language editing (Microsoft Copilot) only for spelling, grammar, and flow checks. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

Supplementary Material

Supplementary material associated with this article can be found in the online version at https://doi.org/10.31083/IJP53160.

References

[1] International Diabetes Federation. IDF Diabetes Atlas (10th ed.). International Diabetes Federation: Brussels. 2021.

[2] American Diabetes Association. 2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes-2021*. Diabetes Care. 2021; 44: S15–S33. https://doi.org/10.2337/dc21-S002

[3] Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. Diabetes Research and Clinical Practice. 2014; 105: 141–150. https://doi.org/10.1016/j.diabres.2014.04.006

[4] Thilakarathna M, Appuhami K, Darshana N, Perera J. Complementary and alternative medicine use among patients with type-2 diabetes mellitus attending a suburban tertiary healthcare centre in Sri Lanka. BMC Complementary Medicine and Therapies. 2025; 25: 363. https://doi.org/10.1186/s12906-025-05077-5

[5] Dugbartey GJ, Alornyo KK, Dapaa-Addo CO, Kwashie EK, Harley Y, Asiedu BN. Toxicological profile of anti-diabetic drugs and emerging measures to reduce the toxic burden. Toxicology Reports. 2026; 16: 102247. https://doi.org/10.1016/j.toxrep.2026.102247

[6] Newman DJ, Cragg GM. Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. Journal of Natural Products. 2020; 83: 770–803. https://doi.org/10.1021/acs.jnatprod.9b01285

[7] Al-Yasiry ARM, Kiczorowska B. Frankincense–therapeutic properties. Postepy Higieny i Medycyny Doswiadczalnej. 2016; 70: 380–391. https://doi.org/10.5604/17322693.1200553

[8] Mahdian D, Abbaszadeh-Goudarzi K, Raoofi A, Dadashizadeh G, Abroudi M, Zarepour E, et al. Effect of *Boswellia* species on the metabolic syndrome: A review. Iranian Journal of Basic Medical Sciences. 2020; 23: 1374–1381. https://doi.org/10.22038/ijbms.2020.42115.9957

[9] Al-Matubsi H, Rashan L, Aburayyan W, Al Hanbali O, Abuarqoub D, Efferth T. Antidiabetic and antioxidant properties of Boswellia sacra oleo-gum in streptozotocin-induced diabetic rats. Journal of Ayurveda and Integrative Medicine. 2024; 15: 101014. https://doi.org/10.1016/j.jaim.2024.101014

[10] Kherouf A, Aouacheri O, Tichati L, Tebboub I, Kherouf M, Saka S. Potential antioxidant properties and antidiabetic and hepatic/pancreatic protective effects of dietary *Boswellia serrata* gum resin powder against oxidative damage in streptozotocin-induced diabetic rats. Comparative Clinical Pathology. 2021; 30: 891–904. https://doi.org/10.1007/s00580-021-03284-3

[11] AlTamimi JZ, AlFaris NA, Alshammari GM, Alagal RI, Aljabryn DH, Yahya MA. The Protective Effect of 11-Keto-β-Boswellic Acid against Diabetic Cardiomyopathy in Rats Entails Activation of AMPK. Nutrients. 2023; 15: 1660. https://doi.org/10.3390/nu15071660

[12] Khan A, Khan I, Halim SA, Rehman NU, Karim N, Ahmad W, et al. Anti-diabetic potential of β-boswellic acid and 11-keto-β-boswellic acid: Mechanistic insights from computational and biochemical approaches. Biomedicine & Pharmacotherapy. 2022; 147: 112669. https://doi.org/10.1016/j.biopha.2022.112669

[13] Al-Edany ZT, Alhelfi N. Study the Effects of Frankincense Aqueous Extract With/Without Synbiotic on Diabetic Male Rats. Basrah Journal of Veterinary Research. 2024; 23: 97–109. https://doi.org/10.23975/bjvr.2024.150474.1095

[14] Radenković M, Stojanović M, Prostran M. Experimental diabetes induced by alloxan and streptozotocin: The current state of the art. Journal of Pharmacological and Toxicological Methods. 2016; 78: 13–31. https://doi.org/10.1016/j.vascn.2015.11.004

[15] Taherzadeh D, Baradaran Rahimi V, Amiri H, Ehtiati S, Yahyazadeh R, Hashemy SI, et al. Acetyl-11-Keto-β-Boswellic

Acid (AKBA) Prevents Lipopolysaccharide-Induced Inflammation and Cytotoxicity on H9C2 Cells. Evidence-Based Complementary and Alternative Medicine. 2022; 2022: 2620710. https://doi.org/10.1155/2022/2620710

[16] Abo-Zalam HB, Gendy AM, Ali BM, Ragab GM, Selim HMRM, Hamed NO, et al. Acetyl-11-keto-beta-boswellic acid ameliorates monosodium iodoacetate-induced osteoarthritis in rats: implications of HMGB1/TLR4/NF-κB and Nrf2/HO-1. Frontiers in Pharmacology. 2025; 16: 1694803. https://doi.org/10.3389/fphar.2025.1694803

[17] Ammon HPT. Modulation of the immune system by Boswellia serrata extracts and boswellic acids. Phytomedicine. 2010; 17: 862–867. https://doi.org/10.1016/j.phymed.2010.03.003

[18] Shadfar S, Parakh S, Jamali MS, Atkin JD. Redox dysregulation as a driver for DNA damage and its relationship to neurodegenerative diseases. Translational Neurodegeneration. 2023; 12: 18. https://doi.org/10.1186/s40035-023-00350-4

[19] Abdel-Tawab M, Werz O, Schubert-Zsilavecz M. Boswellia serrata: an overall assessment of in vitro, preclinical, pharmacokinetic and clinical data. Clinical Pharmacokinetics. 2011; 50: 349–369. https://doi.org/10.2165/11586800-000000000-00000

[20] Karimi M, Vakili K, Rashidian P, Razavi-Amoli S-K, Akhbari M and Kazemi K. Effect of boswellia (Boswellia serrata L.) supplementation on glycemic markers and lipid profile in type 2 diabetic patients: a systematic review and meta-analysis. Frontiers in Clinical Diabetes and Healthcare. 2024; 5:1466408. https://doi.org/10.3389/fcdhc.2024.1466408

[21] Roy NK, Parama D, Banik K, Bordoloi D, Devi AK, Thakur KK, et al. An Update on Pharmacological Potential of Boswellic Acids against Chronic Diseases. International Journal of Molecular Sciences. 2019; 20: 4101. https://doi.org/10.3390/ijms20174101

[22] Siddiqui MZ. Boswellia serrata, a potential antiinflammatory agent: an overview. Indian Journal of Pharmaceutical Sciences. 2011; 73: 255–261. https://doi.org/10.4103/0250-474X.93507

[23] Zou C, Jiang S, Li H, Zhao K, Cao D, Yang G. The NLRP3 Inflammasome: Mechanisms of Activation, Regulation, and Therapeutic Opportunities. MedComm. 2026; 7: e70660. https://doi.org/10.1002/mco2.70660

[24] Javed S, Salawi A, Moni SS, Ahsan W, Khuwaja G, Alam MS, et al. Qualitative phytochemical profiling, antioxidant activity, and development of a water-in-oil cream containing combined oil and water infusions of frankincense resin (*Boswellia spp.*): a preliminary *in vitro* study. Journal of Pharmacy & Pharmaceutical Sciences. 2026; 29: 15609. https://doi.org/10.3389/jps.2026.15609

[25] Zou Y, Dai J, Li J, Liu M, Li R, Li G, et al. Role of the TGF-β/Smad signaling pathway in the transition from acute kidney injury to chronic kidney disease (Review). International Journal of Molecular Medicine. 2025; 56: 162. https://doi.org/10.3892/ijmm.2025.5603

[26] Chen F, Lyu L, Xing C, Chen Y, Hu S, Wang M, et al. The pivotal role of TGF-β/Smad pathway in fibrosis pathogenesis and treatment. Frontiers in Oncology. 2025; 15: 1649179. https://doi.org/10.3389/fonc.2025.1649179

[27] Novianti Y, Nur'aeny N. Exploring Interleukin-10 Levels in Diabetes Patients with and without Oral Diseases: A Systematic Review. Journal of Inflammation Research. 2024; 17: 541–552. https://doi.org/10.2147/JIR.S449546

[28] Saito T, Muramatsu M, Ishii Y, Saigo Y, Konuma T, Toriniwa Y, et al. Pathophysiological analysis of the progression of hepatic lesions in STAM mice. Physiological Research. 2017; 66: 791–799. https://doi.org/10.33549/physiolres.933592

[29] Salih ND, Muslih RK, Hamoodi SR. Histological liver changes in streptozotocin-induced diabetic mice. International Medical Journal Malaysia. 2009; 8: 1–4.

[30] Kumaş M, Eşrefoğlu M, Karataş E, Duymaç N, Kanbay S, Ergün IS, et al. Investigation of dose-dependent effects of berberine against renal ischemia/reperfusion injury in experimental diabetic rats. Nefrologia. 2019; 39: 411–423. https://doi.org/10.1016/j.nefro.2018.10.006

[31] Ma SY, Yin X, Zhang Z, Li YS, Tang HB. Topical frankincense treatment on relieving high-risk diabetic foot in rats by reducing inflammation and improving microcirculation. Frontiers in Pharmacology. 2025; 16: 1564236. https://doi.org/10.3389/fphar.2025.1564236

[32] Al-Marhoon MS, Al-Harrasi A, Siddiqui K, Ashique M, Ali H, Ali BH. Effects of frankincense on experimentally induced renal stones in rats. BJUI Compass. 2023; 4: 437–445. https://doi.org/10.1002/bco2.227

[33] Faried MA, El-Mehi AES. Aqueous anise extract alleviated the pancreatic changes in streptozotocin-induced diabetic rat model via modulation of hyperglycaemia, oxidative stress, apoptosis and autophagy: a biochemical, histological and immunohistochemical study. Folia Morphologica. 2020; 79: 489–502. https://doi.org/10.5603/FM.a2019.0117

[34] Nawar MH, Obaid RM, Al-Chalabi SM. Physiological and histological effects of aqueous extract of cinnamon and frankincense on albino rats with induced diabetes. Journal of Animal Health and Production. 2025; 13: 542–549. https://doi.org/10.17582/journal.jahp/2025/13.s1.542.549