Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 11 July 2026
Revised 26 Aug 2026
Accepted 14 Sep 2026

Natural Resources for Human Health 2026, Vol. 6 (20s): 450–467

KEYWORDS:
Shadawi coffee leaves; diabetes mellitus; diabetic rats; polyphenols; antioxidants; hyperglycemia; pancreatic histopathology; oxidative stress; phytochemicals.

Antidiabetic Potential of Shadawi Coffee (Coffea arabica L.) Leaves: Integrated Biochemical, Antioxidant, Polyphenolic, and Pancreatic Histopathological Evaluation in Diabetic Rats

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ABSTRACT: **Background**: Diabetes mellitus is a chronic metabolic disorder associated with hyperglycemia, dyslipidemia, oxidative imbalance, and alterations in organ function. Coffee leaves contain diverse bioactive compounds, including phenolic acids and flavonoids, but their potential metabolic effects remain less investigated than those of coffee beans.

Objective: This study aimed to evaluate the potential antidiabetic effects of dried Shadawi coffee (Coffea arabica L.) leaf powder in streptozotocin-induced diabetic rats, with emphasis on biochemical, antioxidant, polyphenolic, and pancreatic histopathological responses.

Methods: Thirty adult male albino rats were randomly assigned to five groups (n = 6): normal control, diabetic control, and diabetic rats receiving diets supplemented with 3%, 6%, or 9% dried Shadawi coffee leaf powder for 28 days. Feed intake, body weight gain, serum glucose, insulin, lipid profile, liver enzymes, and kidney function parameters were assessed. The total phenolic and flavonoid contents, DPPH radical-scavenging activity, and individual phenolic compounds were also determined. Pancreatic tissues were

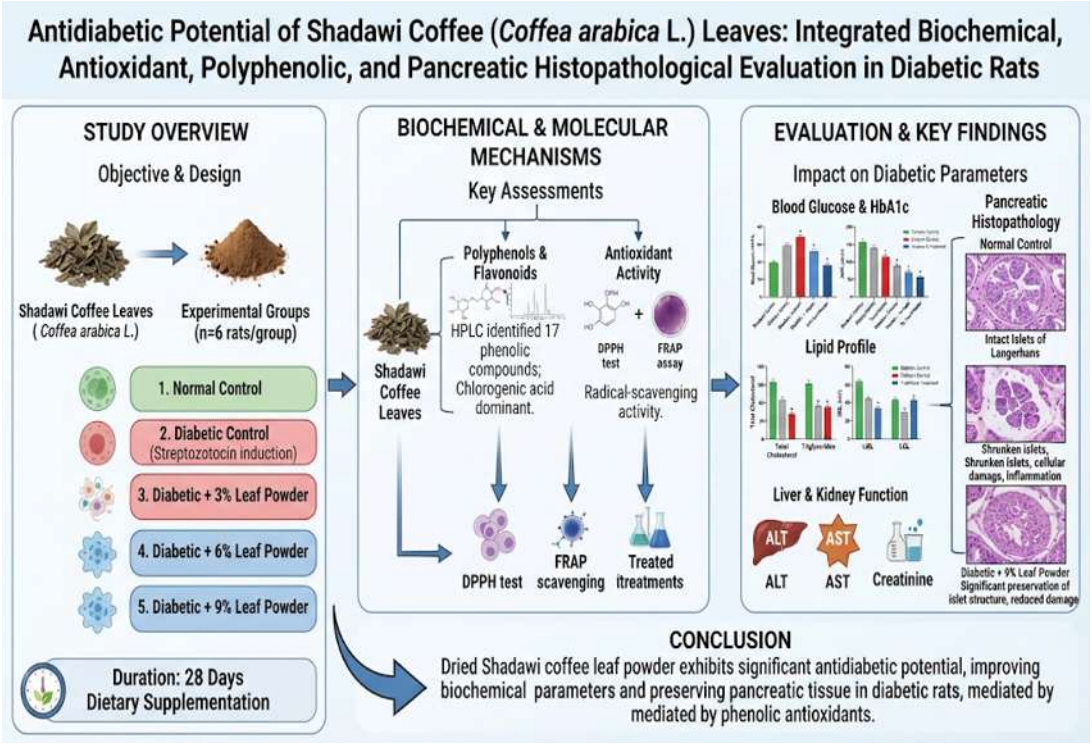
Natural Resources for Human Health
eISSN: 2583-1194

examined histopathologically.

Results: Diabetes was associated with increased serum glucose, HbA1c, total cholesterol, triglycerides, LDL-C, VLDL-C, ALT, AST, urea, creatinine, and uric acid, together with decreased serum insulin, HDL-C, and hepatic glycogen. Dietary supplementation with Shadawi coffee leaf powder produced progressive changes in these parameters, with greater responses generally observed at the higher supplementation levels. The leaf powder contained measurable phenolic and flavonoid compounds and demonstrated antioxidant activity. HPLC analysis identified 17 quantified phenolic compounds, with chlorogenic acid being the predominant constituent. Histopathological examination indicated changes in pancreatic tissue associated with diabetes and varying degrees of tissue preservation following supplementation.

Conclusion: Dried Shadawi coffee leaf powder showed potential biological activity in diabetic rats, accompanied by improvements in several biochemical parameters and the presence of phenolic and antioxidant constituents. These findings support further investigation of Shadawi coffee leaves and their bioactive compounds using mechanistic and dose-response studies.

Graphical Abstract: Antidiabetic Potential of Shadawi Coffee Leaves: Biochemical, Antioxidant, and Pancreatic Evaluation



1- INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent abnormalities in glucose homeostasis and represents one of the major global public health challenges. Diabetes is associated not only with chronic hyperglycemia but also with a range of metabolic disturbances, including insulin resistance, impaired pancreatic β-cell function, dyslipidemia, inflammation, and oxidative stress. According to the 11th edition of the International Diabetes Federation (IDF) Diabetes Atlas, an estimated 589 million adults aged 20–79 years were living with diabetes worldwide in 2024, corresponding to

approximately 11.1% of the adult population in this age group. This number is projected to increase to approximately 853 million by 2050, emphasizing the continuing global burden of diabetes and the need for effective preventive and therapeutic strategies (Genitsaridi et al., 2026). Chronic hyperglycemia is a central metabolic abnormality in diabetes and contributes to a series of biochemical and cellular alterations. Persistent exposure to elevated glucose concentrations can increase the generation of reactive oxygen species (ROS), promote oxidative modification of cellular macromolecules, and interfere with intracellular signaling pathways. Consequently, oxidative stress is considered an important component of diabetes pathophysiology and may contribute to both insulin resistance and pancreatic β-cell dysfunction. Experimental studies have demonstrated that oxidative stress can impair insulin gene expression and β-cell function, thereby contributing to the deterioration of glucose homeostasis (Kaneto et al., 2005a, 2005b). Pancreatic β-cells are particularly vulnerable to oxidative damage because their antioxidant defense capacity is relatively limited compared with that of several other tissues. Excessive production of ROS can adversely affect insulin gene expression, β-cell survival, and insulin secretory function. In addition, oxidative stress can interact with cellular stress and inflammatory signaling pathways, potentially amplifying β-cell dysfunction and contributing to the progression of metabolic abnormalities associated with diabetes (Kaneto et al., 2005a, 2005b). Therefore, controlling oxidative stress, in addition to improving glucose regulation, has attracted considerable scientific interest as a potential approach to reducing diabetes-associated cellular damage. In this context, plant-derived bioactive compounds have received increasing attention as potential complementary approaches for the management of metabolic disorders. Among these compounds, polyphenols are of particular interest because of their diverse biological activities, including antioxidant and metabolic regulatory effects. Experimental and mechanistic evidence suggests that dietary polyphenols may influence glucose metabolism through several mechanisms, including modulation of carbohydrate digestion, glucose transport, insulin signaling, oxidative stress, and pancreatic β-cell function (Farias et al., 2021). The potential antidiabetic effects of polyphenols extend beyond their direct ability to scavenge ROS. Different classes of phenolic compounds may interact with cellular pathways involved in glucose metabolism, insulin signaling, inflammation, and cellular antioxidant defense. For example, Farias et al. (2021) reviewed evidence suggesting that dietary polyphenols may contribute to blood glucose regulation, reduction of oxidative stress and protein glycation, modulation of enzymes involved in carbohydrate metabolism, and preservation of pancreatic β-cell function. Similarly, Williamson and Sheedy (2020) discussed the potential effects of polyphenols on insulin resistance and related metabolic pathways. However, the magnitude of these effects varies among individual compounds and is influenced by factors such as chemical structure, dose, bioavailability, metabolism, and the experimental or clinical context. The nuclear factor erythroid 2-related factor 2 (Nrf2) pathway is another important component of the cellular antioxidant defense system. Nrf2 regulates the expression of several genes involved in protection against oxidative and electrophilic stress. Accordingly, modulation of Nrf2-associated signaling has been investigated as a potential mechanism through which phytochemicals may enhance endogenous antioxidant defenses (Qin et al., 2023). Nevertheless, much of the evidence concerning the interaction between individual phytochemicals and Nrf2 signaling is derived from experimental models, and further research is required to establish the clinical relevance of these mechanisms in humans. Coffee plants represent a potentially valuable source of bioactive phytochemicals. Although coffee research has traditionally focused on the beans, coffee leaves also contain a variety of phenolic and other secondary metabolites. Studies of *Coffea arabica* leaves have identified phenolic compounds and procyanidins and have demonstrated measurable antioxidant activity in coffee-leaf preparations (Ngamsuk et al., 2019). Ngamsuk et al. (2019) investigated the phenolic composition, procyanidin content, and antioxidant activity of processed *C. arabica* leaves and reported that leaf maturity and drying conditions influenced the measured phytochemical content and antioxidant activity. In particular, young leaves subjected to drying showed higher total phenolic content, total procyanidin content, and DPPH radical-scavenging activity under the conditions examined in their study. The authors also identified several phenolic constituents in coffee leaves, supporting the view that coffee leaves may serve as a source of bioactive phenolic compounds. Importantly, the phytochemical composition and biological activity of coffee leaves cannot be considered constant (Chen et al., 2018). They may vary according to coffee species and cultivar, leaf maturity, environmental conditions, geographical origin, harvesting practices, and processing conditions (Yohannis et al., 2024). The findings of Ngamsuk et al. (2019) further demonstrate that leaf maturity and drying conditions can influence phenolic content, procyanidin content, and antioxidant activity. Therefore, characterization of the specific coffee-leaf material used in a biological experiment is essential when attempting to establish a relationship between its phytochemical composition and biological effects. Taken together, the established relationship between oxidative stress and metabolic dysfunction in diabetes, along with the biological activities reported for dietary polyphenols and the presence of phenolic compounds in coffee leaves, provides a scientific rationale for further investigation

of coffee leaves as a potential source of bioactive compounds. However, evidence demonstrating antioxidant activity or phytochemical richness in coffee leaves does not, by itself, establish an antidiabetic therapeutic effect. Therefore, experimental studies evaluating the effects of coffee-leaf preparations on glucose regulation, oxidative stress, insulin sensitivity, and pancreatic β-cell function are warranted to clarify their potential biological significance. In this context, investigating the polyphenolic composition and antioxidant properties of Shadawi coffee leaves (*Coffea arabica* L.) may provide valuable insights into their potential biological activities. Previous studies have demonstrated that *C. arabica* leaves contain diverse bioactive compounds, including chlorogenic acids, flavonoids, mangiferin, procyanidins, and other phenolic constituents, and exhibit considerable antioxidant activity (de Almeida et al., 2019; Ngamsuk et al., 2019). Moreover, *C. arabica* leaf extracts have shown antioxidant and antiglycation activities, inhibition of carbohydrate-digesting enzymes in vitro, and hypoglycemic effects in a zebrafish model (Nascimento et al., 2023). Martina et al. (2021) reported a reduction in homeostatic model assessment of insulin resistance (HOMA-IR) following administration of *C. arabica* Gayo leaf extract to rats with type 2 diabetes mellitus. Furthermore, Fibrianto et al. (2023) evaluated the potential antidiabetic effects of Arabica and Robusta coffee-leaf infusions, including their effects on blood glucose levels and pancreatic β-cell counts in streptozotocin (STZ)-induced diabetic rats. Despite these findings, the effects of graded dietary supplementation with whole Shadawi coffee-leaf powder on diabetes-associated biochemical alterations and pancreatic tissue integrity remain insufficiently characterized. Therefore, the present study was designed to evaluate the potential antidiabetic effects of powdered Shadawi coffee leaves (*Coffea arabica* L.) in experimentally induced diabetic albino rats. Coffee-leaf powder was administered at dietary inclusion levels of 3%, 6%, and 9% for 28 days, with assessment of biochemical parameters and pancreatic histopathological changes. In addition, the antioxidant capacity and polyphenolic constituents of the leaves were characterized to explore their possible association with the observed metabolic effects.

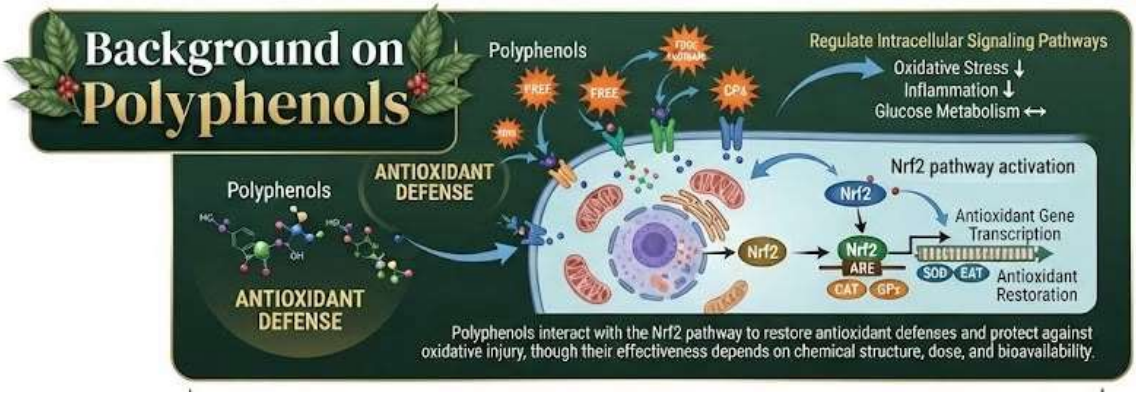


Figure 1. Mechanisms of action of polyphenols in regulating intracellular signaling pathways, activating the Nrf2 antioxidant defense system, and mitigating oxidative stress and inflammation in metabolic disorders.

2. MATERIALS AND METHOD

2.1. Plant Material and Preparation of Shadawi Coffee Leaves

Fresh Shadawi coffee leaves (*Coffea arabica* L.) were collected and carefully inspected to remove damaged or contaminated material. The leaves were thoroughly washed with clean water to eliminate adhering dust and other foreign materials. They were subsequently dried under controlled conditions and protected from direct sunlight to minimize potential degradation of light- and heat-sensitive phytochemicals, following previously reported procedures for the preparation of coffee leaves (Almeida et al., 2019; Chen et al., 2019). After complete drying, the leaves were mechanically ground into a fine, homogeneous powder using an electric grinder. The resulting powder was transferred to clean, airtight containers, protected from light, and stored under appropriate conditions until further use in the experimental diets and phytochemical analyses.

2.2. Phytochemical Characterization of Shadawi Coffee Leaves

The powdered Shadawi coffee leaves were subjected to phytochemical characterization to assess their phenolic composition and antioxidant properties. The total phenolic content and antioxidant activity were determined using established analytical methods, as previously applied to coffee leaves (Chen et al., 2019). Individual phenolic constituents were identified and

quantified by high-performance liquid chromatography (HPLC) using chromatographic conditions appropriate for the separation and determination of phenolic compounds. Identification was based on comparison with authentic reference standards and their corresponding chromatographic characteristics, while quantification was performed using calibration curves generated from the respective standards. Similar HPLC-based approaches have been successfully applied for the characterization and quantification of phenolic and other bioactive compounds in coffee leaves (Almeida et al., 2019). The resulting phytochemical profile was considered in the interpretation of the biochemical and histopathological findings, particularly regarding the potential contribution of phenolic and antioxidant constituents to the observed biological effects.

2.3. Experimental Animals and Housing Conditions

Thirty healthy adult male white albino Sprague–Dawley rats, weighing 150 ± 10 g, were used in the present study. The animals were obtained from the National Agricultural Research Center, Cairo, Egypt. The experiment was conducted in the Animal House of the Faculty of Home Economics, Menoufia University, Egypt. Before initiation of the experimental procedures, the animals were allowed to acclimatize to the laboratory environment for an appropriate acclimatization period. The rats were housed under controlled environmental conditions, with a 12-h light/12-h dark cycle and appropriate room temperature and humidity. Animals had free access to drinking water and the basal diet throughout the acclimatization and experimental periods, except where otherwise specified by the experimental protocol. The animals were monitored regularly throughout the study for general health status, food intake, body weight, and any clinical signs associated with diabetes or the experimental treatments. The reporting of the animal experiment was structured with reference to the ARRIVE 2.0 recommendations for transparent reporting of in vivo animal research (Percie du Sert et al., 2020).

2.4. Induction of Experimental Diabetes

Following the acclimatization period, experimental diabetes was induced in the designated rats by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 75 mg/kg body weight, as previously described (Adewole & Ojewole, 2007). Following STZ administration, fasting blood glucose levels were monitored to confirm the successful induction of diabetes. Rats with fasting blood glucose concentrations exceeding 250 mg/dL were considered diabetic and included in the corresponding experimental groups. Animals that failed to meet the predefined hyperglycemic criterion, as well as those that died during the induction procedure, were excluded from subsequent experimental procedures.

2.5. Basal Diet

The animals were provided with a nutritionally balanced basal diet throughout the experimental period. The basal diet consisted of 10% protein, 10% corn oil, 0.2% choline chloride, 5% cellulose, 1% vitamin mixture, 4% mineral salt mixture, and corn starch to complete the formulation to 100%, based on established purified diet formulations for laboratory rodents (Reeves et al., 1993). The experimental diets were prepared by incorporating the specified concentrations of powdered Shadawi coffee leaves into the basal diet.

2.6. Experimental Design and Dietary Treatments

After confirmation of diabetes, the animals were randomly allocated into five experimental groups, with six rats in each group (n = 6):

Group 1: Normal Control (NC) Six non-diabetic rats were fed the basal diet and received distilled water throughout the 28-day experimental period.

- Group 2: Diabetic Control (DC) Six diabetic rats were fed the basal diet and received distilled water throughout the 28-day experimental period. This group served as the untreated diabetic control.
- Group 3: Diabetic + 3% Shadawi Coffee Leaves (DC + SCL3%) Six diabetic rats were fed the basal diet supplemented with 3% powdered Shadawi coffee leaves throughout the 28-day experimental period.
- Group 4: Diabetic + 6% Shadawi Coffee Leaves (DC + SCL6%) Six diabetic rats were fed the basal diet supplemented with 6% powdered Shadawi coffee leaves throughout the 28-day experimental period.
- Group 5: Diabetic + 9% Shadawi Coffee Leaves (DC + SCL9%) Six diabetic rats were fed the basal diet supplemented with 9% powdered Shadawi coffee leaves throughout the 28-day experimental period.

The graded dietary concentrations of Shadawi coffee leaves were used to investigate the potential dose-related biological effects of the plant material in diabetic rats.

2.7. Preparation of Experimental Diets: The required amounts of powdered Shadawi coffee leaves were thoroughly mixed with the basal diet to obtain final dietary concentrations of 3%, 6%, and 9%. The experimental diets were prepared under appropriate hygienic conditions, and the ingredients were thoroughly mixed to ensure relatively uniform distribution of the plant material throughout each dietary formulation. The prepared diets were stored under suitable conditions and provided to the animals according to the experimental schedule.

2.8. Assessment of Body Weight and Food Intake: Body weights were recorded at the beginning of the experiment and at regular intervals throughout the experimental period. Food intake was also recorded throughout the study to evaluate the effects of diabetes and Shadawi coffee leaf supplementation on dietary consumption and body-weight changes. Body weight gain (BWG), body weight gain percentage (BWG%), and feed efficiency ratio (FER) were calculated where applicable. Body weight gain was calculated as follows: BWG (g) = Final body weight (g) − Initial body weight (g)

Body weight gain percentage was calculated as: BWG (%) = [(Final body weight − Initial body weight) / Initial body weight] × 100

Feed efficiency ratio was calculated as: FER = Body weight gain (g) / Food intake (g)

2.9. Blood Sampling and Serum Preparation: At the end of the 28-day experimental period, the rats were fasted overnight before blood collection, with free access to water. Blood samples were collected under appropriate anesthesia and humane conditions. The blood samples were transferred into clean, dry centrifuge tubes and allowed to clot. Serum was separated by centrifugation at 4000 rpm for 10 min. The separated serum was carefully transferred into labeled Eppendorf tubes and stored at −20°C until biochemical analyses were performed. All samples were handled carefully to minimize hemolysis and preanalytical variation.

2.10. Biochemical Analyses: Serum biochemical parameters were determined using commercially available diagnostic kits and standard enzymatic or colorimetric procedures according to the manufacturers' instructions and established analytical methods.

2.10.1. Serum Glucose: Serum glucose concentration was determined using an enzymatic colorimetric method based on the glucose oxidase–peroxidase principle, as described by Trinder (1969). The results were expressed as mg/dL.

2.10.2. Lipid Profile: The serum lipid profile was assessed by determining the concentrations of:

- Total cholesterol (TC)

- Triglycerides (TG)

- High-density lipoprotein cholesterol (HDL-C)

- Low-density lipoprotein cholesterol (LDL-C)

- Very-low-density lipoprotein cholesterol (VLDL-C). Total cholesterol was determined using an enzymatic colorimetric method according to Allain et al. (1974), whereas serum triglycerides were determined using an enzymatic colorimetric procedure according to Fossati and Prencipe (1982). HDL-C was determined using an appropriate precipitation-based analytical procedure according to the method applied in the study (Lopes-Virella et al., 1977). LDL-C was calculated according to the Friedewald equation, where applicable, while VLDL-C was estimated according to the analytical protocol used in the study (Friedewald et al., 1972).

2.10.3. Liver Function Parameters: Selected biochemical indicators of liver function were determined, including:

- Alanine aminotransferase (ALT)

- Aspartate aminotransferase (AST)

ALT and AST activities were determined using the colorimetric method described by Reitman and Frankel (1957). Serum albumin concentration was determined using the bromocresol green method described by Doumas et al. (1971). Serum

globulin concentration was determined according to the standard serum protein procedure described by Gornall et al. (1949), with globulin calculated as the difference between total serum protein and albumin, where applicable.

2.10.4. Kidney Function Parameters

Renal function was evaluated by determining serum concentrations of:

- Urea

- Creatinine

- Uric acid. Serum urea concentration was determined using the method described by Fawcett and Scott (1960). Serum creatinine concentration was determined using a colorimetric method based on the Jaffe reaction, according to Bartels et al. (1972). Serum uric acid concentration was determined using an enzymatic colorimetric method based on uricase, as described by Fossati et al. (1980)

2.11. Pancreatic Tissue Collection

At the end of the 28-day experimental period and following blood collection, the animals were humanely euthanized according to the approved animal-care protocol. The pancreas was carefully excised immediately after euthanasia. Tissue samples were gently rinsed with physiological saline to remove adhering blood and were subsequently placed in an appropriate fixative for histopathological examination.2.12.

2.12. Statistical Analysis

All data are expressed as mean ± standard deviation (SD) (n = 6). Differences among experimental groups were analyzed using one-way analysis of variance (ANOVA), followed by Duncan's multiple range test to determine significant differences between group means. Statistical significance was set at ($P < 0.05$), according to Snedecor and Cochran (1989).

2.13. Ethical Approval

The experimental protocol was reviewed and approved by the Institutional Research Ethics Committee of Al-Baha University, Saudi Arabia (Approval No. 47119677; dated 17 May 2026).

3. RESULTS AND DISCUSSION

3.1.Chemical Results

Chemical composition, bioactive compounds, antioxidant activity, and phenolic profile of dried Shadawi coffee (*Coffea arabica* L.) leaves powder

The chemical composition, bioactive compounds, and antioxidant characteristics of dried Shadawi coffee (*Coffea arabica* L.) leaf powder are presented in Figure 2. On a wet-weight basis, the leaf powder contained 7.85 ± 0.12% moisture, 12.80 ± 0.14% crude protein, 4.90 ± 0.08% crude fat, 6.75 ± 0.11% ash, and 17.40 ± 0.22% crude fiber. Carbohydrates, calculated by difference, accounted for 50.30 ± 0.18% of the powder. On a dry-weight basis, crude protein, crude fat, ash, crude fiber, and carbohydrates represented 13.89 ± 0.15, 5.32 ± 0.10, 7.33 ± 0.09, 18.88 ± 0.18, and 54.58 ± 0.15%, respectively. The corresponding energy values were 304.15 ± 0.05 and 330.22 ± 0.08 kcal/100 g on wet- and dry-weight bases, respectively. In addition to its proximate composition, the dried coffee leaf powder contained appreciable levels of phenolic and flavonoid compounds. The total phenolic content was 524.30 ± 10.45 mg GAE/100 g dry matter, whereas the total flavonoid content reached 187.65 ± 6.12 mg RE/100 g dry matter. The sample also exhibited DPPH radical-scavenging activity of 365.40 ± 8.90 mg TE/100 g dry matter. These results demonstrate the presence of phenolic and flavonoid constituents in the dried Shadawi coffee leaves and indicate measurable radical-scavenging activity under the conditions of the assay. The individual phenolic compounds were further characterized by high-performance liquid chromatography (HPLC). Eighteen compounds were examined, of which 17 were detected and quantified, while coumarin was not detected under the analytical conditions used. Chlorogenic acid was the most abundant compound, reaching 11.95 ± 0.38 mg/g dry matter, followed by rutin (3.45 ± 0.15 mg/g) and catechin (3.12 ± 0.12 mg/g). Caffeic acid and ferulic acid were also detected at relatively high concentrations of 2.81 ± 0.12 and 2.34 ± 0.10 mg/g dry matter, respectively. Epicatechin and protocatechuic acid were present at 1.76 ± 0.09 and 1.54 ± 0.08 mg/g, respectively, while *p*-coumaric acid and *p*-hydroxybenzoic acid were detected at

1.48 ± 0.07 and 1.05 ± 0.06 mg/g, respectively. The remaining identified compounds were present at lower concentrations. Gallic acid and vanillic acid were detected at 0.92 ± 0.05 and 0.83 ± 0.04 mg/g dry matter, respectively, whereas syringic acid, sinapic acid, quercetin, myricetin, cinnamic acid, and salicylic acid were detected at concentrations ranging from 0.33 to 0.62 mg/g dry matter. Taken together, the results presented in Figure 3 and Table 3 show that dried Shadawi coffee leaf powder contains a diverse range of nutritional and bioactive constituents, including phenolic acids and flavonoid compounds. Chlorogenic acid was the predominant individual phenolic compound detected by HPLC, while the measurable total phenolic and flavonoid contents were accompanied by detectable DPPH radical-scavenging activity.

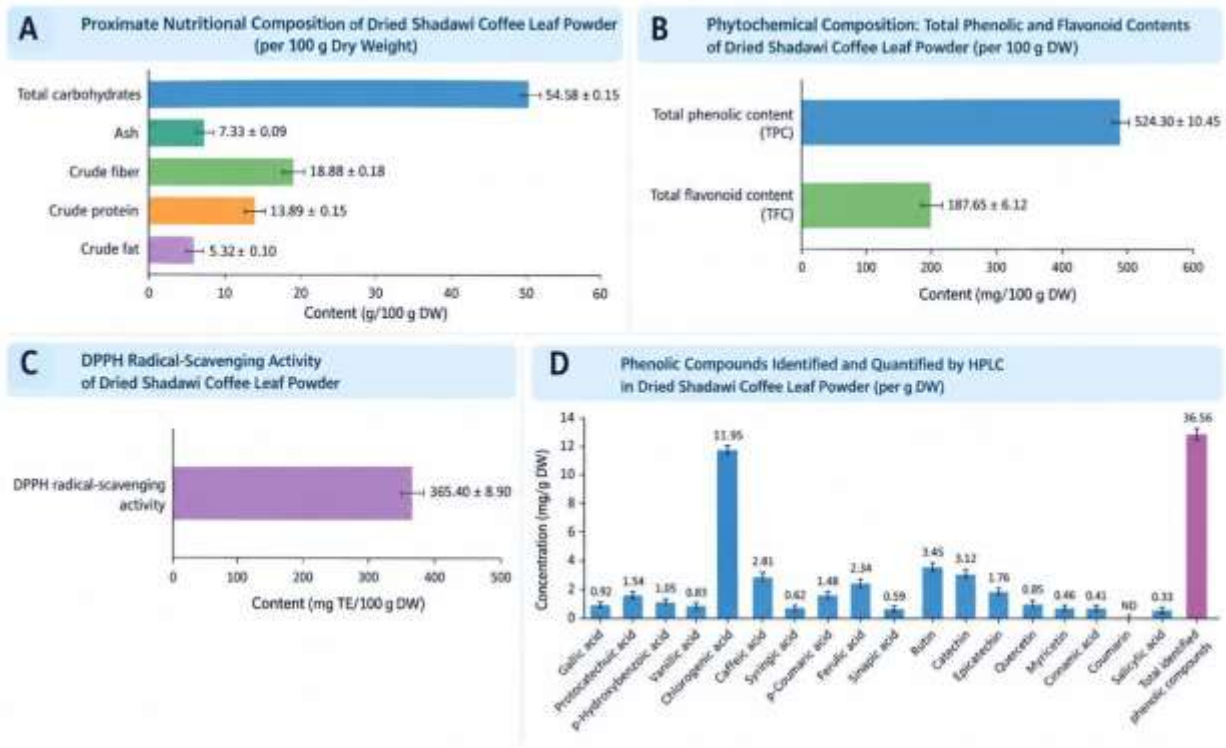


Figure 2. Chemical composition, bioactive compounds, antioxidant activity, and phenolic profile of dried Shadawi coffee (*Coffea arabica* L.) leaves powder.

3.2.Biochemial Results

Effect of dried Shadawi coffee leaf powder on feed intake, body weight gain, and feed efficiency

Figure 3 illustrates the effects of dietary supplementation with dried Shadawi coffee (*Coffea arabica* L.) leaf powder on feed intake, body weight gain, and feed efficiency ratio (FER) in diabetic rats during the 28-day experimental period. The diabetic control group recorded the highest feed intake, at 20.45 ± 0.88 g/day, compared with 14.80 ± 0.65 g/day in the normal control group. Feed intake decreased progressively with increasing levels of dried coffee leaf powder supplementation, reaching 18.75 ± 0.80, 17.40 ± 0.72, and 16.15 ± 0.64 g/day in the 3%, 6%, and 9% supplementation groups, respectively. Body weight gain showed a different pattern among the experimental groups. The normal control group recorded the highest body weight gain (43.10 ± 2.35 g), whereas the diabetic control group showed the lowest value (16.90 ± 2.05 g). Supplementation with dried Shadawi coffee leaf powder increased body weight gain to 22.40 ± 1.95, 28.60 ± 2.10, and 36.20 ± 2.25 g in the 3%, 6%, and 9% groups, respectively. The 9% supplementation group recorded a body weight gain closer to that of the normal control group. The feed efficiency ratio also varied among the experimental groups. The normal control group showed the highest FER (0.102 ± 0.006), while the diabetic control group recorded the lowest value (0.028 ± 0.003). The FER increased to 0.041 ± 0.004, 0.054 ± 0.005, and 0.075 ± 0.006 in the 3%, 6%, and 9% supplementation groups, respectively. Significant differences among the experimental groups were observed for the measured parameters ($P < 0.05$), as indicated by the different superscript letters in Figure 3. Overall, the data show progressive changes in feed intake, body

weight gain, and feed efficiency across the different levels of dried Shadawi coffee leaf powder supplementation, with the 9% group generally showing values closer to those observed in the normal control group.

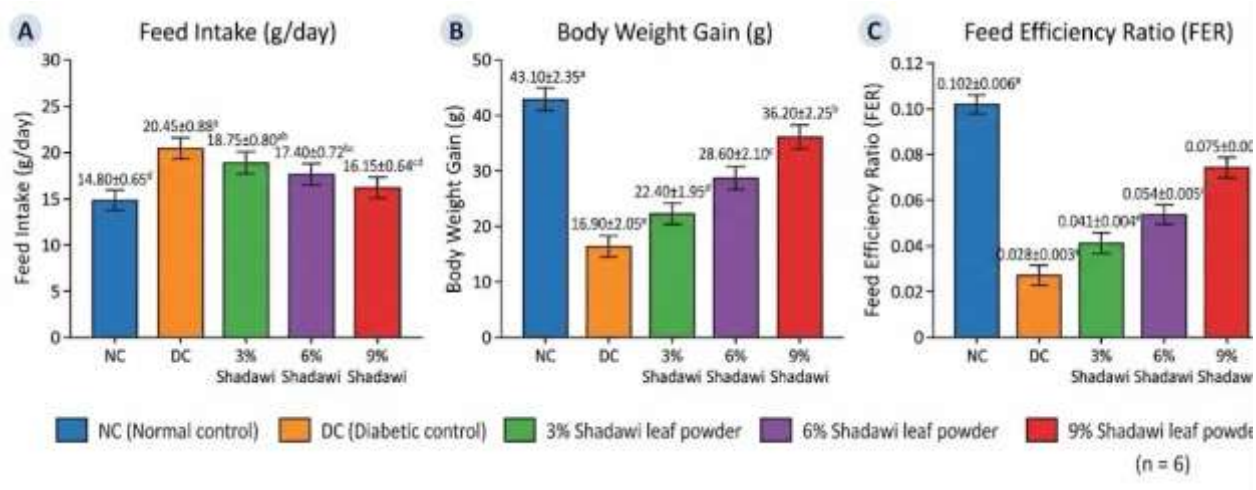


Figure 3. Effect of Shadawi coffee leaf powder on feed intake, body weight gain, and FER in diabetic rats. Values are presented as mean ± standard deviation (SD) (n = 6). Within each panel, bars bearing different superscript letters (a–d) indicate statistically significant differences among groups, as determined by Duncan's multiple range test ($P < 0.05$).

3.3.Biochemial Results

- **Effect of dried Shadawi coffee leaf powder on glycemic parameters**

Figure 4 illustrates the effects of dietary supplementation with dried Shadawi coffee (*Coffea arabica* L.) leaf powder on selected glycemic parameters in diabetic rats after 28 days of treatment. The diabetic control group showed substantially higher serum glucose and HbA1c levels than the normal control group, together with lower serum insulin concentrations and hepatic glycogen content. Serum glucose increased from 92.15 ± 4.85 mg/dL in the normal control group to 255.30 ± 14.10 mg/dL in the diabetic control group. Supplementation with 3%, 6%, and 9% dried coffee leaf powder was associated with progressively lower serum glucose concentrations, reaching 210.45 ± 11.50, 178.20 ± 9.30, and 144.60 ± 8.15 mg/dL, respectively.

Serum insulin concentration was 2.05 ± 0.16 μIU/mL in the normal control group and decreased to 0.65 ± 0.07 μIU/mL in the diabetic control group. Following dietary supplementation, serum insulin levels increased to 0.92 ± 0.08, 1.30 ± 0.10, and 1.65 ± 0.13 μIU/mL in the 3%, 6%, and 9% groups, respectively. A similar trend was observed for hepatic glycogen content, which decreased from 185.20 ± 7.10 mg/g tissue in the normal control group to 112.50 ± 6.05 mg/g tissue in the diabetic control group. The values increased to 132.80 ± 5.80, 152.40 ± 6.60, and 170.15 ± 7.25 mg/g tissue following supplementation with 3%, 6%, and 9% coffee leaf powder, respectively.

The HbA1c level was 5.05 ± 0.28% in the normal control group compared with 9.45 ± 0.52% in the diabetic control group. Dietary supplementation with dried Shadawi coffee leaf powder was associated with lower HbA1c levels, which reached 8.25 ± 0.44%, 7.35 ± 0.38%, and 6.15 ± 0.31% in the 3%, 6%, and 9% supplementation groups, respectively. Significant differences among the experimental groups were observed for the measured parameters ($P < 0.05$), as indicated by the different superscript letters shown in Figure 4. Overall, the data demonstrate a consistent pattern of improvement across the measured glycemic parameters with increasing levels of dried Shadawi coffee leaf powder supplementation, with the 9% group showing values closer to those of the normal control group.

Natural Resources for Human Health
eISSN: 2583-1194

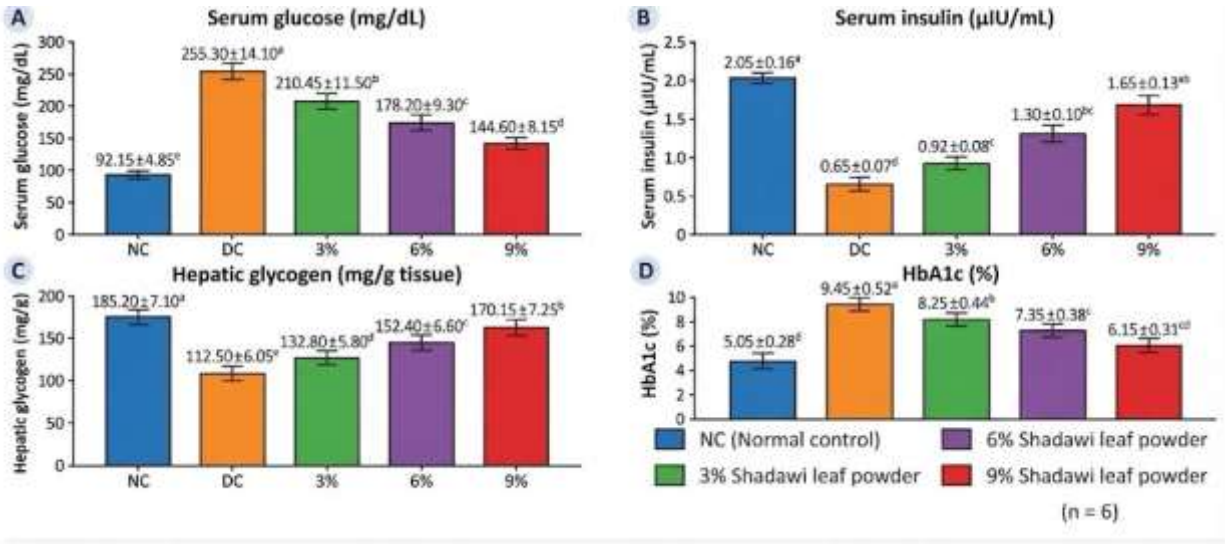


Figure 4. Effect of dietary supplementation with dried Shadawi coffee (Coffea arabica L.) leaf powder on glycemic parameters in diabetic rats. Values are presented as mean ± standard deviation (SD) (n = 6). Within each panel, bars bearing different superscript letters (a–d) indicate statistically significant differences among groups, as determined by Duncan's multiple range test ($P < 0.05$).

- **Effect of dried Shadawi coffee leaf powder on serum lipid profile**

Figure 5 illustrates the effect of dietary supplementation with dried Shadawi coffee (*Coffea arabica* L.) leaf powder on the serum lipid profile of diabetic rats after 28 days of treatment. The diabetic control group exhibited higher serum total cholesterol and triglyceride concentrations than the normal control group. Total cholesterol increased from 75.60 ± 3.10 mg/dL in the normal control group to 132.40 ± 5.45 mg/dL in the diabetic control group. Supplementation with 3%, 6%, and 9% dried coffee leaf powder reduced total cholesterol levels to 116.80 ± 4.90, 104.20 ± 4.30, and 93.75 ± 3.90 mg/dL, respectively. These differences were statistically significant ($P < 0.05$). Serum triglycerides showed a similar pattern, increasing from 60.20 ± 2.65 mg/dL in the normal control group to 112.50 ± 4.80 mg/dL in the diabetic control group. Following supplementation with 3%, 6%, and 9% dried Shadawi coffee leaf powder, triglyceride concentrations decreased to 97.10 ± 4.30, 85.40 ± 3.90, and 73.20 ± 3.40 mg/dL, respectively. The 9% supplementation group showed a triglyceride level comparable to that of the normal control group.

In contrast, HDL-C concentration decreased in the diabetic control group to 36.10 ± 1.05 mg/dL compared with 49.80 ± 1.60 mg/dL in the normal control group. Dietary supplementation with coffee leaf powder was associated with a gradual increase in HDL-C, reaching 39.40 ± 1.20, 42.80 ± 1.30, and 45.60 ± 1.45 mg/dL in the 3%, 6%, and 9% groups, respectively. LDL-C showed an opposite trend, with the highest concentration recorded in the diabetic control group (89.70 ± 3.60 mg/dL) compared with 45.20 ± 1.65 mg/dL in the normal control group. Supplementation with 3%, 6%, and 9% coffee leaf powder reduced LDL-C concentrations to 74.20 ± 2.95, 62.80 ± 2.70, and 54.10 ± 2.30 mg/dL, respectively. For VLDL-C, the diabetic control group recorded a higher concentration (14.20 ± 0.48 mg/dL) than the normal control group (10.10 ± 0.25 mg/dL). The values decreased to 12.50 ± 0.55, 11.30 ± 0.52, and 9.50 ± 0.35 mg/dL in the 3%, 6%, and 9% supplementation groups, respectively. Overall, Figure 5 shows that supplementation with dried Shadawi coffee leaf powder was associated with improvements in the serum lipid profile of diabetic rats, characterized by reductions in total cholesterol, triglycerides, LDL-C, and VLDL-C and an increase in HDL-C. The changes generally became more pronounced as the level of coffee leaf powder supplementation increased, with the 9% group showing values closer to those of the normal control group.

Natural Resources for Human Health
eISSN: 2583-1194

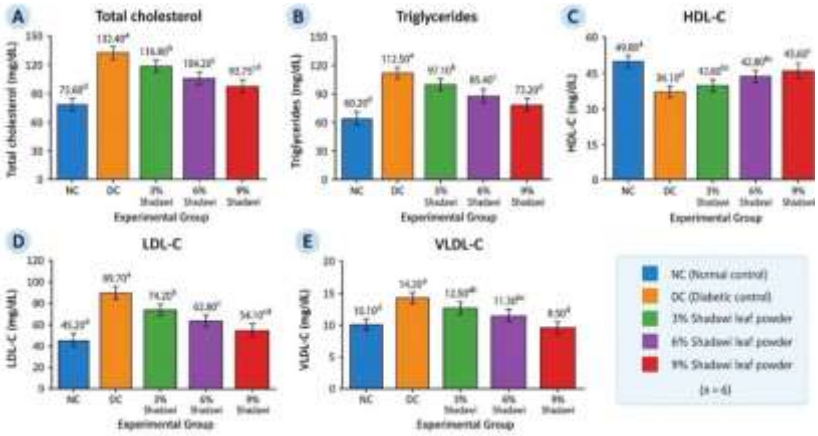


Figure 5. Effect of dietary supplementation with dried Shadawi coffee (Coffea arabica L.) leaf powder on serum lipid profile parameters in diabetic rats (A) Total cholesterol, (B) Triglycerides, (C) HDL-C, (D) LDL-C, and (E) VLDL-C. Values are presented as mean ± standard deviation (SD) (n = 6). Within each panel, bars bearing different superscript letters (a–d) indicate statistically significant differences among groups, as determined by Duncan's multiple range test ($P < 0.05$).

- **Effect of dried Shadawi coffee leaf powder on serum liver enzyme activities**

Figure 6 illustrates the effect of dietary supplementation with dried Shadawi coffee (*Coffea arabica* L.) leaf powder on serum liver enzyme activities in diabetic rats after 28 days of treatment. The diabetic control group exhibited markedly higher activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) compared with the normal control group. Serum ALT activity increased from 25.80 ± 1.30 U/L in the normal control group to 55.10 ± 2.65 U/L in the diabetic control group. Following dietary supplementation with 3%, 6%, and 9% dried Shadawi coffee leaf powder, ALT activity decreased to 47.30 ± 2.10, 39.50 ± 1.85, and 32.20 ± 1.45 U/L, respectively. These differences among the experimental groups were statistically significant ($P < 0.05$). A comparable pattern was observed for AST activity. The normal control group recorded an AST activity of 46.50 ± 1.55 U/L, whereas the diabetic control group showed a substantially higher value of 99.80 ± 4.20 U/L. Supplementation with 3%, 6%, and 9% dried Shadawi coffee leaf powder reduced AST activity to 85.40 ± 3.90, 71.20 ± 3.10, and 57.90 ± 2.50 U/L, respectively. The differences between the experimental groups were statistically significant ($P < 0.05$), as indicated by the different superscript letters in Figure 6.

Overall, Figure 6 shows that diabetes was associated with elevated serum ALT and AST activities, whereas dietary supplementation with dried Shadawi coffee leaf powder was associated with a progressive reduction in both enzyme activities. The reduction became more pronounced with increasing supplementation levels, and the values observed in the 9% group were closer to those of the normal control group.

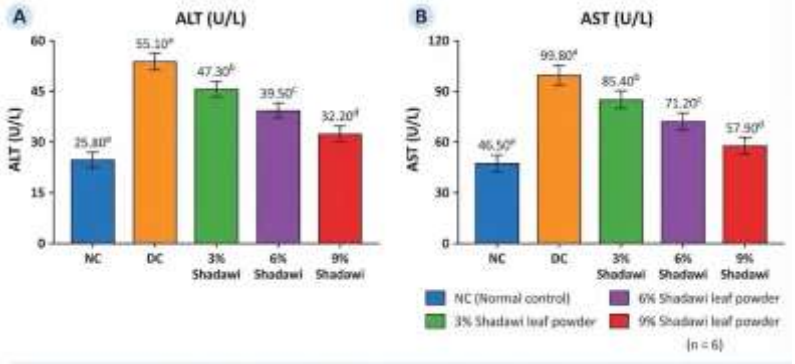


Figure 6. Effect of dietary supplementation with dried Shadawi coffee (*Coffea arabica* L.) leaf powder on serum ALT and AST activities in diabetic rats after 28 days of treatment. Values are presented as mean ± standard deviation (SD) (n = 6). Within each panel, bars bearing different superscript letters (a–d) indicate statistically significant differences among groups, as determined by Duncan's multiple range test ($P < 0.05$).

- **Effect of dried Shadawi coffee leaf powder on serum kidney function parameters**

Figure 7 illustrates the effect of dietary supplementation with dried Shadawi coffee (*Coffea arabica* L.) leaf powder on selected serum kidney function parameters in diabetic rats after 28 days of treatment. The diabetic control group showed higher serum concentrations of urea, creatinine, and uric acid than the normal control group. Serum urea concentration increased from 32.80 ± 1.65 mg/dL in the normal control group to 64.20 ± 2.90 mg/dL in the diabetic control group. Following supplementation with 3%, 6%, and 9% dried Shadawi coffee leaf powder, serum urea concentrations decreased to 55.10 ± 2.50, 47.80 ± 2.25, and 40.50 ± 1.85 mg/dL, respectively. The differences among the experimental groups were statistically significant ($P < 0.05$).

Serum creatinine exhibited a similar pattern. The normal control group recorded a creatinine concentration of 0.68 ± 0.04 mg/dL, whereas the diabetic control group showed a higher value of 1.42 ± 0.08 mg/dL. Dietary supplementation with 3%, 6%, and 9% dried coffee leaf powder reduced serum creatinine concentrations to 1.22 ± 0.07, 1.05 ± 0.06, and 0.82 ± 0.05 mg/dL, respectively. The creatinine concentration in the 9% supplementation group was statistically comparable to that of the normal control group, as indicated by the shared superscript letter.

A comparable response was observed for serum uric acid. Its concentration increased from 2.70 ± 0.15 mg/dL in the normal control group to 5.45 ± 0.28 mg/dL in the diabetic control group. Supplementation with 3%, 6%, and 9% dried Shadawi coffee leaf powder reduced uric acid concentrations to 4.65 ± 0.24, 3.95 ± 0.22, and 3.30 ± 0.18 mg/dL, respectively. The differences among the experimental groups were statistically significant ($P < 0.05$), with the lowest uric acid concentration among the supplemented groups recorded at the 9% supplementation level.

Overall, Figure 7 demonstrates a consistent pattern of changes in the measured serum kidney function parameters. Diabetes was associated with elevated serum urea, creatinine, and uric acid concentrations, whereas dietary supplementation with dried Shadawi coffee leaf powder was associated with progressive reductions in these parameters. The values observed in the 9% supplementation group were closer to those of the normal control group.

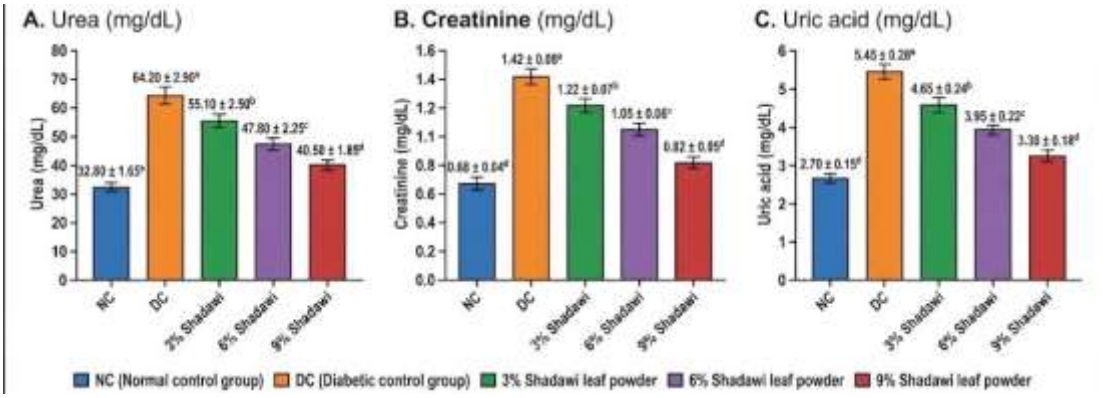


Figure 7. Effect of dietary supplementation with dried Shadawi coffee (Coffea arabica L.) leaf powder on serum urea, creatinine, and uric acid concentrations in diabetic rats after 28 days of treatment. Values are presented as mean ± standard deviation (SD) (n = 6). Within each panel, bars bearing different superscript letters (a–d) indicate statistically significant differences among groups, as determined by Duncan's multiple range test ($P < 0.05$).

3.4. Histopathological Results

Histopathological examination of pancreatic tissue sections stained with hematoxylin and eosin (H&E) revealed distinct morphological differences among the experimental groups (Figure 8). The normal control group showed well-preserved pancreatic architecture, characterized by clearly defined islets of Langerhans surrounded by normally arranged exocrine acinar tissue. The islets exhibited relatively compact cellular organization, with endocrine cells displaying preserved nuclear and cytoplasmic morphology. The surrounding acini were regularly arranged, with no apparent evidence of cellular degeneration, edema, or inflammatory changes.

In contrast, pancreatic sections from the diabetic control group showed marked histopathological alterations. The islets of Langerhans appeared reduced in size and irregular in architecture, with apparent cellular depletion and degenerative changes.

The surrounding exocrine tissue also exhibited architectural disruption, accompanied by increased intercellular spaces and areas of cytoplasmic vacuolation. These findings were consistent with substantial pancreatic tissue alterations associated with streptozotocin-induced diabetes. Dietary supplementation with 3% dried Shadawi coffee (Coffea arabica L.) leaf powder was associated with partial improvement in pancreatic morphology. The islets appeared relatively more organized than those observed in the diabetic control group, although some reduction in islet size and cellular irregularity remained evident. The surrounding acinar tissue showed improved preservation, with less apparent vacuolation and tissue disruption compared with the untreated diabetic group. The 6% supplementation group exhibited more pronounced preservation of pancreatic architecture. The islets of Langerhans appeared larger and more clearly defined, with improved cellular organization and fewer apparent degenerative changes. The exocrine acinar tissue was also relatively well preserved and showed more regular organization compared with the diabetic control and 3% supplementation groups. The 9% supplementation group showed the most pronounced morphological preservation among the diabetic groups. Pancreatic sections demonstrated relatively well-defined islets with improved cellular organization and preserved surrounding acinar architecture.

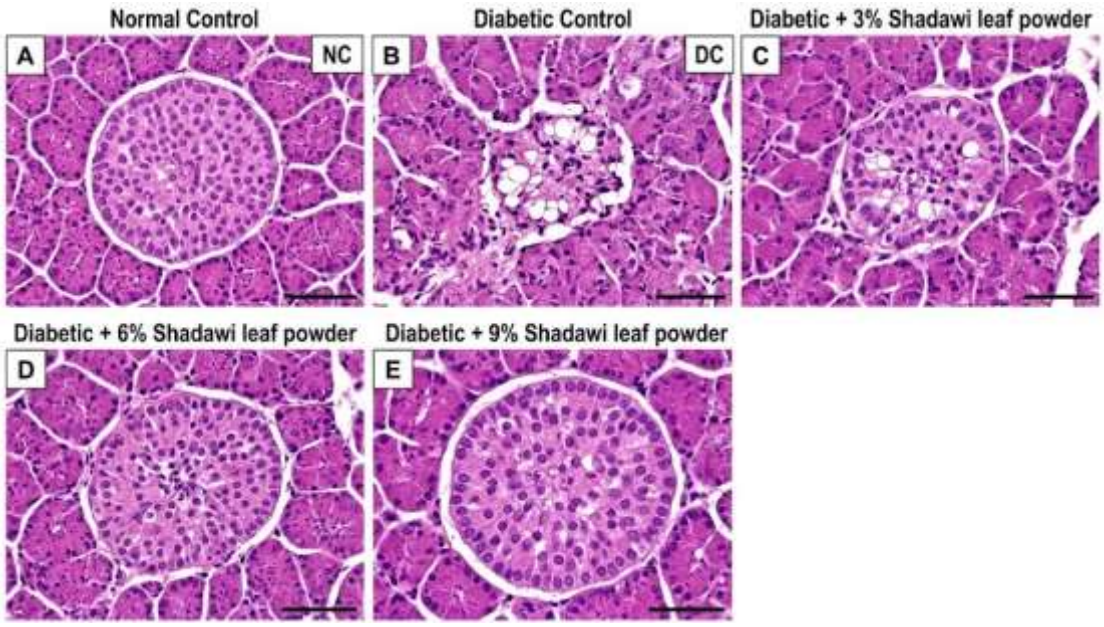


Fig. 8. Representative photomicrographs of pancreatic tissue sections (H&E, scale bar = 50 μm) showing the protective effects of *Shadawi* coffee leaf powder against diabetes-induced histopathological alterations in rats: (A) Normal control, (B) Diabetic control, (C) Diabetic + 3% leaf powder, (D) Diabetic + 6% leaf powder, and (E) Diabetic + 9% leaf powder.

5. DISCUSSION

The present study investigated the potential antidiabetic activity of dried Shadawi coffee (*Coffea arabica* L.) leaf powder in streptozotocin (STZ)-induced diabetic rats. The findings demonstrated that diabetes was associated with marked disturbances in glucose and lipid metabolism, alterations in hepatic and renal biochemical parameters, and pronounced pancreatic histopathological changes. Dietary supplementation with Shadawi coffee leaf powder was associated with progressive improvement in several of these parameters, particularly at the 6% and 9% supplementation levels. These findings may be related, at least in part, to the phytochemical composition of the coffee leaves, which contained appreciable levels of phenolic and flavonoid compounds and exhibited measurable radical-scavenging activity.

The marked elevation of serum glucose and HbA1c, together with the reduction in serum insulin and hepatic glycogen observed in the diabetic control group, is consistent with the metabolic consequences of STZ-induced pancreatic β-cell injury. STZ is widely used to induce experimental diabetes because of its diabetogenic effects on pancreatic β-cells, leading to impaired insulin secretion and persistent hyperglycemia (Ghasemi & Jeddi, 2023). In the present study, supplementation with Shadawi coffee leaf powder progressively reduced serum glucose and HbA1c while increasing serum insulin and hepatic glycogen, indicating an improvement in glucose homeostasis. This interpretation is supported by previous experimental evidence showing that *C. arabica* leaf extracts and their major bioactive constituents can exert hypoglycemic effects

(Nascimento et al., 2023). In addition, evidence from clinical studies has suggested that coffee consumption may influence glucose metabolism and insulin responses, although the magnitude and direction of these effects may depend on the duration of exposure and other characteristics of coffee consumption (Reis et al., 2019). However, the present study cannot establish the precise mechanism responsible for the observed effects. The improvement may involve multiple pathways, including attenuation of oxidative stress, modulation of carbohydrate metabolism, and preservation of pancreatic endocrine function.

The phytochemical findings provide a plausible basis for the observed biological effects. The Shadawi coffee leaf powder contained considerable total phenolic and flavonoid contents and showed DPPH radical-scavenging activity. HPLC analysis further identified 17 quantified phenolic compounds, with chlorogenic acid representing the predominant compound, followed by rutin and catechin. These findings are consistent with previous chemical investigations of *C. arabica* leaves, which have demonstrated the presence of diverse polyphenolic constituents, including chlorogenic acids, flavonoids, and xanthones, and have reported positive associations between polyphenolic content and antioxidant activity (de Almeida et al., 2019). A recent review similarly identified chlorogenic acids, rutin, mangiferin, and other phytochemicals among the important constituents of coffee leaves and discussed their potential antioxidant and metabolic activities (Yohannis et al., 2024). Moreover, experimental evidence obtained using *C. arabica* leaf extracts has demonstrated hypoglycemic activity, supporting the biological relevance of the phytochemical constituents detected in coffee leaves (Nascimento et al., 2023).

Chlorogenic acid is of particular interest because it is a major coffee polyphenol and has been investigated for its potential effects on glucose metabolism, lipid metabolism, oxidative stress, and inflammatory pathways. A recent systematic review summarized evidence indicating that chlorogenic acid may modulate metabolic and oxidative processes relevant to diabetes and other metabolic disorders (Nguyen et al., 2024). Nevertheless, because the present study evaluated the whole leaf powder rather than isolated compounds, the contribution of any individual constituent to the observed effects cannot be established. Therefore, the observed biological responses should be interpreted as effects of the complex phytochemical matrix of the coffee leaves rather than as effects attributable specifically to chlorogenic acid, rutin, catechin, or any other individual compound.

Diabetic rats also exhibited an unfavorable serum lipid profile, characterized by increased total cholesterol, triglycerides, LDL-C, and VLDL-C and reduced HDL-C. Such alterations are consistent with the well-established association between impaired insulin action and diabetic dyslipidemia. Insulin deficiency or resistance can promote increased availability of circulating free fatty acids, enhance hepatic VLDL production, and impair the clearance of triglyceride-rich lipoproteins, thereby contributing to hypertriglyceridemia and abnormalities in LDL-C and HDL-C concentrations (Thambiah & Lai, 2021). In the present study, supplementation with Shadawi coffee leaf powder progressively improved these lipid parameters. This improvement may be related to the phenolic-rich composition of the leaves and the metabolic activities reported for coffee-derived polyphenols. Chlorogenic acid, in particular, has been investigated for its potential effects on glucose and lipid metabolism and on pathways related to oxidative stress and inflammation (Nguyen et al., 2024). Nevertheless, direct assessment of lipid-metabolizing enzymes and molecular signaling pathways would be required to confirm this interpretation.

The diabetic control group also showed increased serum ALT and AST activities, indicating biochemical evidence of hepatic disturbance. The progressive reduction in these enzymes following coffee leaf supplementation suggests an improvement in hepatic biochemical status. This finding may be associated with improved glycemic control and the antioxidant properties of the leaf constituents. Phenolic compounds may contribute to antioxidant defense by scavenging reactive species and modulating endogenous antioxidant systems; however, the present study did not directly measure hepatic oxidative-stress markers. Therefore, ALT and AST should be considered biochemical indicators of hepatic disturbance rather than direct measures of hepatic structural integrity. Additional liver histopathology and oxidative-stress biomarkers would be required to determine whether the observed biochemical improvement is accompanied by direct hepatoprotective effects(Alzahrani et al.,2026) .

Similarly, the increases in serum urea, creatinine, and uric acid observed in diabetic rats indicate alterations in renal biochemical status. Diabetes-associated metabolic abnormalities and oxidative stress contribute to renal injury and are important factors in the development and progression of diabetic kidney disease (Jha et al., 2016). In the present study, the progressive reduction of these renal biomarkers following supplementation may partly reflect improved glycemic control and reduced metabolic stress. However, these findings should be interpreted cautiously because serum urea, creatinine, and uric acid alone do not provide a comprehensive assessment of renal structure and function. Future studies incorporating urinary

biomarkers, renal histopathology, and molecular markers of oxidative stress and inflammation would provide stronger evidence regarding a potential renoprotective effect.

The pancreatic histopathological findings were consistent with the biochemical observations. The diabetic control group showed marked alterations in the islets of Langerhans and surrounding exocrine tissue, including reduced islet size, cellular irregularity, vacuolation, and disruption of pancreatic architecture. These changes are compatible with pancreatic injury associated with STZ-induced diabetes, which involves preferential toxicity toward pancreatic β-cells and consequent impairment of insulin secretion (Ghasemi & Jeddi, 2023). In contrast, the 3%, 6%, and 9% supplementation groups showed progressively better preservation of pancreatic architecture, with comparatively improved islet organization and preservation of acinar tissue. The greater morphological preservation observed at 6% and 9% was accompanied by higher serum insulin concentrations and improved glycemic parameters, suggesting a possible association between pancreatic structural preservation and metabolic improvement. However, this interpretation should remain cautious because qualitative histopathology alone cannot demonstrate β-cell regeneration or definitively quantify endocrine-cell preservation. Quantitative morphometric analysis and immunohistochemical staining for insulin and other β-cell markers would therefore be valuable in future studies (Labban & Abd Elmeged,2026). Overall, the present findings suggest that dried Shadawi coffee leaf powder exhibits potential biological activity in experimental diabetes, particularly with respect to glucose regulation, lipid metabolism, hepatic and renal biochemical status, and pancreatic tissue preservation. The phytochemical profile of the leaves, particularly their phenolic and flavonoid constituents and the predominance of chlorogenic acid, provides a plausible biochemical basis for these effects. Previous investigations have confirmed that *C. arabica* leaves contain diverse polyphenolic compounds and possess antioxidant activity, while experimental evidence has also demonstrated hypoglycemic activity of coffee-leaf extracts (de Almeida et al., 2019). However, the findings of the present study should be regarded as preliminary experimental evidence rather than proof of a therapeutic effect. Further studies should investigate the molecular mechanisms involved, establish a more comprehensive dose-response relationship, evaluate long-term safety, and determine whether the observed effects can be reproduced using standardized extracts or isolated bioactive constituents. Such investigations would help clarify the biological significance of Shadawi coffee leaves and their potential as a source of bioactive compounds relevant to experimental diabetes.

6. CONCLUSION

The present study demonstrated that dried Shadawi coffee (*Coffea arabica* L.) leaf powder contains appreciable amounts of phenolic and flavonoid compounds and exhibits measurable antioxidant activity, with chlorogenic acid identified as the predominant phenolic constituent. In streptozotocin-induced diabetic rats, dietary supplementation with Shadawi coffee leaf powder was associated with progressive improvements in glycemic parameters, including reductions in serum glucose and HbA1c and increases in serum insulin and hepatic glycogen. Improvements were also observed in the serum lipid profile, as well as in hepatic and renal biochemical parameters. Histopathological examination further indicated improved preservation of pancreatic architecture, particularly at the higher supplementation levels. Collectively, these findings suggest that Shadawi coffee leaves may represent a promising source of bioactive compounds with potential metabolic and antioxidant activities. However, the present findings are limited to an experimental animal model and do not establish clinical efficacy or safety in humans. Further investigations are warranted to clarify the molecular mechanisms underlying the observed effects, determine the optimal dose and duration of supplementation, evaluate long-term safety, and identify the specific bioactive constituents responsible for the biological activities. Such studies would help determine the potential application of Shadawi coffee leaves or standardized extracts as a complementary source of bioactive compounds relevant to metabolic health.

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