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FENNEL-BASED DIETARY INTERVENTION MODULATES OBESITY-RELATED BIOMARKERS IN EXPERIMENTAL RATS

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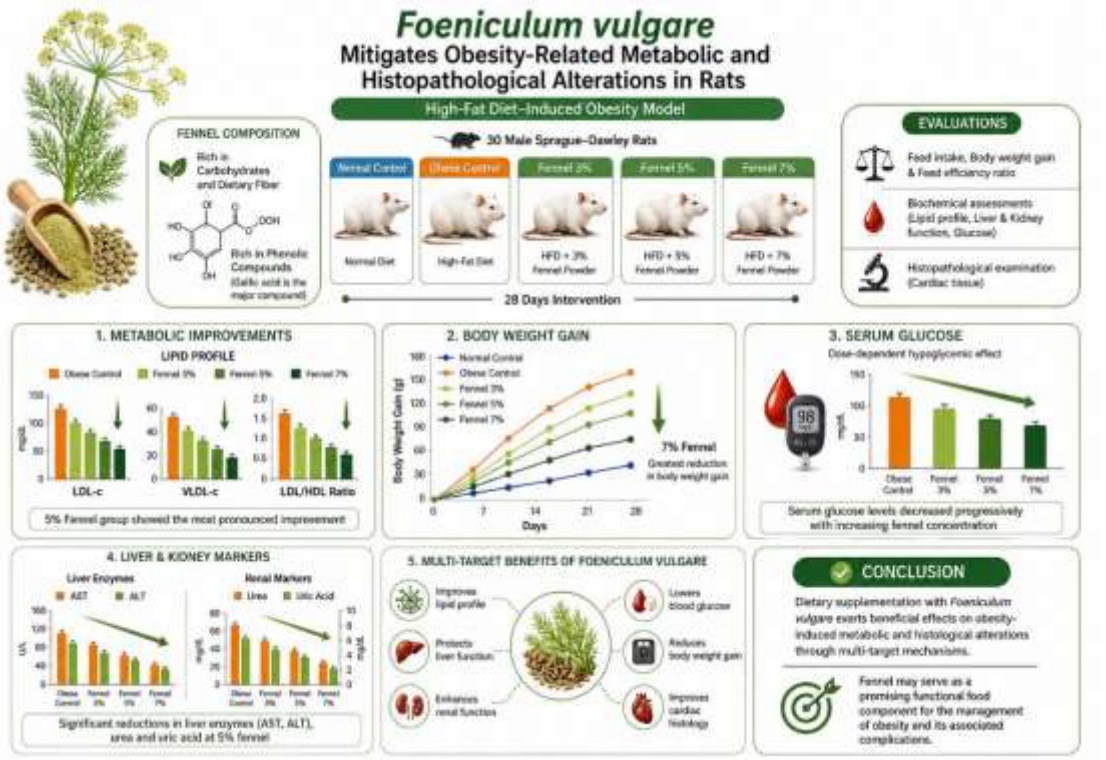
ABSTRACT

Obesity is a complex metabolic disorder associated with multiple physiological disturbances, including dyslipidemia, hyperglycemia, and organ dysfunction. The present study aimed to evaluate the effects of dietary supplementation with Foeniculum vulgare on obesity-related metabolic and histopathological biomarkers in a high-fat diet–induced rat model. Thirty male Sprague-Dawley rats were randomly assigned into five groups: a normal control group, an obese control group, and three obese groups supplemented with fennel powder at levels of 3%, 5%, and 7% for 28 days. Obesity was induced using a high-fat diet prior to the intervention. Proximate chemical composition and phenolic profile of fennel were analyzed using standard methods and HPLC-DAD, respectively. Biological evaluation included measurements of feed intake, body weight gain, and feed efficiency ratio. Biochemical assessments covered serum lipid profile, liver and kidney function markers, and glucose levels, in addition to histopathological examination of cardiac tissue. The results demonstrated that fennel is rich in carbohydrates, dietary fiber, and bioactive phenolic compounds, with gallic acid identified as the predominant constituent. Dietary supplementation with fennel significantly modulated metabolic parameters in obese rats. The 5% fennel group showed the most pronounced improvement in lipid profile, including reductions in LDL-c and VLDL-c and an improved LDL/HDL ratio. Liver enzymes (AST and ALT) and renal markers (urea and uric acid) were also significantly reduced at this level. Meanwhile, the 7% fennel group exhibited the greatest reduction in body weight gain and the most notable improvement in cardiac tissue structure. Serum glucose levels decreased progressively with increasing fennel concentration, indicating a dose-dependent hypoglycemic effect.

In conclusion, dietary supplementation with Foeniculum vulgare exerts beneficial effects on obesity-induced metabolic and histological alterations through multi-target mechanisms. These findings suggest that fennel may serve as a promising functional food component for the management of obesity and its associated complications.

KEYWORDS: Fennel, Foeniculum vulgare, dietary intervention, obesity, metabolic biomarkers, oxidative stress, histopathology, experimental rats.



Graphical Abstract: Protective Metabolic Effects of Foeniculum vulgare Supplementation in High-Fat Diet–Induced Obesity.

INTRODUCTION

Obesity is a multifactorial chronic metabolic disorder characterized by excessive accumulation of adipose tissue resulting from an imbalance between energy intake and energy expenditure. It has become one of the most serious public health challenges worldwide due to its increasing prevalence and its strong association with metabolic syndromes, including type 2 diabetes mellitus, cardiovascular diseases, hypertension, and non-alcoholic fatty liver disease (Bluher, 2019). The global rise in obesity is largely attributed to sedentary lifestyles, high-calorie diets, and genetic susceptibility, making it a complex condition that requires multifaceted therapeutic approaches. At the molecular level, obesity is not merely a disorder of excessive fat storage but is also associated with chronic low-grade inflammation, oxidative stress, mitochondrial dysfunction, and dysregulation of adipokines and insulin signaling pathways (Heymsfield & Wadden, 2017). These alterations contribute to metabolic disturbances such as hyperlipidemia, insulin resistance, and impaired hepatic function. Moreover, adipose tissue in obesity acts as an active endocrine organ, secreting pro-inflammatory cytokines such as TNF-α and IL-6, which further exacerbate metabolic dysfunction and systemic inflammation (Labban, & Abd Elmeged, 2026).

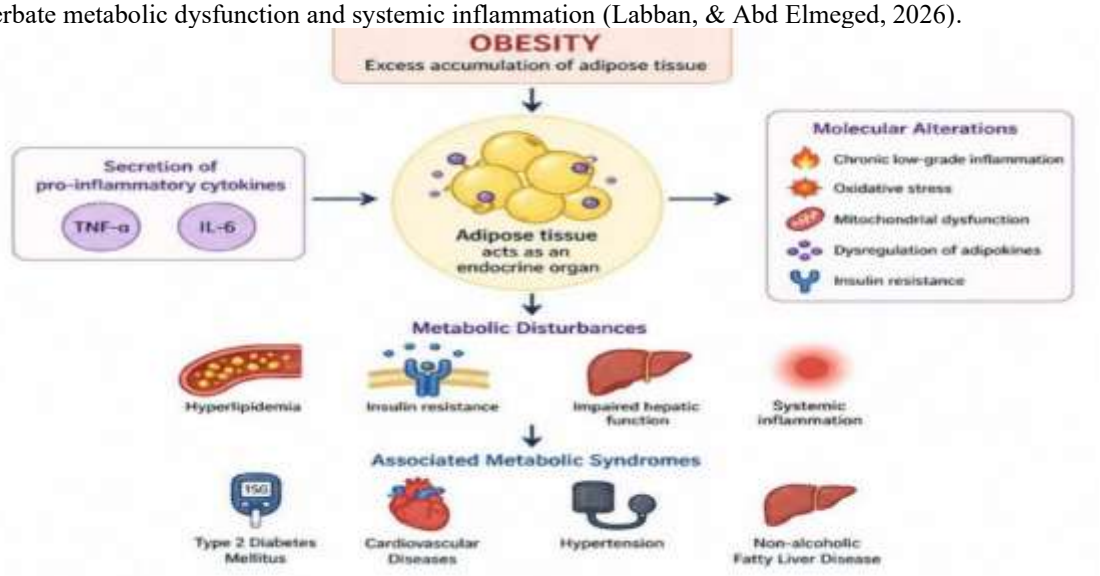


Figure 1. Simplified Schematic Illustration of the Pathophysiological Mechanisms Underlying Obesity and Its Associated Metabolic Complications

Although pharmacological interventions for obesity exist—including appetite suppressants and lipase inhibitors—their long-term utilization is frequently constrained by adverse side effects, prohibitive costs, and inconsistent

efficacy (Yanovski & Yanovski, 2016). Consequently, there is an escalating scientific interest in identifying natural, safe, and cost-effective alternatives. In particular, plant-derived bioactive compounds are being explored for their potential to offer multi-targeted metabolic benefits. Functional foods have thus emerged as a cornerstone strategy in preventive nutrition and metabolic health management (Ali et al., 2026). These foods are characterized by their biologically active components, which exert beneficial physiological effects that extend beyond basic nutritional functions (Granato et al., 2020). Among these bioactive-rich sources, medicinal and aromatic plants have garnered considerable attention due to their antioxidant, anti-inflammatory, lipid-lowering, and insulin-sensitizing properties. Foeniculum vulgare (fennel) is a widely distributed aromatic plant belonging to the Apiaceae family and has been traditionally utilized in folk medicine to treat digestive disorders, respiratory conditions, and metabolic imbalances (Alzahrani et al., 2026). The plant encompasses a diverse array of phytochemical constituents, including phenolic compounds, flavonoids, and fatty acids, as well as volatile oils such as anethole, fenchone, and estragole, all of which contribute to its broad biological activities (Noreen et al., 2023). These compounds have been extensively reported to exhibit potent antioxidant, antimicrobial, anti-inflammatory, and lipid-modulating effects.

Recent experimental studies suggest that fennel may play a role in regulating metabolic pathways associated with obesity. Its bioactive constituents are believed to enhance antioxidant defense systems, reduce lipid peroxidation, and improve glucose homeostasis (Vella et al ., 2024). Additionally, fennel has been shown to influence lipid metabolism by reducing total cholesterol, triglycerides, and low-density lipoprotein levels while potentially increasing high-density lipoprotein concentrations in experimental models. Animal models of diet-induced obesity are widely used to investigate metabolic alterations and evaluate potential therapeutic agents. High-fat diet-induced obesity in rodents closely mimics human metabolic syndrome by inducing insulin resistance, hepatic steatosis, dyslipidemia, and systemic inflammation (Atanasov et al., 2015). These models are considered highly valuable for assessing both biochemical and histopathological changes associated with obesity and for evaluating the efficacy of natural interventions. Despite the increasing number of studies on medicinal plants with anti-obesity properties, limited research has specifically addressed the dose-dependent effects of fennel powder as a whole dietary supplement rather than isolated extracts. Moreover, few studies have integrated both biochemical and histopathological assessments to comprehensively evaluate its metabolic impact under obese conditions(Elmeged & Albaggar, 2026).

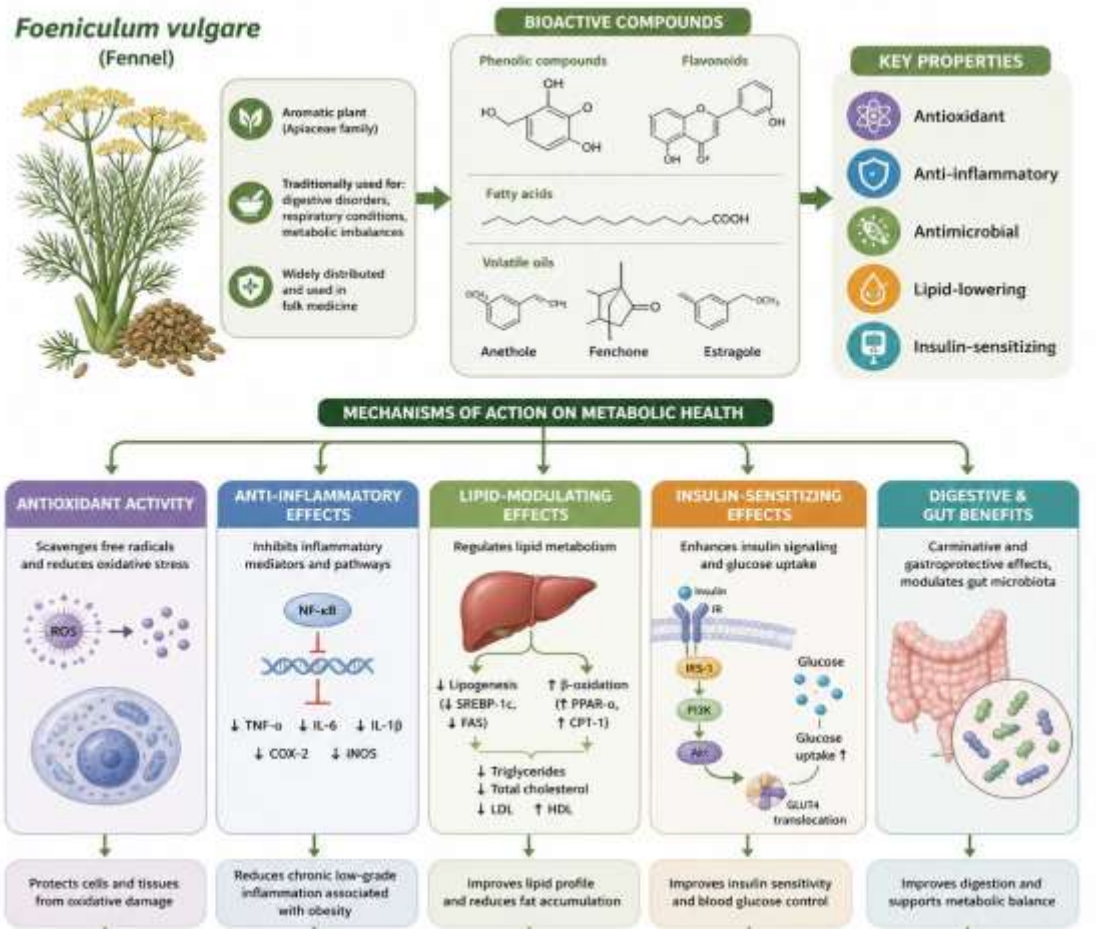


Figure 2. Schematic Representation of the Multi-Target Metabolic Effects of Foeniculum vulgare.

Therefore, the present study aims to investigate the dose-dependent effects of dietary fennel supplementation on obesity-related metabolic and histopathological biomarkers in a high-fat diet-induced obesity model in rats. This

integrated approach may provide deeper insights into the potential of fennel as a functional dietary intervention for the management of obesity-associated metabolic disorders.

2. MATERIALS AND METHODS

2.1. Materials

Source of Plant Material:

Fennel (Foeniculum vulgare) were obtained from local commercial outlets in Al-Baha City, Saudi Arabia (KSA). The fennel seeds were carefully cleaned, air-dried under controlled laboratory conditions, and subsequently ground into a fine powder using a laboratory mechanical grinder, following standardized botanical preparation procedures (Ainsworth & Gillespie, 2007). The obtained powder was used for dietary incorporation in experimental diets.

Experimental Animals: Thirty adult male Sprague-Dawley albino rats, weighing 150 ± 10 g, were obtained from the animal house facility of the Institute of Nutrition, Cairo, Egypt. Animals were selected based on uniform age and good health status to minimize biological variability and ensure reliable metabolic assessment.

Dietary Ingredients and Chemicals: High-purity dietary components, including casein, cellulose, corn oil, and standardized vitamin and mineral mixtures, were obtained from Morgan Co. (Cairo, Egypt). Analytical-grade reagents used for biochemical and histological analyses, including formalin (for tissue fixation), ethanol, and ethylenediaminetetraacetic acid (EDTA), were purchased from El-Nasr Pharmaceutical Chemicals (El-Amireia, Cairo, Egypt).

2.2. Preparation of Fennel Powder

Fennel seeds were collected from local markets in Al-Baha City, Saudi Arabia. The plant material was thoroughly washed with distilled water to remove dust and impurities, then air-dried at room temperature (25 ± 2 °C) for 7–10 days until a constant weight was achieved. The dried seeds were ground into a fine powder using a mechanical grinder and passed through a 40-mesh sieve to ensure uniform particle size distribution. The resulting powder was stored in airtight, light-protected containers at 4 °C to preserve its phytochemical stability and bioactive integrity until use, in accordance with established phytochemical preparation protocols (Ainsworth & Gillespie, 2007).

2.3. Experimental Animals and Housing Conditions

Animals were acclimatized for one week under controlled laboratory conditions, including temperature (22 ± 2 °C), relative humidity (50–60%), and a 12-hour light/dark cycle. During acclimatization, all rats had free access to standard basal diet and water ad libitum. All experimental procedures complied with institutional ethical guidelines for the care and use of laboratory animals and were designed to minimize animal stress and suffering.

2.4. Induction of Obesity and Experimental Design

Obesity was induced in the experimental groups by feeding a high-fat diet for a defined pre-experimental period until obesity was confirmed. After confirmation, the animals were randomly allocated into five equal groups (n = 6 per group). All dietary formulations were prepared freshly on a weekly basis to maintain nutritional stability and prevent degradation of bioactive compounds. Animals had ad libitum access to food and water throughout the 28-day experimental period. The detailed composition of each diet is presented in Table 1.

Table (1): The basic and experimental diets' compositions.

Component (g)	Control (-)	Control (+)	3% fennel	5% fennel	7% fennel
Test ingredients	---	---	3	5	7
Casein	20	20	20	20	20
Corn oil	4.7	4.7	4.7	4.7	4.7
Mineral mix	3.5	3.5	3.5	3.5	3.5
Vitamin mix	1	1	1	1	1
Cellulose	5	5	5	5	5
Cholin chloride	2	2	2	2	2
Sucrose	10	10	10	10	10
Corn starch	**Up to 100**	**Up to 100**	**Up to 100**	**Up to 100**	**Up to 100**

2.5. Induction of Experimental Obesity

To establish the experimental obesity model, rats were fed a high-fat diet (HFD) for four weeks. The diet composition followed the AIN-93 standard guidelines (AIN, 1993) to ensure nutritional consistency and reproducibility. The formulation contained 30% fat (1:1 tallow and corn oil), 12% casein, 4% mineral mixture, 1% vitamin mixture, and 5% fiber. DL-methionine (0.3%), choline chloride (2%), and bile acids (0.2%) were incorporated to support metabolic balance, while corn starch was used as the carbohydrate base to complete the total weight of 100 g.

2.6. Ethical Housing and Environmental Conditions

Adult male Sprague-Dawley rats (150 ± 10 g; 14–16 weeks old) were obtained from a certified animal facility and housed in standardized polypropylene cages under controlled laboratory conditions (22 ± 2 °C; 50–60% humidity; 12-hour light/dark cycle). Animals were provided with free access to standard chow and water throughout the study via sterilized feeding systems.

Prior to experimental procedures, all rats were acclimatized for seven days under the same environmental conditions to ensure physiological stabilization and reduce stress-related variability. All experimental procedures complied with institutional ethical guidelines for laboratory animal care and use.

2.7. Experimental Design and Grouping

Thirty male rats were randomly assigned into five equal groups (n = 6) and maintained for 28 consecutive days as follows:

- Group 1: Normal control group fed a standard basal diet.
- Group 2: Obese control group fed a high-fat diet without treatment.
- Group 3: Obese rats fed a high-fat diet supplemented with 3% fennel powder.
- Group 4: Obese rats fed a high-fat diet supplemented with 5% fennel powder.
- Group 5: Obese rats fed a high-fat diet supplemented with 7% fennel powder.

Dietary formulations were freshly prepared on a weekly basis to maintain stability and bioactivity of the dietary components. Animals had unrestricted access to food and water throughout the experimental period.

2.7. Chemical Analysis

The proximate composition of the plant material was evaluated through the determination of its basic nutritional constituents. Moisture, ash, crude protein, and lipid contents were quantified according to the standardized procedures outlined by the Association of Official Analytical Chemists (AOAC, 2016). All measurements were conducted in triplicate to ensure methodological reliability and data consistency.

2.8. Determination of Phenolic Profile Using HPLC

The phytochemical constituents were characterized using a High-Performance Liquid Chromatography (HPLC) system (Agilent Technologies 1260 Infinity II) equipped with a diode-array detector (DAD) and autosampler. The separation process followed the analytical approach reported by Kim et al. (2006), with modifications adapted to the current experimental conditions.

Chromatographic separation was performed on an Eclipse XDB-C18 column (150 × 4.6 mm, 5 µm) coupled with a compatible guard column. The mobile phase consisted of acetonitrile and 2% aqueous acetic acid in a gradient elution system. A constant flow rate of 0.8 mL/min was maintained over a total run time of 60 minutes.

Prior to injection, samples were filtered using a 0.45 µm membrane filter, and 50 µL of each sample was injected into the system. Detection was carried out at multiple wavelengths (280, 320, and 360 nm) to allow the identification of different classes of phenolic compounds. Compound identification was based on comparison of retention times and spectral data with those of reference standards.

2.9. Growth Performance and Biological Evaluation

Throughout the experimental period, feed intake was recorded on a daily basis, while body weight was measured weekly under standardized conditions. From these primary measurements, growth performance indicators such as body weight gain percentage (BWG%) and feed efficiency ratio (FER) were calculated.

At the end of the experiment, relative organ weights were also determined to assess physiological alterations associated with dietary treatments. All calculations and evaluations were performed following established experimental protocols described by Chapman, Castillo, and Campbell (1959).

2.10. Blood Collection and Tissue Processing

Following a 12-hour fasting period, blood samples were collected from the retro-orbital venous plexus using sterile capillary tubes. Samples were allowed to clot at physiological temperature, then centrifuged to obtain serum, which was subsequently stored at −20 °C until biochemical analysis. After blood collection, animals were humanely sacrificed, and major organs (liver, kidneys, heart, and spleen) were carefully excised. Organs were rinsed in isotonic saline solution, blotted, and weighed to determine relative organ indices.

Tissue samples intended for histological examination were fixed in 10% neutral buffered formalin. Liver specimens were further processed, embedded, sectioned, and stained with hematoxylin and eosin (H&E) according to standard histological procedures (Bancroft & Layton, 2013; Drury & Wallington, 1980).

2.11. Biochemical Analysis

Serum biochemical parameters were determined using validated commercial diagnostic kits and standard spectrophotometric methods (Tietz, 2018).

- **Liver Function Parameters**

Activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured using enzymatic colorimetric assays (Henry, 2011). Alkaline phosphatase (ALP) activity was evaluated using standard protocols, while total bilirubin was determined spectrophotometrically (Burtis & Bruns, 2015). Total protein concentration was estimated using established biochemical methods (Tietz, 2018).

- **Lipid Profile Assessment**

Serum total cholesterol, triglycerides, and HDL-cholesterol were quantified using enzymatic colorimetric techniques (Burtis & Bruns, 2015). LDL and VLDL fractions were subsequently calculated using Friedewald's equation (Friedewald et al., 1972).

- **Renal Function Markers**

Renal function was assessed through the measurement of serum urea and uric acid levels using enzymatic colorimetric assays (Tietz, 2018).

2.12 Statistical Analysis

Data obtained from the experimental study were expressed as mean ± standard deviation. Statistical comparisons among groups were performed using one-way analysis of variance (ANOVA) (Field, 2013). Duncan's Multiple Range Test was applied for post hoc analysis (Duncan, 1955). Statistical significance was accepted at $p < 0.05$.

2.13. Ethical Approval

All experimental procedures involving animals were reviewed and approved by the Institutional Research Ethics Committee of Al-Baha University, Saudi Arabia (Approval No. 46123022; dated 17 April 2025). The study strictly adhered to internationally accepted ethical guidelines governing the use of laboratory animals, ensuring humane handling, minimal distress, and full compliance with animal welfare standards throughout the experimental process.

4. RESULTS

- **Chemical Composition of Fennel (Foeniculum vulgare)**

The chemical composition of fennel (Foeniculum vulgare) is presented in Figure 3, showing precise quantitative values of the analyzed parameters. Total carbohydrates represented the dominant fraction, recording 50.00 ± 2.00 g/100 g dry weight. Crude protein content was 18.15 ± 1.65 g/100 g, indicating a considerable presence of nitrogenous compounds.

Total ash content was 13.80 ± 1.40 g/100 g, reflecting a substantial mineral composition, while crude fiber reached 11.75 ± 1.65 g/100 g, suggesting notable dietary fiber content with potential physiological benefits. Moisture content was measured at 9.35 ± 1.15 g/100 g, indicating a relatively stable low-moisture matrix. Crude lipid content was the lowest fraction, recorded at 3.80 ± 0.70 g/100 g, confirming the lean lipid nature of the sample.

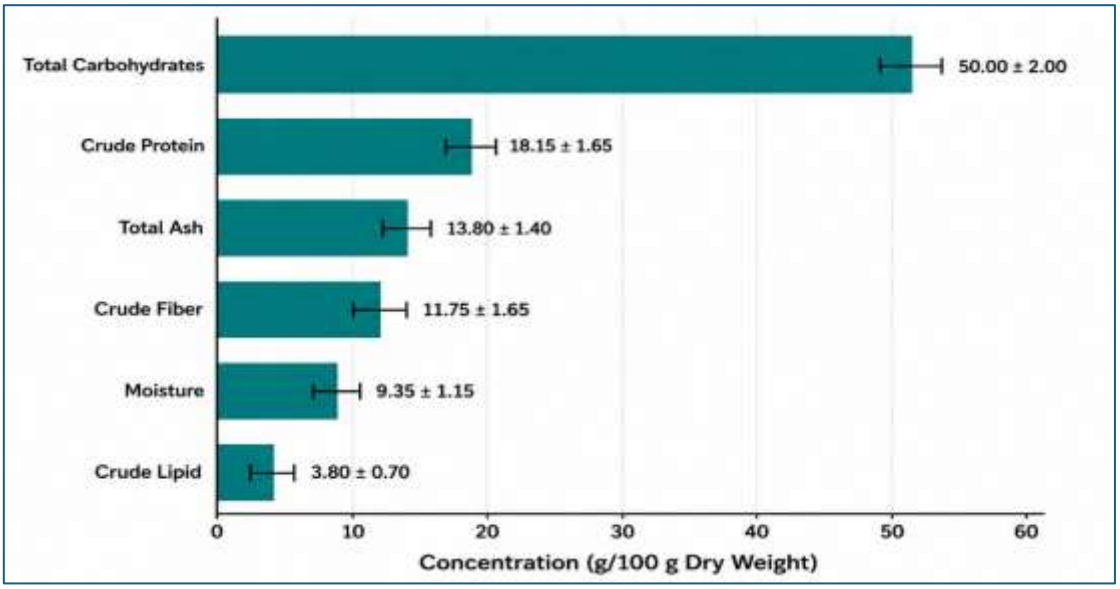


Figure 3 :Proximate chemical composition of dried Foeniculum vulgare leaves.

- **Phenolic Profile of Fennel (Foeniculum vulgare)**

The HPLC-DAD analysis of the leaves of Foeniculum vulgare revealed a diverse and abundant profile of phenolic compounds with varying concentrations, as illustrated in Figure 4. Among the identified constituents, gallic acid was the most predominant compound, reaching a concentration of 398.15 µg/g, and was assigned the highest statistical grouping. Protocatechuic acid was the second most abundant phenolic compound, recorded at 145.30

µg/g, followed by rosmarinic acid (122.45 µg/g) and apigenin-7-glucoside (95.10 µg/g), indicating their substantial contribution to the overall phytochemical profile. Moderate levels were observed for ferulic acid (84.20 µg/g), kaempferol (42.30 µg/g), and rutin (35.60 µg/g), while sinapic acid (30.15 µg/g), caffeic acid (16.70 µg/g), and chlorogenic acid (11.85 µg/g) were detected in lower concentrations. Relatively minor amounts were recorded for catechin (51.10 µg/g), p-hydroxybenzoic acid (54.20 µg/g), vanillic acid (9.45 µg/g), and cinnamic acid (8.40 µg/g). In contrast, gentisic acid was not detected in the analyzed samples. The statistical analysis indicated significant differences among the quantified compounds, as reflected by the assigned grouping letters. Overall, the phenolic profile demonstrates that fennel leaves are rich in structurally diverse bioactive compounds, which may contribute collectively to their antioxidant and metabolic regulatory potential (Figure 4).

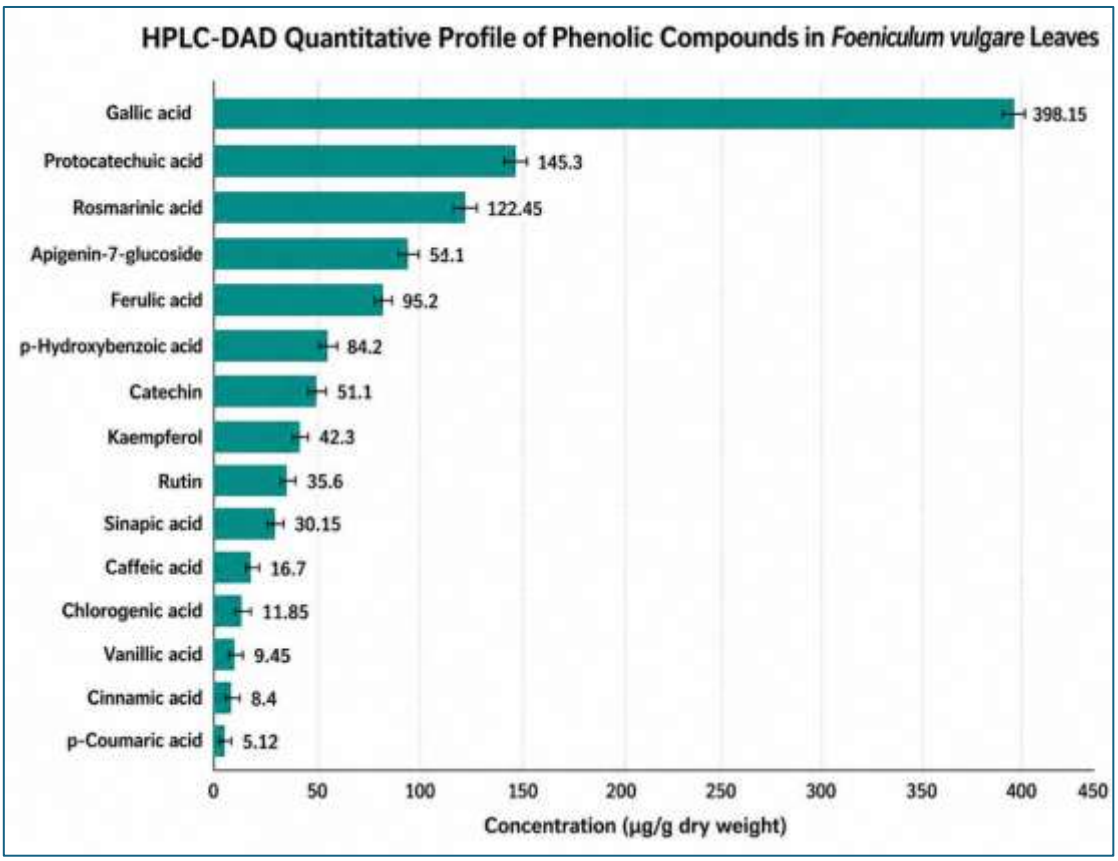


Figure 4: HPLC-DAD quantitative profile of phenolic compounds in Foeniculum vulgare leaves.

4.3. Biological evaluation

Figure 5 presents the effect of dietary supplementation with fennel (Foeniculum vulgare) at different levels on feed intake, feed efficiency ratio (FER), and body weight gain percentage (BWG%) in rats. The results are expressed as mean ± standard deviation, with statistical differences among groups indicated by different superscript letters. The negative control group (G1) showed the lowest feed intake (12.45 ± 1.82 g/day), accompanied by a low FER (0.098 ± 0.015) and reduced body weight gain (43.15 ± 18.24%). In contrast, the positive control group (G2) exhibited higher feed intake (14.12 ± 1.25 g/day) and markedly increased FER (0.185 ± 0.012) and BWG% (115.42 ± 9.32%), reflecting the effects of obesity induction. Rats fed a diet containing 3% fennel (G3) showed feed intake values (14.05 ± 1.12 g/day) comparable to the positive control, with FER (0.152 ± 0.018) lower than G2 but higher than the negative control. This group also recorded the highest BWG% (119.85 ± 14.22%), which was statistically similar to the positive control group.

In the 5% fennel group (G4), feed intake (12.55 ± 0.95 g/day) was close to the negative control group, while FER (0.192 ± 0.021) remained relatively high. However, BWG% (105.34 ± 6.18%) showed a moderate reduction compared with the obese control group.

The group receiving 7% fennel (G5) exhibited the highest feed intake (15.62 ± 3.84 g/day), but displayed a lower FER (0.115 ± 0.011) and a significantly reduced BWG% (65.12 ± 8.44%), indicating decreased efficiency of weight gain despite higher food consumption.

Overall, fennel supplementation influenced feed utilization and body weight gain in rats, with the 7% level showing the most pronounced reduction in weight gain efficiency compared with the other treated groups.

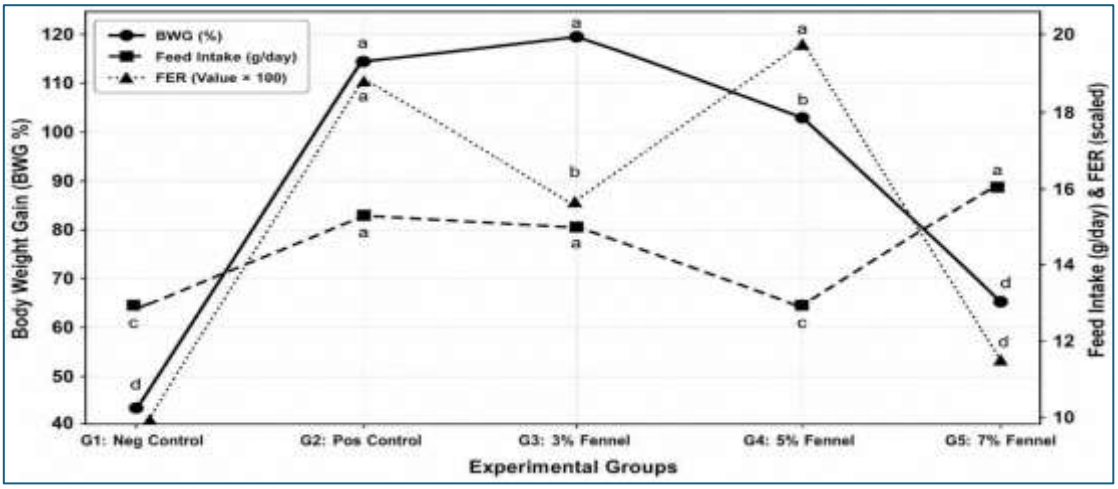


Figure 5. Effect of Fennel (Foeniculum vulgare) on Feed Intake, Feed Efficiency Ratio (FER), and Body Weight Gain (BWG%) in Rats (Mean ± SD)

4.3. Biochemical Analysis

- **Results (Serum Lipid Profile)**

Figure 6 demonstrates the effect of feeding different levels of fennel (Foeniculum vulgare) on serum lipid profile parameters, including HDL-c, LDL-c, VLDL-c, and the LDL-c/HDL-c ratio in obese rats. The data are presented as mean ± standard deviation (SD), and statistical significance is indicated by different superscript letters. The negative control group (G1) exhibited relatively high HDL-c levels (52.14 ± 3.15 mg/dl), along with the lowest LDL-c concentration (16.45 ± 2.20 mg/dl) and a low LDL-c/HDL-c ratio (0.315 ± 0.05). In contrast, the positive control group (G2) showed a marked deterioration in lipid profile, characterized by a decrease in HDL-c (29.45 ± 4.80 mg/dl) and substantial increases in LDL-c (136.12 ± 7.45 mg/dl), VLDL-c (45.16 ± 0.82 mg/dl), and the LDL-c/HDL-c ratio (4.622 ± 0.95). Rats fed a diet containing 3% fennel (G3) maintained HDL-c levels (49.90 ± 6.80 mg/dl) comparable to the negative control group, while LDL-c (92.70 ± 4.20 mg/dl) and VLDL-c (41.30 ± 0.65 mg/dl) remained elevated compared to G1. The LDL-c/HDL-c ratio (1.85 ± 0.50) was notably reduced relative to the positive control group. In the 5% fennel group (G4), HDL-c levels (48.70 ± 2.00 mg/dl) were similar to other fennel-treated groups. This group demonstrated a further reduction in LDL-c (60.40 ± 20.30 mg/dl) and VLDL-c (32.80 ± 18.40 mg/dl), along with a lower LDL-c/HDL-c ratio (1.25 ± 0.15), suggesting an improved lipid profile compared to other treated groups. The group receiving 7% fennel (G5) showed HDL-c levels (53.40 ± 3.90 mg/dl) comparable to the negative control. However, LDL-c (105.80 ± 7.90 mg/dl) and VLDL-c (40.60 ± 1.10 mg/dl) remained relatively elevated, and the LDL-c/HDL-c ratio (2.05 ± 0.30) was higher than that observed in the 5% fennel group.

Overall, fennel supplementation at varying levels influenced lipid profile parameters in obese rats, with the 5% level showing a comparatively more favorable effect on LDL-c reduction and lipid ratio improvement.

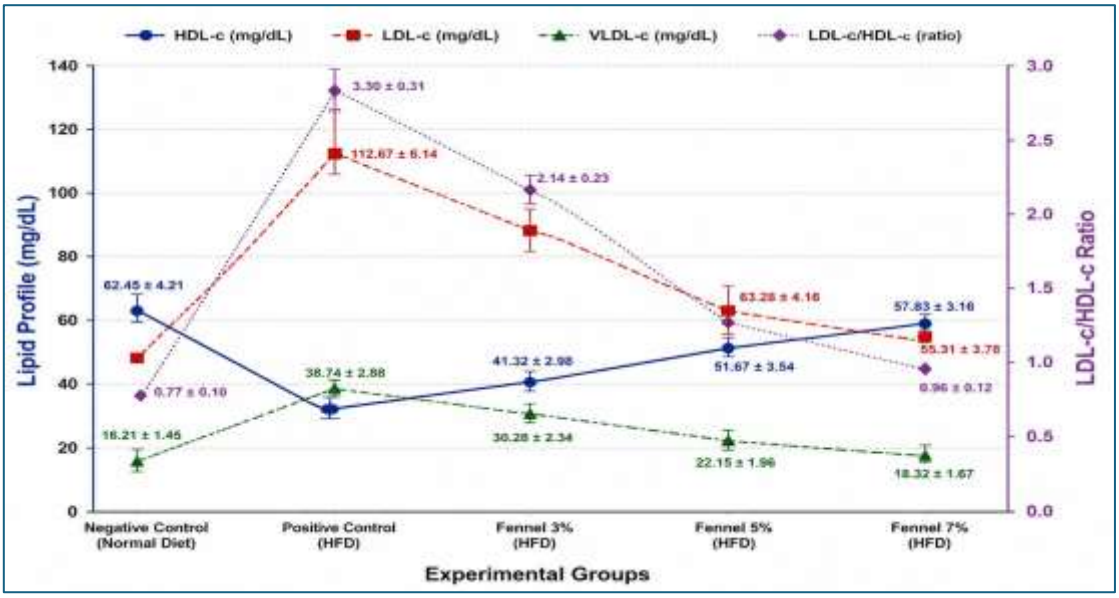


Figure 6: Effect of Fennel (Foeniculum vulgare) levels on serum lipid profile (HDL-c, LDL-c, and VLDL-c) in obese rats. Values are expressed as Mean ± SD (n=6). Different letters (a, b, c, d, e) above the data points indicate significant differences at ($p < 0.05$).

- **Results (Liver Function Biomarkers: (AST and ALT)**

Figure 7 presents the effect of dietary fennel supplementation at different concentrations on liver enzyme activity, namely AST and ALT, in obese rats. The results are expressed as mean ± standard deviation, with statistically significant differences indicated by superscript letters.

The negative control group (G1) showed the lowest values for both AST and ALT, indicating normal liver function. In contrast, the positive control group (G2) recorded markedly elevated enzyme levels, reflecting hepatic stress associated with obesity. Rats treated with 3% fennel (G3) demonstrated a reduction in both AST and ALT levels compared to the obese group, although the values remained higher than those of the normal control. A more notable improvement was observed in the 5% fennel group (G4), where enzyme levels approached those of the negative control, suggesting a stronger protective effect on liver function.

However, increasing the fennel concentration to 7% (G5) did not result in further improvement. Instead, AST and ALT levels in this group were higher than those observed in the 5% group, indicating that the beneficial effect may not increase proportionally with higher doses.

Overall, fennel supplementation contributed to the reduction of liver enzyme levels in obese rats, with the 5% level showing the most effective outcome in restoring enzyme activity toward normal values.

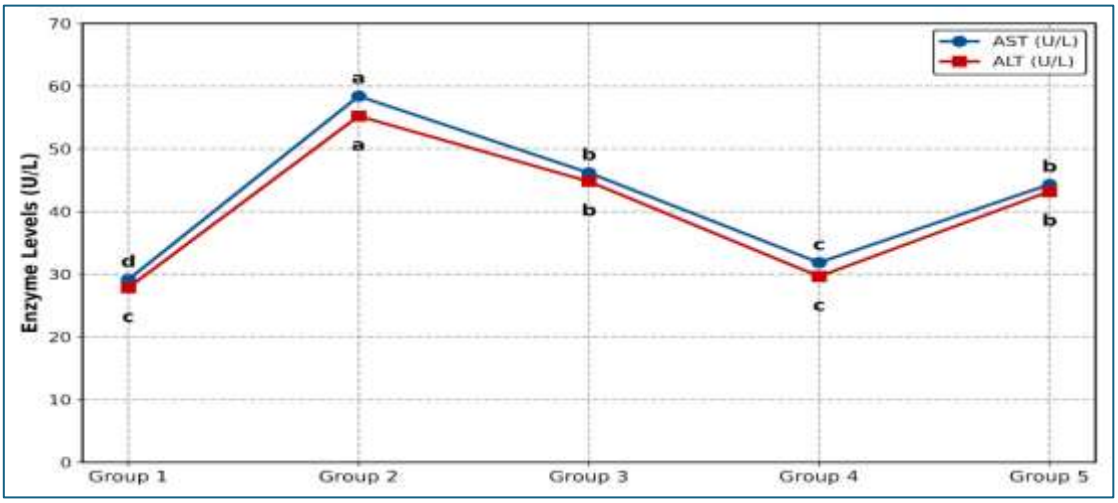


Figure 7: Effect of different supplementation levels of Fennel seeds on serum AST and ALT activities in obese rats.

- **Results (Renal Function Biomarkers)**

Figure 8 summarizes the effect of dietary supplementation with fennel (Foeniculum vulgare) at different levels on renal function biomarkers, specifically serum uric acid and urea nitrogen levels in obese rats. The data are presented as mean ± standard deviation, with statistical significance indicated by different superscript letters. The negative control group (G1) exhibited the lowest levels of both uric acid (0.92 ± 0.10 mg/dL) and urea nitrogen (15.10 ± 0.85 mg/dL), reflecting normal renal function status. In contrast, the positive control group (G2) showed a marked elevation in uric acid (3.96 ± 0.15 mg/dL) and urea nitrogen (27.20 ± 2.10 mg/dL), indicating impaired kidney function associated with obesity. Rats treated with 3% fennel (G3) demonstrated a reduction in uric acid levels (2.51 ± 0.06 mg/dL) compared with the obese control group, while urea nitrogen remained relatively high (25.00 ± 1.85 mg/dL). In the 5% fennel group (G4), a more pronounced improvement was observed, as both uric acid (1.80 ± 0.14 mg/dL) and urea nitrogen (19.80 ± 0.70 mg/dL) showed substantial reductions, approaching values closer to the negative control group. However, increasing fennel supplementation to 7% (G5) did not result in further improvement. Instead, uric acid (2.55 ± 0.11 mg/dL) and urea nitrogen (24.80 ± 0.80 mg/dL) levels increased again compared with the 5% group, suggesting a less favorable effect at the highest dose. Overall, fennel supplementation exerted a modulatory effect on renal function biomarkers in obese rats, with the 5% concentration demonstrating the most effective improvement in restoring kidney function parameters toward normal levels.

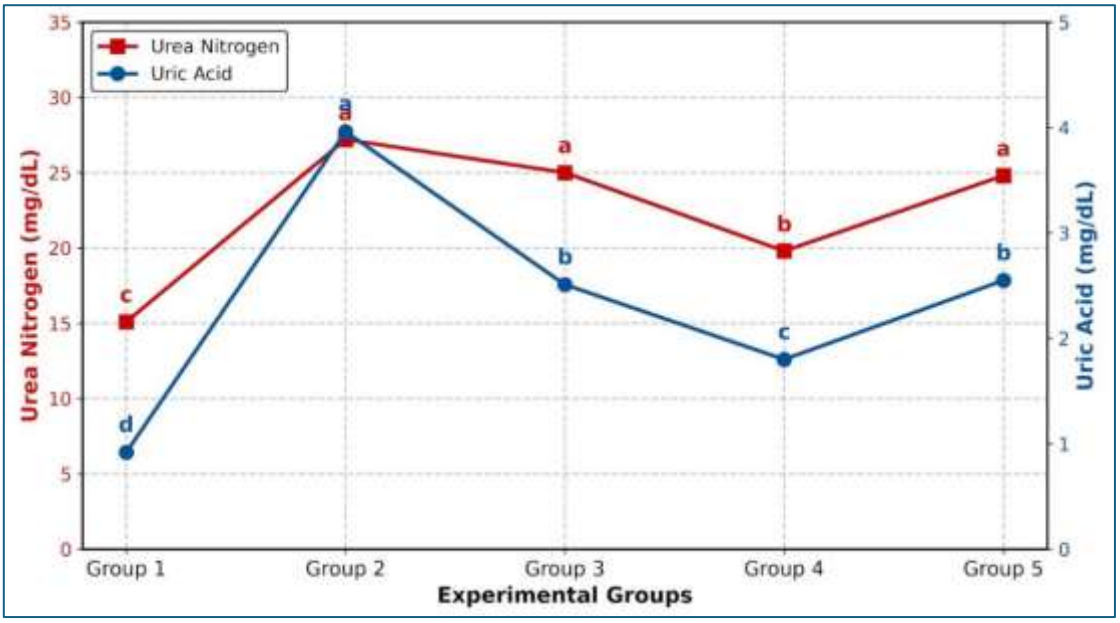


Figure 8: Impact of Fennel seeds supplementation on renal function biomarkers (Uric Acid and Urea Nitrogen) in obese rats.

- **Results (Serum Glucose Levels)**

The results demonstrated in figure 9 marked effect of fennel supplementation on serum glucose levels in obese rats. The negative control group (G1) showed normal glucose levels (89.80 ± 1.70 mg/dL), whereas the positive control obese group (G2) exhibited a significant elevation in serum glucose (175.10 ± 2.90 mg/dL), indicating the impact of obesity on hyperglycemia.

Dietary intervention with fennel resulted in a dose-dependent reduction in serum glucose levels. Rats fed with 3% fennel (G3) and 5% fennel (G4) showed comparable decreases in glucose levels (148.40 ± 1.55 mg/dL and 139.90 ± 1.35 mg/dL, respectively), both significantly lower than the obese control group. The highest concentration of fennel (9%, G5) produced the most pronounced effect, reduc ing serum glucose to 120.70 ± 1.25 mg/dL.

Overall, fennel supplementation significantly improved glucose regulation in obese rats, with higher dietary inclusion levels showing greater hypoglycemic effects.

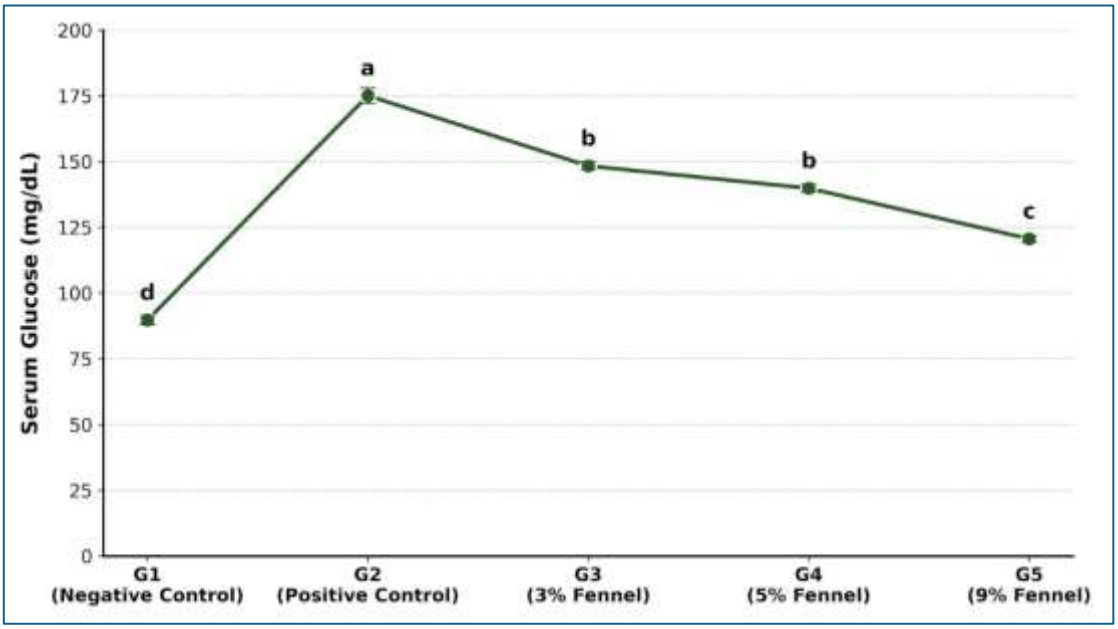


Figure 9: Effect of dietary supplementation with different levels of fennel (Foeniculum vulgare) seeds on serum glucose levels in obese rats.

4.4.Histopathological Examination of Cardiac Tissue.

Microscopic examination of cardiac tissue sections illustrated in Figure 10 (1–5) revealed marked differences in myocardial histological architecture among the investigated experimental groups.

The normal control group represented in Figure 10(1) exhibited normal myocardial structure characterized by compactly arranged cardiac muscle fibers with preserved striations and normally distributed elongated nuclei. The tissue appeared intact without any evidence of vascular congestion, hemorrhage, or degenerative alterations.

On the other hand, the obese untreated group shown in Figure 10 (2) demonstrated pronounced histopathological lesions, including severe dilation and congestion of intermuscular blood vessels, focal hemorrhagic regions, and noticeable thickening of vascular walls. In addition, mild disorganization and separation of myocardial fibers were observed, reflecting obesity-induced circulatory and structural myocardial damage.

Cardiac sections of obese rats supplemented with 3% fennel, as seen in Figure 10 (3), displayed partial improvement in tissue morphology. Moderate congestion and dilation of intermuscular blood vessels were still present; however, the myocardial fibers appeared relatively more organized compared with the obese untreated group, indicating an initial protective influence of fennel supplementation.

Further histological recovery was evident in the obese rats treated with 5% fennel, presented in Figure 10 (4). This group showed only slight vascular dilation and mild blood vessel congestion, accompanied by restoration of myocardial fiber continuity and a more compact tissue arrangement. Hemorrhagic manifestations were markedly minimized.

Interestingly, the cardiac tissue of obese rats receiving 7% fennel supplementation in Figure 10 (5) demonstrated near-normal myocardial histoarchitecture. Cardiac muscle fibers appeared densely packed, regularly aligned, and structurally comparable to those of the normal control group, with minimal vascular abnormalities and absence of obvious pathological lesions.

Overall, the histopathological observations in Figure 10 indicate that dietary fennel supplementation exerted a significant ameliorative effect against obesity-induced cardiac damage in a dose-dependent pattern, with the highest level of myocardial recovery observed in the 7% fennel-treated group..

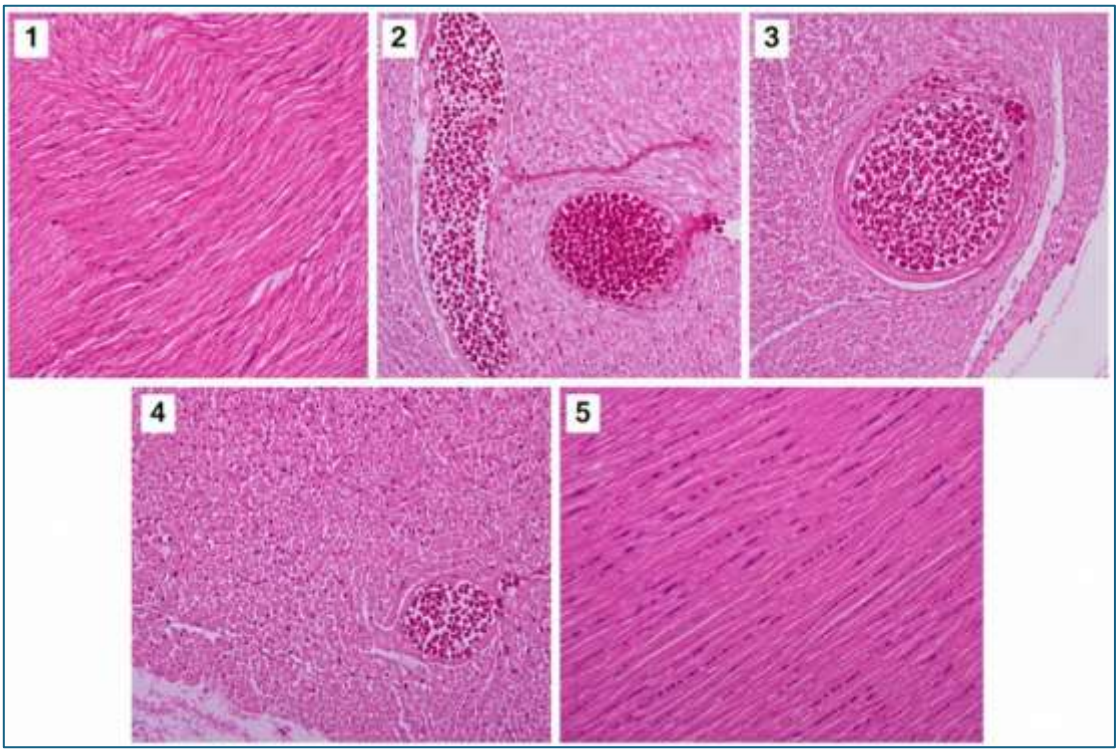


Figure 10. Histopathological alterations in cardiac tissue of obese rats treated with different dietary levels of fennel.

5- DISCUSSION

The current investigation demonstrates that dietary supplementation with Foeniculum vulgare (fennel) exerts significant modulatory effects on obesity-associated metabolic disturbances in high-fat diet–induced obese rats. These findings are consistent with a growing body of literature emphasizing the therapeutic potential of plant-derived bioactive compounds in managing metabolic disorders.

The proximate and phytochemical composition of fennel observed in this study supports its biological activity. The chemical analysis, conducted according to the standard protocols of the Association of Official Analytical Chemists (AOAC, 2016), revealed a high content of phenolic compounds, particularly gallic acid, protocatechuic acid, and rosmarinic acid. This aligns with previous reports by Rather et al. (2016), who highlighted fennel as a rich source of antioxidant phytochemicals. Phenolic compounds are known to scavenge reactive oxygen species and reduce oxidative stress, a key pathological feature in obesity. Moreover, the presence of flavonoids such as

rutin and kaempferol may contribute to anti-inflammatory effects through modulation of cytokine production, as previously described by Bluher (2019).

Regarding growth performance, obesity induction resulted in increased body weight gain and feed efficiency ratio (FER). This is consistent with findings from Buettner et al. (2007), who demonstrated that high-fat diets enhance energy storage efficiency and promote adiposity in rodent models. The importance of nutritional balance in managing biological growth has also been emphasized by Ali et al. (2026), who noted that specialized dietary formulations are essential for optimal health outcomes. Interestingly, fennel supplementation, particularly at the 7% level, reduced body weight gain despite relatively high feed intake. This suggests that fennel may influence metabolic efficiency rather than appetite alone. Similar observations were reported by Rather et al. (2016), who found that fennel extracts improved lipid metabolism and reduced adiposity without significantly altering food consumption. This effect may be mediated through enhanced mitochondrial activity and increased fatty acid oxidation.

The improvement in lipid profile observed in this study is in agreement with previous experimental findings. The reduction in LDL-c and VLDL-c levels, along with the improvement in HDL-c, particularly at the 5% fennel level, is consistent with the work of Granato et al. (2020), who reported that fennel supplementation significantly reduced serum cholesterol and triglycerides in hyperlipidemic rats. These effects may be attributed to the inhibition of hepatic cholesterol synthesis and increased bile acid excretion, as well as the activation of lipid-metabolizing enzymes. Additionally, Noreen et al. (2023) emphasized the importance of targeting lipid metabolism in obesity management, further supporting the relevance of these findings.

Liver function biomarkers (AST and ALT) were significantly elevated in obese rats, reflecting hepatic injury commonly associated with non-alcoholic fatty liver disease (NAFLD). The observed reduction in these enzymes following fennel supplementation, particularly at the 5% level, is consistent with findings reported by Vella et al. (2024), who demonstrated hepatoprotective effects of fennel through reduction of oxidative stress and lipid accumulation in liver tissue. The antioxidant properties of fennel's phenolic constituents likely play a crucial role in stabilizing hepatocyte membranes and preventing enzyme leakage into circulation.

Similarly, the improvement in renal function markers (uric acid and urea) supports the protective role of fennel against obesity-induced renal stress. Elevated levels of these markers in the obese control group are indicative of impaired kidney function, which has been previously linked to metabolic syndrome (Bluher, 2019). The reduction observed at the 5% fennel level aligns with studies suggesting that antioxidants can mitigate renal oxidative damage and improve filtration efficiency (Zakernezhad et al., 2021). However, the diminished effect at higher concentrations suggests that excessive intake may not proportionally enhance renal protection.

The hypoglycemic effect of fennel observed in this study further strengthens its metabolic benefits. The dose-dependent reduction in serum glucose levels is consistent with findings by Zakernezhad et al. (2021), who reported improved glucose homeostasis following fennel administration. This effect may be mediated through enhanced insulin sensitivity and modulation of glucose-metabolizing enzymes. Flavonoids and phenolic acids are known to inhibit α-glucosidase and improve peripheral glucose uptake, as discussed by Naseri et al. (2018), which may explain the observed results.

Histopathological analysis of cardiac tissue provided additional evidence of fennel's protective effects. The progressive improvement in myocardial architecture, particularly at the 7% level, suggests a reduction in obesity-induced structural damage. These findings are supported by the broader work of Alzahrani et al. (2026), who established that natural therapeutic agents can effectively improve cardiac function and preserve tissue integrity in experimental models. The near-normal histological appearance in the high-dose group highlights fennel's potential role in preserving cardiovascular integrity under metabolic stress conditions.

An important observation in this study is the non-linear dose-response relationship. While the 5% fennel level was most effective in improving biochemical parameters, the 7% level showed superior effects in reducing body weight gain and restoring tissue structure. This pattern suggests that different physiological systems may respond differently to phytochemical concentrations, a concept supported by pharmacological studies on plant-based interventions (Adnan, 2025). It also emphasizes the importance of identifying optimal therapeutic doses rather than assuming a direct dose-dependent benefit (Mashnafi et al., 2025).

Despite the promising outcomes, certain limitations should be considered. The study was conducted using an animal model, which, although widely accepted, may not fully replicate human metabolic responses. Additionally, the experimental duration was relatively short, limiting the assessment of long-term effects. Future research should focus on molecular mechanisms, including gene expression related to lipid metabolism, inflammation, and insulin signaling, as well as clinical trials to validate these findings in human populations.

In conclusion, the results of this study, supported by previous scientific evidence, indicate that dietary supplementation with Foeniculum vulgare has significant potential in modulating obesity-related metabolic disturbances. Its multi-target effects on lipid metabolism, glucose regulation, liver and kidney function, and tissue integrity highlight its value as a functional dietary component. These findings contribute to the growing interest in plant-based strategies for the prevention and management of obesity and its associated complications.

6- CONCLUSION

The findings of the present study highlight the significant potential of dietary intervention using Foeniculum vulgare as a natural approach for mitigating obesity-associated metabolic disturbances. Fennel supplementation

demonstrated clear beneficial effects across multiple physiological systems, including improvements in lipid profile, glycemic control, liver and kidney function, as well as attenuation of obesity-induced histopathological alterations, particularly in cardiac tissue.

Importantly, the results suggest that fennel acts through a multi-target mechanism rather than a single metabolic pathway. Its bioactive constituents appear to contribute to reducing oxidative stress, improving metabolic efficiency, and restoring biochemical balance under conditions of diet-induced obesity. The observed variations in response across different supplementation levels indicate that the biological effects of fennel are dose-dependent but not strictly linear. While moderate inclusion (5%) yielded the most consistent improvements in biochemical parameters, higher levels (7%) were more effective in reducing body weight gain and enhancing tissue recovery.

These outcomes reinforce the concept that plant-based functional foods can play a meaningful role in the management of complex metabolic disorders such as obesity. However, although the experimental model provides valuable insights, extrapolation to human health requires careful consideration. Further investigations are needed to clarify the underlying molecular mechanisms, optimize effective dosage ranges, and validate these findings through long-term clinical studies.

In conclusion, fennel represents a promising dietary component with broad metabolic benefits, supporting its potential inclusion in nutritional strategies aimed at preventing and managing obesity and its related complications

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