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MOLECULAR EVALUATION OF A NELUMBO NUCIFERA NANOFORMULATION IN HIGH-FAT DIET-INDUCED OBESITY THROUGH ADIPOGENIC, INFLAMMATORY, AND METABOLIC GENE EXPRESSION ANALYSIS

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ABSTRACT
Obesity is a major metabolic disorder associated with dyslipidemia, oxidative stress, chronic inflammation, and altered gene expression. The present study investigated the anti-obesity potential of a Nelumbo nucifera leaf nanoemulsion in a high-fat diet (HFD)-induced obese rat model. The nanoemulsion was prepared by the ultrasonication method and characterized for particle size, polydispersity index, zeta potential, and entrapment efficiency. HFD-fed rats were treated with low- and high-dose nanoemulsion, while Orlistat served as the standard drug. Treatment significantly reduced body weight gain, improved serum lipid profile, enhanced antioxidant enzyme activities, decreased lipid peroxidation, and suppressed pro-inflammatory cytokines compared with the HFD control group. Histopathological examination revealed marked improvement in hepatic and adipose tissue architecture following nanoemulsion treatment. RT-qPCR analysis demonstrated downregulation of adipogenic and inflammatory genes and restoration of metabolic gene expression. Overall, Nelumbo nucifera nanoemulsion exhibited potent anti-obesity activity through modulation of adipogenesis, inflammation, oxidative stress, and metabolic signalling pathways, highlighting its promise as a phytopharmaceutical candidate for obesity management.

KEYWORDS: Nelumbo nucifera; Nanoemulsion; Obesity; High-fat diet; Gene expression.

1. INTRODUCTION
Obesity has emerged as one of the most significant global public health challenges of the twenty-first century, affecting individuals across all age groups and socioeconomic backgrounds. Characterized by excessive accumulation of adipose tissue resulting from chronic energy imbalance, obesity substantially increases the risk of developing numerous metabolic disorders, including type 2 diabetes mellitus, dyslipidemia, hypertension, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases, and several forms of cancer. The worldwide prevalence of obesity has risen dramatically over the past few decades owing to sedentary lifestyles, increased consumption of calorie-dense diets, and reduced physical activity, thereby imposing a considerable economic and healthcare burden on society [1]. Beyond excessive fat deposition, obesity is now recognized as a complex multifactorial metabolic disease involving dysregulation of endocrine, inflammatory, and molecular signaling pathways that contribute to progressive metabolic dysfunction [2].
Experimental models employing a high-fat diet (HFD) closely mimic the metabolic alterations observed in human obesity and have therefore become the most widely accepted model for investigating obesity-associated pathophysiological mechanisms and evaluating potential therapeutic interventions [3]. Prolonged consumption of an HFD promotes adipocyte hypertrophy and hyperplasia, insulin resistance, hepatic steatosis, oxidative stress, and chronic low-grade inflammation. These alterations collectively disturb systemic energy homeostasis and accelerate metabolic syndrome progression. Consequently, HFD-induced obesity models provide a valuable platform for studying the molecular mechanisms regulating lipid metabolism, adipogenesis, inflammatory responses, and energy expenditure [4].

Adipogenesis, the process through which preadipocytes differentiate into mature lipid-filled adipocytes, represents one of the central mechanisms responsible for obesity development. This highly coordinated biological process is regulated by several transcription factors, including peroxisome proliferator-activated receptor gamma (PPAR-γ), CCAAT/enhancer-binding protein alpha (C/EBP-α), and sterol regulatory element-binding protein-1c (SREBP-1c). Activation of these transcription factors stimulates downstream lipogenic genes such as fatty acid synthase (FASN) and acetyl-CoA carboxylase (ACC), ultimately promoting triglyceride synthesis and adipocyte maturation [5]. Conversely, genes involved in mitochondrial β-oxidation and energy expenditure, including AMP-activated protein kinase (AMPK), carnitine palmitoyltransferase-1A (CPT-1A), peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α), and uncoupling protein-1 (UCP-1), play essential roles in regulating fatty acid oxidation and thermogenesis. Impaired expression of these metabolic regulators contributes significantly to excessive lipid accumulation and obesity progression [6].

In addition to altered lipid metabolism, obesity is increasingly recognized as a chronic inflammatory disorder characterized by excessive secretion of pro-inflammatory cytokines from hypertrophied adipose tissue. Enlarged adipocytes recruit macrophages and other immune cells that produce inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), and monocyte chemoattractant protein-1 (MCP-1). Activation of the nuclear factor-kappa B (NF-κB) signaling pathway further amplifies inflammatory responses, leading to insulin resistance, endothelial dysfunction, oxidative stress, and progressive metabolic impairment [7]. Simultaneously, circulating adiponectin levels decrease whereas leptin production increases, disrupting appetite regulation and insulin sensitivity. Therefore, simultaneous modulation of adipogenic, inflammatory, and metabolic gene expression has become an attractive therapeutic strategy for obesity management [8].

Current pharmacological therapies for obesity, including orlistat and glucagon-like peptide-1 receptor agonists, demonstrate clinical efficacy but are frequently associated with gastrointestinal disturbances, high treatment costs, limited patient compliance, or adverse systemic effects. These limitations have intensified interest in plant-derived bioactive compounds that exhibit multiple pharmacological actions while maintaining a favorable safety profile [9]. Nanotechnology-based herbal formulations have recently attracted considerable attention because nanoencapsulation can enhance the solubility, gastrointestinal stability, bioavailability, and tissue distribution of phytoconstituents, thereby improving therapeutic efficacy. Such nanoformulations also facilitate targeted modulation of molecular pathways involved in obesity and metabolic syndrome [10].

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

Analytical-grade ethanol, Tween 80, Span 80, soybean oil, medium-chain triglyceride (MCT) oil, phosphate-buffered saline (PBS), TRIzol reagent, reverse transcription kit, SYBR Green Master Mix, ELISA kits, and biochemical diagnostic kits were obtained from standard commercial suppliers. All chemicals used in the study were of analytical grade, and ultrapure water was used throughout the experimental procedures [11].

2.2 Collection and Authentication of Plant Material

Fresh leaves of Nelumbo nucifera Gaertn. were collected from pesticide-free ponds during the flowering season. The plant was authenticated by a qualified taxonomist, and a voucher specimen was deposited in the institutional herbarium for future reference. The collected leaves were washed thoroughly with distilled water, shade-dried at room temperature (25–30°C) for 10–14 days, pulverized using a mechanical grinder, and stored in airtight containers until extraction [12].

2.3 Preparation of Hydroalcoholic Extract

Approximately 500 g of powdered leaves were extracted with 70% ethanol using the Soxhlet extraction method for 8 h. The extract was filtered through Whatman No.1 filter paper and concentrated under reduced pressure using a rotary evaporator maintained below 40°C. The concentrated extract was freeze-dried to obtain a dry powder, and the percentage yield was calculated before storage at 4°C until further analysis [13].

2.4 Preliminary Phytochemical Screening

The hydroalcoholic extract was subjected to qualitative phytochemical screening for alkaloids, flavonoids, phenolic compounds, tannins, glycosides, saponins, steroids, terpenoids, proteins, and carbohydrates using standard phytochemical procedures described by Harborne and Trease & Evans [14,15].

2.5 Preparation of Nelumbo nucifera Nano-emulsion

The nanoemulsion was prepared using the ultrasonication method with soybean oil as the oil phase, Tween 80 as the surfactant, and ethanol as the co-surfactant. The hydroalcoholic extract was dispersed in the oil phase, followed by the addition of the surfactant mixture under continuous magnetic stirring. Distilled water was added dropwise to form a coarse emulsion, which was subsequently subjected to probe ultrasonication for 10 min using intermittent pulses to obtain a stable nanoemulsion with nanosized droplets [16,17].

2.6 Characterization of Nanoemulsion

The mean particle size, polydispersity index (PDI), and zeta potential were determined by dynamic light scattering using a Zetasizer Nano instrument after appropriate dilution with distilled water [18]. Morphological characteristics of the nanoemulsion droplets were examined using transmission electron microscopy after negative staining with phosphotungstic acid [19]. Entrapment efficiency was determined by ultracentrifugation, and the amount of free extract in the supernatant was estimated spectrophotometrically [10]. Stability studies were

performed at 4°C, 25°C, and 40 ± 2°C/75 ± 5% RH for three months according to ICH stability recommendations [20].

2.7 Experimental Animals

Healthy adult male Wistar rats weighing 180–220 g were housed under standard laboratory conditions (22 ± 2°C, 55 ± 5% humidity, 12 h light/dark cycle) with free access to standard pellet diet and water. Animals were acclimatized for one week before the experiment and maintained according to CPCSEA [21].

2.8 Induction of High-Fat Diet-Induced Obesity

Experimental obesity was induced by feeding animals a high-fat diet containing approximately 45–60% of calories derived from fat for 12 weeks. Body weight and food intake were monitored weekly throughout the study [22].

2.9 Experimental Design

Thirty rats were randomly divided into five groups (n = 6):

- Group I: Normal Control
- Group II: High-Fat Diet Control
- Group III: High-Fat Diet + Orlistat (10 mg/kg)
- Group IV: High-Fat Diet + Nelumbo nucifera Nanoemulsion (Low Dose)
- Group V: High-Fat Diet + Nelumbo nucifera Nanoemulsion (High Dose)

All treatments were administered orally once daily for eight weeks.

2.10 Biochemical Investigations

At the end of the treatment period, overnight-fasted blood samples were collected for biochemical investigations. Serum glucose, total cholesterol, triglycerides, HDL, LDL, VLDL, ALT, AST, ALP, and insulin were estimated using commercial diagnostic kits according to the manufacturer's instructions. HOMA-IR was calculated to assess insulin resistance [23].

2.11 Oxidative Stress Parameters

Liver and adipose tissues were homogenized in ice-cold phosphate buffer. Superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and malondialdehyde (MDA) were estimated using standard biochemical methods [24, 25].

2.12 Estimation of Inflammatory Cytokines

Serum concentrations of TNF-α, IL-6, IL-1β, MCP-1, leptin, and adiponectin were measured using commercially available ELISA kits according to the manufacturer's protocol [26].

2.13 Histopathological Examination

Liver and epididymal adipose tissues were fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned at 5 μm thickness, and stained with hematoxylin and eosin (H&E). Histological changes were examined under a light microscope [27-28].

2.14 Gene Expression Analysis

Total RNA was isolated from liver and adipose tissues using TRIzol reagent. RNA purity and concentration were determined spectrophotometrically. One microgram of RNA was reverse-transcribed into cDNA, followed by quantitative real-time PCR using SYBR Green chemistry. Relative expression of PPAR-γ, C/EBP-α, SREBP-1c, FASN, ACC, TNF-α, IL-6, IL-1β, NF-κB, MCP-1, AMPK, CPT-1A, PGC-1α, UCP-1, GLUT4, SIRT1, and adiponectin was determined using the comparative 2^−ΔΔCt method with GAPDH as the internal control [29, 30].

2.15 Statistical Analysis

Results were expressed as mean ± SEM. Statistical analysis was performed using GraphPad Prism software. One-way ANOVA followed by Tukey's post hoc test was used for comparison among groups. Differences were considered statistically significant at $p < 0.05$. [31].

3. RESULTS

3.1 Characterization of Nelumbo nucifera Nanoemulsion

The prepared Nelumbo nucifera nanoemulsion exhibited satisfactory physicochemical characteristics with a transparent appearance and no evidence of phase separation. The optimized formulation showed a mean particle size of 128.6 ± 4.3 nm, a polydispersity index (PDI) of 0.218 ± 0.012, indicating a narrow particle size distribution, and a zeta potential of −31.8 ± 2.1 mV, suggesting good colloidal stability. The entrapment efficiency was found to be 89.7 ± 1.8%. Stability studies demonstrated no significant changes in particle size, PDI, zeta potential, or physical appearance after three months under refrigerated and room temperature storage conditions.

Table 1. Physicochemical characterization of optimized Nelumbo nucifera nanoemulsion

Parameter	Result
Particle size (nm)	128.6 ± 4.3
Polydispersity Index	0.218 ± 0.012
Zeta potential (mV)	−31.8 ± 2.1
Entrapment efficiency (%)	89.7 ± 1.8
Physical appearance	Clear, homogeneous

3.2 Effect on Body Weight

Rats receiving a high-fat diet exhibited a significant increase in body weight compared with the normal control group. Treatment with Nelumbo nucifera nanoemulsion significantly reduced body weight gain in a dose-dependent manner. The high-dose nanoemulsion group showed a reduction comparable to the Orlistat-treated group.

Table 2. Effect on body weight

Group	Initial (g)	Final (g)
Normal Control	186 ± 5	253 ± 8
HFD Control	187 ± 6	372 ± 10***
Orlistat	185 ± 5	289 ± 9###
Nanoemulsion Low Dose	186 ± 4	318 ± 8###
Nanoemulsion High Dose	187 ± 5	279 ± 7###

Values are Mean ± SEM.

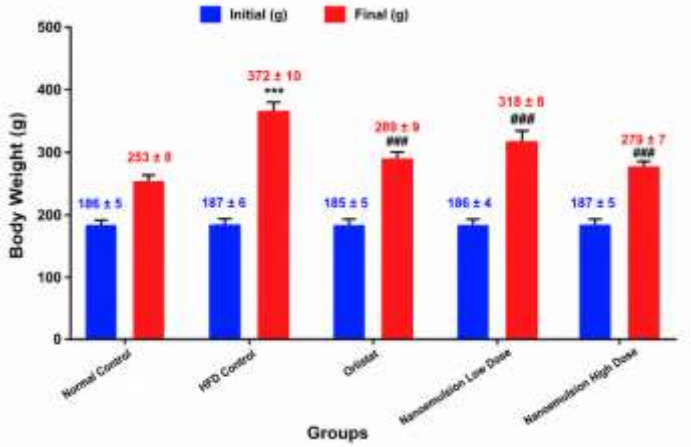

Figure 1. Effect of Nelumbo nucifera nanoemulsion on body weight in high-fat diet-induced obese rats.

3.3 Effect on Serum Lipid Profile

The HFD group demonstrated significant dyslipidemia characterized by elevated total cholesterol, triglycerides, LDL, and VLDL levels, along with decreased HDL cholesterol. Administration of Nelumbo nucifera nanoemulsion significantly improved the lipid profile in a dose-dependent manner.

Table 3. Serum lipid profile

Parameter	NC	HFD	Orlistat	Nano-L	Nano-H
Total cholesterol (mg/dL)	86	176	102	122	95
Triglycerides (mg/dL)	72	168	95	118	92
HDL (mg/dL)	48	26	44	39	46
LDL (mg/dL)	28	110	42	61	38

3.4 Effect on Blood Glucose and Insulin Resistance

High-fat diet feeding significantly increased fasting blood glucose, serum insulin, and HOMA-IR values. Both doses of Nelumbo nucifera nanoemulsion significantly improved glucose homeostasis and insulin sensitivity, with the high-dose group producing results comparable to Orlistat.

3.5 Effect on Oxidative Stress Markers

Oxidative stress was markedly elevated in obese rats, as evidenced by increased malondialdehyde (MDA) levels and decreased antioxidant enzyme activities (SOD, CAT, and GSH). Nanoemulsion treatment significantly restored antioxidant defense mechanisms in a dose-dependent fashion.

Table 4. Oxidative stress markers

Parameter	NC	HFD	Orlistat	Nano-L	Nano-H
SOD (U/mg protein)	15.6	8.2	14.3	12.4	14.8
CAT (U/mg protein)	61.2	34.5	56.8	49.3	58.4
GSH (µmol/g tissue)	9.1	4.2	8.3	7.1	8.6
MDA (nmol/mg protein)	1.8	5.9	2.4	3.2	2.2

3.6 Effect on Inflammatory Cytokines

The serum levels of TNF-α, IL-6, IL-1β, MCP-1, and leptin were significantly elevated in obese rats, whereas adiponectin levels were markedly decreased. Treatment with Nelumbo nucifera nanoemulsion significantly suppressed pro-inflammatory cytokines while increasing adiponectin concentrations.

3.7 Histopathological Findings

Histological examination of liver sections from the normal control group revealed normal hepatic architecture with intact hepatocytes and well-organized hepatic cords. The HFD control group exhibited marked macrovesicular steatosis, hepatocyte ballooning, inflammatory cell infiltration, and sinusoidal congestion. Orlistat treatment markedly improved hepatic morphology with only mild fatty degeneration. Rats treated with Nelumbo nucifera nanoemulsion showed dose-dependent hepatoprotection. The high-dose group demonstrated nearly normal hepatic architecture with minimal lipid accumulation and reduced inflammatory infiltration.

Examination of epididymal adipose tissue revealed normal adipocyte size and organization in the control group. The HFD group showed marked adipocyte hypertrophy and inflammatory infiltration. Nanoemulsion-treated animals exhibited a progressive reduction in adipocyte size and inflammatory changes, with the high-dose group closely resembling normal adipose tissue.

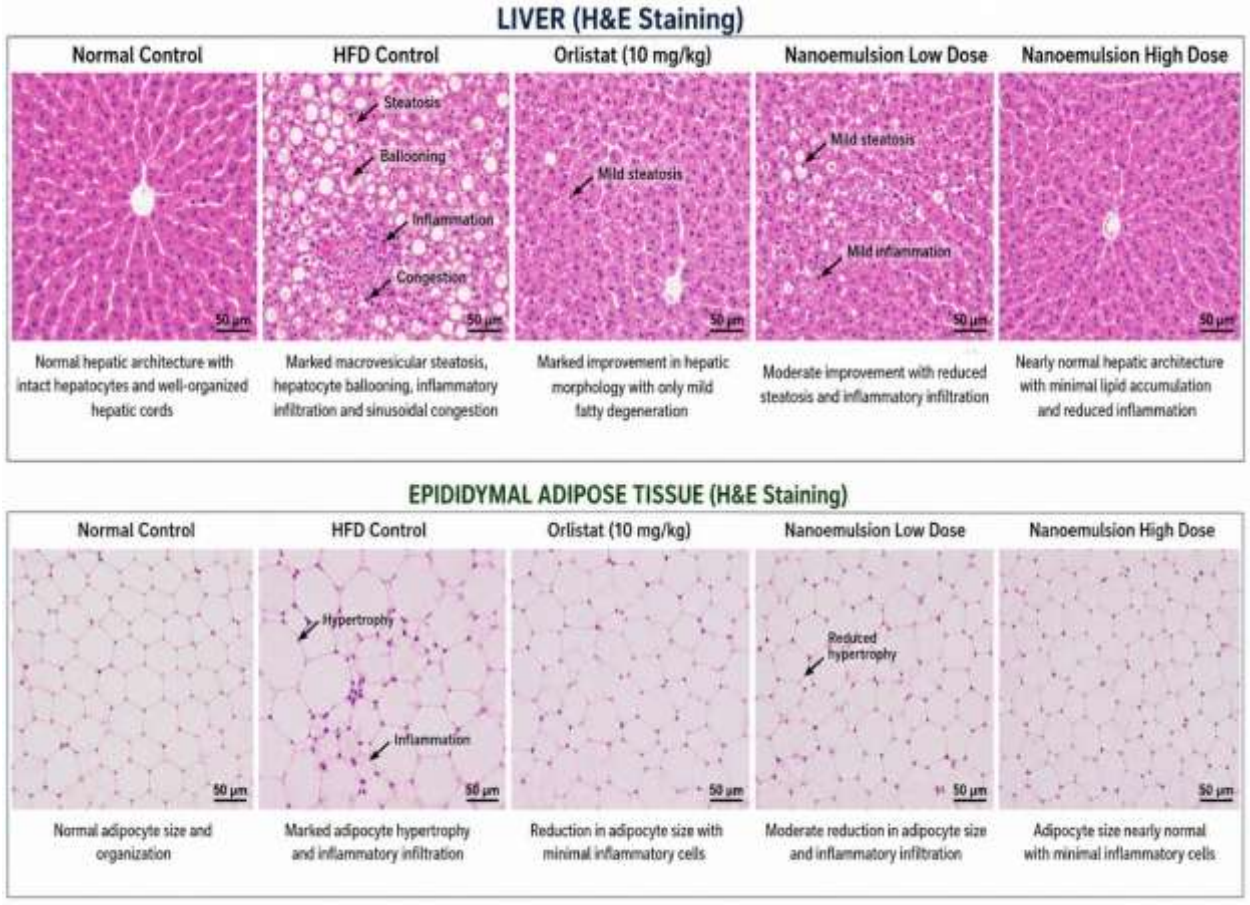

Figure 2. Histopathological evaluation of liver and epididymal adipose tissues in high-fat diet-induced obese rats following treatment with Nelumbo nucifera nanoemulsion.

3.8 Gene Expression Analysis

RT-qPCR analysis demonstrated significant upregulation of adipogenic genes (PPAR-γ, C/EBP-α, SREBP-1c, FASN, and ACC) in the HFD group compared with normal controls. Treatment with Nelumbo nucifera nanoemulsion significantly downregulated these genes, particularly in the high-dose group.

Similarly, inflammatory mediators (TNF-α, IL-6, IL-1β, NF-κB, and MCP-1) were markedly overexpressed in obese animals. Nanoemulsion treatment significantly suppressed the expression of these inflammatory genes.

Conversely, metabolic genes associated with fatty acid oxidation and energy homeostasis (AMPK, CPT-1A, PGC-1α, UCP-1, GLUT4, SIRT1, and Adiponectin) were significantly downregulated in HFD-fed rats. Administration of the nanoemulsion restored the expression of these genes in a dose-dependent manner, with the high-dose group showing values approaching those of the normal control and Orlistat-treated groups.

Table 5. Relative fold change in gene expression (2^-ΔΔCt)

Gene	HFD	Orlistat	Nano-L	Nano-H
PPAR-γ	3.62	1.34	2.14	1.48
C/EBP-α	3.21	1.28	1.95	1.41
SREBP-1c	3.88	1.42	2.22	1.56

TNF-α	4.32	1.52	2.56	1.71
IL-6	3.84	1.47	2.31	1.63
AMPK	0.42	0.91	0.74	0.96
SIRT1	0.38	0.89	0.69	0.94
GLUT4	0.45	0.95	0.73	0.97

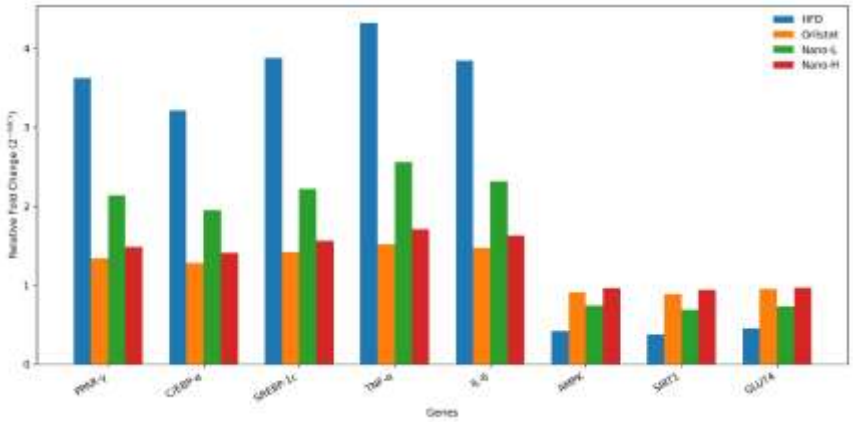

Figure 3. Effect of Nelumbo nucifera Nanoemulsion on Relative Gene Expression in High-Fat Diet-Induced Obese Rats

4. DISCUSSION

Obesity is a multifactorial metabolic disorder characterized by excessive adipose tissue accumulation, dyslipidemia, insulin resistance, oxidative stress, and chronic low-grade inflammation. The present study demonstrated that Nelumbo nucifera nanoemulsion effectively attenuated high-fat diet (HFD)-induced obesity by improving body weight, lipid metabolism, oxidative stress, inflammatory cytokine production, histopathological alterations, and molecular markers regulating adipogenesis and energy metabolism. These findings suggest that nanoformulation of N. nucifera significantly enhances its anti-obesity potential through simultaneous modulation of multiple metabolic pathways.

One of the characteristic features of diet-induced obesity is excessive body weight gain resulting from increased adipocyte hypertrophy and lipid accumulation. In the present study, HFD-fed rats exhibited a marked increase in body weight compared with normal controls, whereas treatment with N. nucifera nanoemulsion significantly reduced body weight gain in a dose-dependent manner. The high-dose nanoemulsion produced an effect comparable to Orlistat, suggesting improved regulation of energy homeostasis. Similar reductions in body weight following administration of N. nucifera extracts have been reported previously, where the anti-obesity activity was attributed to abundant flavonoids, phenolic compounds, and alkaloids capable of suppressing adipogenesis and enhancing lipid metabolism [32,33].

Obesity-induced dyslipidemia is characterized by elevated serum cholesterol, triglycerides, LDL, and VLDL levels together with decreased HDL cholesterol, thereby increasing cardiovascular risk. In the present investigation, HFD markedly altered the serum lipid profile, whereas nanoemulsion treatment restored lipid homeostasis. The high-dose nanoemulsion substantially reduced total cholesterol, triglycerides, and LDL while elevating HDL levels. These observations are consistent with previous reports demonstrating that N. nucifera polyphenols inhibit lipid accumulation through regulation of hepatic lipid metabolism and increased fatty acid oxidation [34,35]. Furthermore, nanoemulsion technology may enhance intestinal absorption and systemic bioavailability of phytoconstituents, thereby improving therapeutic efficacy compared with conventional herbal preparations [36].

Oxidative stress plays a central role in obesity-associated metabolic dysfunction through excessive generation of reactive oxygen species (ROS), lipid peroxidation, and depletion of endogenous antioxidant defenses. Consistent with previous investigations, HFD feeding significantly increased malondialdehyde (MDA) while reducing SOD, CAT, and GSH activities. Administration of N. nucifera nanoemulsion significantly restored antioxidant enzyme activities and reduced lipid peroxidation. These antioxidant effects may be attributed to the high content of flavonoids and phenolic constituents, which effectively scavenge free radicals and protect cellular membranes against oxidative injury [37,38].

Chronic inflammation represents another hallmark of obesity and contributes significantly to insulin resistance and metabolic syndrome. Hypertrophied adipocytes recruit macrophages that secrete inflammatory cytokines including TNF-α, IL-6, IL-1β, and MCP-1, resulting in activation of NF-κB signaling and progressive metabolic impairment [39]. In the present study, serum concentrations of pro-inflammatory cytokines were markedly elevated in HFD-fed animals but were significantly reduced following treatment with N. nucifera nanoemulsion.

Simultaneously, adiponectin levels increased, indicating restoration of adipose tissue endocrine function. These findings agree with earlier studies demonstrating potent anti-inflammatory properties of N. nucifera mediated through inhibition of NF-κB activation and suppression of inflammatory cytokine production [40,41].

Histopathological observations further confirmed the biochemical findings. Liver sections obtained from HFD-fed animals demonstrated macrovesicular steatosis, hepatocyte ballooning, inflammatory infiltration, and sinusoidal congestion, whereas epididymal adipose tissue exhibited marked adipocyte hypertrophy with inflammatory cell infiltration. These pathological alterations are widely recognized features of obesity-associated hepatic steatosis and adipose tissue dysfunction [42]. Treatment with N. nucifera nanoemulsion markedly improved hepatic architecture and reduced adipocyte hypertrophy in a dose-dependent manner. The high-dose formulation restored nearly normal tissue morphology, indicating substantial hepatoprotective and anti-adipogenic activity. Similar histological improvements have previously been reported following administration of N. nucifera extracts in experimental obesity and metabolic syndrome models [43].

The molecular findings obtained by RT-qPCR provide mechanistic evidence supporting the anti-obesity activity of the nanoformulation. Expression of adipogenic transcription factors including PPAR-γ, C/EBP-α, and SREBP-1c was markedly increased in HFD-fed animals, confirming enhanced adipocyte differentiation and lipogenesis. Nanoemulsion treatment significantly downregulated these genes, suggesting inhibition of adipogenesis and lipid accumulation. Comparable suppression of adipogenic gene expression by N. nucifera flavonoids has been demonstrated in both in vitro and in vivo models [44,45].

The inflammatory genes TNF-α and IL-6 were also significantly overexpressed following HFD feeding but were markedly reduced after nanoemulsion treatment, indicating attenuation of obesity-induced inflammatory signaling. These observations further support previous reports demonstrating inhibition of NF-κB-mediated inflammatory pathways by lotus-derived phytochemicals [46].

Conversely, metabolic regulators including AMPK, SIRT1, and GLUT4 were significantly downregulated in obese animals but were restored following treatment with N. nucifera nanoemulsion. Activation of the AMPK/SIRT1 signaling axis is known to promote fatty acid β-oxidation, improve glucose utilization, enhance mitochondrial function, and suppress hepatic lipogenesis. Restoration of these metabolic genes suggests improved insulin sensitivity and energy expenditure, thereby contributing to the observed anti-obesity effects [47,48].

The enhanced therapeutic efficacy observed with the nanoemulsion may be explained by improved physicochemical characteristics of the formulation. The optimized nanoemulsion exhibited nanoscale particle size, narrow particle size distribution, high entrapment efficiency, and excellent stability, which are known to increase gastrointestinal absorption, cellular uptake, and bioavailability of poorly soluble phytoconstituents [49-68]. Consequently, nanoencapsulation likely facilitated more efficient delivery of N. nucifera bioactive compounds to metabolically active tissues, thereby enhancing pharmacological activity.

Overall, the present findings demonstrate that Nelumbo nucifera nanoemulsion exerts significant anti-obesity activity through coordinated regulation of adipogenic, inflammatory, oxidative stress, and metabolic pathways. The formulation effectively reduced body weight gain, improved serum lipid abnormalities, restored antioxidant defense mechanisms, suppressed inflammatory responses, ameliorated histopathological damage, and normalized obesity-associated gene expression. These observations indicate that N. nucifera nanoemulsion represents a promising phytopharmaceutical strategy for the management of obesity and associated metabolic disorders. Future investigations involving detailed phytochemical characterization, pharmacokinetic evaluation, protein expression studies, and long-term safety assessment will further clarify its translational potential for clinical application.

5. CONCLUSION

The present study demonstrated that Nelumbo nucifera nanoemulsion effectively ameliorated high-fat diet-induced obesity through significant improvements in body weight, serum lipid profile, oxidative stress, inflammatory cytokines, and histopathological alterations. Furthermore, the nanoemulsion favorably modulated the expression of key adipogenic, inflammatory, and metabolic genes, indicating inhibition of adipogenesis and restoration of metabolic homeostasis. The high-dose nanoemulsion exhibited therapeutic efficacy comparable to Orlistat, suggesting enhanced anti-obesity activity through improved bioavailability of phytoconstituents. These findings indicate that Nelumbo nucifera nanoemulsion represents a promising phytopharmaceutical candidate for the management of obesity and its associated metabolic complications. Further studies focusing on pharmacokinetics, long-term safety, and clinical evaluation are warranted to validate its therapeutic potential.

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