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Original Communication

Fermented *Solanum nigrum* L. Fruit Beverages by *Lactiplantibacillus plantarum* Improve Obesity in a Rat Model

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Abstract

Background: Obesity constitutes a pervasive global health challenge, with herbal therapeutic interventions gaining increasing public attention. This study aimed to evaluate the efficacy of a homemade beverage derived from *Solanum nigrum* L. fruit fermented with *Lactiplantibacillus plantarum* (fermented *Solanum nigrum* L. fruit, FSNF) in ameliorating obesity-related pathophysiology in a rat model. **Methods:** In the animal experiment (n = 15), Sprague-Dawley rats were allocated into three groups: normal diet control (Con, n = 5), high-fat diet (HFD, n = 5), and HFD supplemented with FSNF (n = 5, 1 mL per 100 g of body weight). All groups were maintained under identical housing conditions, differing only in terms of dietary composition and feeding interventions. Following an 8-week feeding period (comprising 4 weeks of a high-fat diet to induce obesity and 4 weeks of FSNF intervention, excluding the adaptation period), blood and fecal samples were collected. Blood and liver tissues were assayed for inflammatory and oxidative stress biomarkers, while fecal specimens were subjected to 16S rDNA high-throughput sequencing to characterize the gut microbiota. **Results:** After 4 weeks of intervention, FSNF administration significantly reduced the release of pro-inflammatory cytokines (interleukin-6 (IL-6), $p = 0.0128$; tumor necrosis factor-α (TNF-α), $p = 0.0092$) and lowered oxidative damage markers (malondialdehyde (MDA), $p = 0.0202$). Moreover, FSNF administration promoted favorable modulation of obesity-associated hormonal parameters (adiponectin (ADPN), $p = 0.0003$; glucagon-like peptide-1 (GLP-1), $p = 0.0037$) and lipid profiles (cholesterol (CHOl), $p = 0.0088$ in liver tissue; triglycerides (TG), $p = 0.0458$ in liver tissue and $p = 0.0334$ in serum; high-density lipoprotein cholesterol (HDL-C), $p = 0.0009$ in liver tissue and $p = 0.0405$ in serum). Notably, FSNF remodeled the relative abundance of multiple gut microbiota, including *Ligilactobacillus*, *Lactobacillus*, *Romboutsia*, *Limosilactobacillus*, *Clostridia_UCG-014_Incertae_Sedis*, *Lachnospiraceae_NK4A136 group*, *[Eubacterium] coprostanoligenes group Incertae Sedis*, *Treponema*, and *Oscillospiraceae_NK4A214 group*. These microbial changes may have acted synergistically to modulate host hepatic expression of key metabolic genes (sterol regulatory element-binding protein 1C (SREBP-1C), $p = 0.0138$; protein kinase AMP-activated catalytic subunit Alpha 2 (AMPKα2), $p = 0.0026$; AMP-activated protein kinase (AMPK), $p = 0.0070$; carnitine palmitoyltransferase-1 (CPT-1), $p = 0.0002$) and contributed to improve obesity outcomes. **Conclusions:** Collectively, these findings demonstrate that FSNF effectively reduces systemic inflammation, regulates lipid metabolism and obesity-related hormonal balances, and restructures gut microbiota composition in obese rats. Furthermore, FSNF is capable of modulating the gut microbiota, improving the host's lipid metabolism, and enhance the expression of relevant target genes, thereby alleviating obesity. This work provides preliminary mechanistic insights into the anti-obesity action of FSNF and offers a theoretical foundation and practical strategy for obesity prevention and intervention.

Keywords: obesity; fermented beverages; *Solanum nigrum*; *Lactiplantibacillus plantarum*; cytokines; oxidative stress; lipid metabolism; hormones; gut microbiota; rats

1. Introduction

Obesity is generally defined as a chronic disease resulting from an energy imbalance caused by the combined effects of nutritional, neurological, hormonal, and metabolic factors [1,2]. Obesity is no longer viewed simply as a lifestyle issue, but is more clearly defined as a multifactorial chronic disease requiring lifelong management [3,4]. The global obesity crisis remains severe. According to a report by the World Obesity Atlas, as of 2022, there were nearly 900 million obese adults worldwide, and this number is projected to exceed 1 billion by 2030 and reach 2 billion by 2035 [5,6]. Therefore, obesity is a serious global health issue that is directly linked to the development of many diseases; the underlying mechanism involves subclinical inflammation, which is believed to be the link between obesity and its associated diseases [7,8].

Modern medicine primarily uses methods such as dietary changes, exercise, medication, and surgery to treat obesity, but these approaches have their limitations, including difficulty in adherence, potential side effects, and high costs [9,10]. Obesity, which is characterized by complex causes and multiple metabolic disorders, requires multi-targeted interventions to achieve comprehensive results [9,10,11].

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The application of "Medicine and Food Homology" (substances that are both food and medicine) in obesity management represents a key area of convergence between modern nutritional science and traditional Chinese medicine [12,13]. The effects of these substances are not limited to single-target, drug-like interventions; rather, they exert their effects through the synergistic action of the various natural bioactive compounds they contain [14,15]. In the treatment of obesity, these substances can influence multiple pathways, including the regulation of energy metabolism, modulation of inflammatory responses, and the remodeling of adipocyte function [15,16]. Additionally, the use of food-medicine substances provides the gut microbiota with a rich source of substrates, stimulating the microbiota to counteract the effects of obesity [16].

Solanum nigrum L. (also recorded as *Solanum nigrum* Linn.), commonly known as black nightshade, possesses a wide range of pharmacological activities, with particularly notable effects in the areas of antitumor, anti-inflammatory, antioxidant, and hepatoprotective properties [17,18,19]. With respect to its hepatoprotective action, accumulating evidence demonstrates that extracts of this plant effectively ameliorate chemical- and alcohol-induced liver injury through multifaceted mechanisms, encompassing anti-inflammatory and antioxidative pathways, regulation of the gut microbiota, and inhibition of fibrogenesis [20,21]. Moreover, it exerts preventive and therapeutic effects against fatty liver disease by modulating lipid metabolism, suppressing de novo lipogenesis, and promoting lipid catabolism [21]. In the context of anti-inflammatory activity, the extract markedly suppresses the production of nitric oxide (NO), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) in lipopolysaccharide (LPS)-stimulated macrophages, an effect mechanistically attributed to the downregulation of inducible nitric oxide synthase (iNOS) expression [22]. Furthermore, *Solanum nigrum* L. is rich in antioxidative phytochemicals, particularly polyphenols and flavonoids [23]. Notably, its extract exhibits significant DPPH radical-scavenging activity, and its bioactive constituents, especially quercetin and kaempferol, confer protection against oxidative damage in erythrocytes via their potent antioxidant properties [23]. *Lactiplantibacillus plantarum* (formerly known as *Lactobacillus plantarum*) secretes a natural antibiotic called bacteriocin, which inhibits the growth of harmful microorganisms [24]. It is also a common probiotic in the gut, exhibiting good acid and bile salt tolerance, enabling it to survive in the acidic environment of the stomach and in bile [25]. It produces various beneficial metabolites, such as organic acids, vitamins, and antioxidants [26]. These substances improve the intestinal environment and strengthen the intestinal barrier function, thereby preventing the invasion of harmful substances and pathogens [27], ultimately improving the clinical condition [28].

Therefore, we sought to develop a beverage by fermenting *Solanum nigrum* L. fruit (FSNF) with probiotics (in this study, using *Lactiplantibacillus plantarum*). We then used this beverage to intervene in a rat obesity model to observe whether it exhibits anti-obesity effects, and tried to elucidate the potential mechanisms of action. We aim to provide an alternative new approach for obesity intervention, and try to offer theoretical support for the efficacy of probiotic-fermented products derived from food-medicine dual-use ingredients.

2. Materials and Methods

2.1 Materials

Specified pathogen free (SPF) grade Sprague-Dawley (SD) rats were obtained from Hunan Slaike Jingda Laboratory Animal Co., Ltd. (China). *Solanum nigrum* L. fruits were obtained from a local farmers' market adjacent to the laboratory site. The strain of *Lactiplantibacillus plantarum* employed in this study was HW 006, which is maintained in the laboratory's in-house culture collection. Rat diets were purchased from a commercial feed supplier, with full ingredient details available in the **Supplementary Materials**.

2.2 Study Design

Male 5-week-old SD rats (weighing 140–160 g, N = 15) were acclimatized for one week on a normal diet and then randomly assigned to three groups (N = 5 each): normal control (Con), high-fat diet (HFD), and high-fat diet supplemented with FSNF. The Con group received a normal diet throughout; the HFD and FSNF groups were fed a high-fat diet for four weeks to induce obesity, after which the FSNF group received additional FSNF via oral gavage, while the HFD group continued on a high-fat diet alone. However, at the intervention time point, the Con, HFD, and FSNF groups all underwent gavage administration, with the gavage intervention lasting four weeks. The complete gavage and feeding protocol is detailed in **Supplementary Table 1**. All rats were maintained under controlled conditions (23 ± 2 °C, 50 ± 10% humidity, 12 h light/dark cycle). Daily food intake and weekly body weight were monitored from the start of gavage. At study termination, after a 12 h fast, rats were deeply anesthetized with Zoletil-50 (40 mg/kg) and subsequently euthanized by cervical dislocation. Following the induction of deep anesthesia, blood was collected via ocular enucleation. The rats were then euthanized by cervical dislocation, and necropsy was performed to dissect and weigh the organs. Tissues destined for histological examination were fixed in 4% paraformaldehyde; remaining tissues were snap-frozen in liquid nitrogen and stored at –80 °C for subsequent analyses. Fecal samples from all rats were subjected to next-generation sequencing, and three randomly selected animals per group were further used for relative quantification of target genes to validate the findings. An overview of the experimental design is presented in Fig. 1.

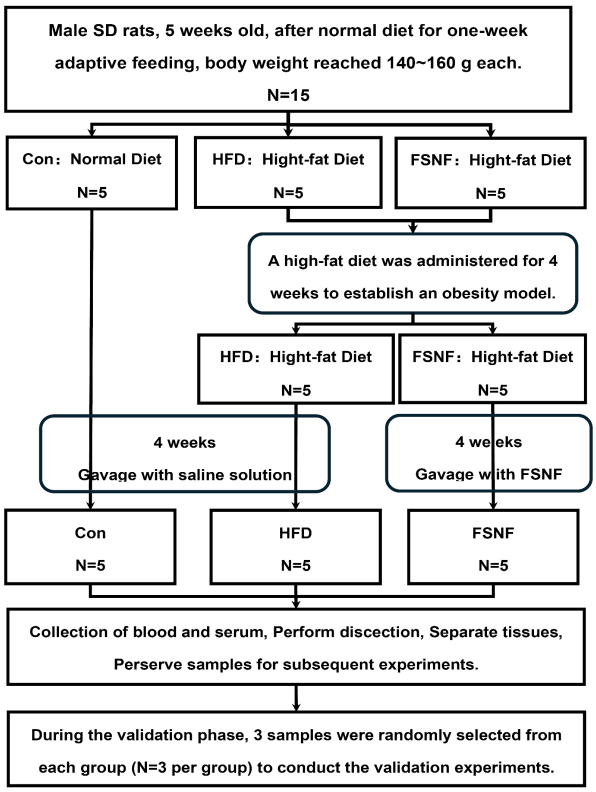


Fig. 1. Study design and experimental workflow. Fifteen rats, assigned to three groups, were included in the study. Liver tissues were collected for histopathological evaluation via hematoxylin and eosin (H&E) staining; faecal samples were subjected to 16S rRNA gene amplicon sequencing on the Illumina platform for gut microbiome characterisation; and both liver tissue and serum were used for the measurement of physiological and biochemical parameters. SD, Sprague-Dawley; Con, normal control; HFD, high-fat diet; FSNF, fermented *Solanum nigrum* L. fruit.

2.3 Preparing Fermented Solanum nigrum L. Fruit Beverages

Ripe, undamaged fruits of *Solanum nigrum* L. were selected, thoroughly washed with running water, and drained. The cleaned fruits were then crushed, and the juice was extracted. The crude juice was filtered through a 60-mesh sieve to obtain a clear filtrate, which was sterilized by autoclaving at 121 °C for 15 min and subsequently cooled to 37 °C. The sterile juice was inoculated with *Lactiplantibacillus plantarum* HW 006 at an inoculum concentration of 3% (v/v) and fermented at 37 °C for 18 h in a temperature-controlled incubator. The resulting fermented beverage (designated as FSNF) was stored at 4 °C until further use.

2.4 Chemical Compounds Analysis of FSNF by Non-targeted Metabolomics Liquid Chromatography Mass Spectrometry (LC-MS)

The FSNF supernatant sample was prepared by centrifuging for 15 min at 4 °C at 1500 ×g, and then transferred to dry ice for further LC-MS analysis. UHPLC (Vanquish UHPLC, Thermo, Waltham, MA, USA) coupled to an Orbitrap Exploris™ 480 was used to analyze the FSNF sample to understand the material components. The sample analysis was conducted in triplicate. A detailed description of the process is provided in the **Supplementary Materials**.

2.5 Analysis of Active Components and Their Content in FSNF

The active components in FSNF and their concentrations were analyzed, primarily including total sugars, total flavonoids, total polyphenols, pH, and total acidity; each component was measured in triplicate. For specific analytical methods, please refer to the **Supplementary Materials**.

2.6 Biochemical Analysis

Serum and liver biochemical parameters were measured using a fully automated biochemical analyzer (AU5800, Beckman, Brea, CA, USA). Corresponding reagent kits, specific to each biochemical index, were procured from Ningbo Meikang Biotechnology Co., Ltd. (Ningbo, Zhejiang, China). The concentrations of TNF-α, IL-6, insulin, glucagon-like peptide-1 (GLP-1), and adiponectin in both serum and liver samples were quantified via enzyme-linked immunosorbent assay (ELISA) using commercial kits obtained from Shanghai Hualan Chemical Technology Co., Ltd. (China). All experimental procedures were performed strictly in accordance with the manufacturers' protocols.

2.7 Next-generation Sequencing for Fecal Samples

The preparation of fecal DNA, the obtaining of sequencing-targeted fragments, the construction of sequencing libraries, and the sequencing process have been described in detail in previous reports [29]. It should be noted that negative controls must be included starting from the DNA extraction stage and must accompany all samples throughout the subsequent experimental procedures; they should only be discarded once it is determined that sequencing is no longer feasible. Negative control samples specific to each experimental step should be incorporated into that step. Additionally, positive control samples with known microbial community structures and abundances should be included to accompany all samples through the entire experimental process, in order to mitigate potential experimental biases.

2.8 Bioinformatics Analysis

For information on how to obtain clean data, α diversity, β diversity matrix, and taxonomic annotation, please refer to our previous report [29]. Specifically, Shannon's diversity index was employed to quantify α diversity. For β diversity, Bray-Curtis dissimilarity was calculated to assess structural variations in gut microbial communities across samples, and the resulting distance matrix was visualized via principal coordinate analysis (PCoA). Taxonomic correlation analysis was conducted by computing Spearman rank

correlation coefficients based on the relative abundances of the top 50 most abundant species. Prediction of gut microbiota function was performed using Tax4Fun version 2 (Tax4Fun2) [30]. Unless otherwise specified, all analytical parameters were set to their default values.

For intergroup comparisons of gut microbial community structures, the Kruskal-Wallis rank-sum test was utilized, with statistical significance set at $p < 0.05$. In the PCoA analysis, the overall similarity between groups was assessed using the Analysis of similarities (ANOSIM) test, with $p < 0.05$ considered to indicate a significant difference. In addition, Linear Discriminant Analysis Effect Size (LEfSe) [31] was performed to detect differentially abundant genera and functionally distinct gene sets, and to estimate their relative contributions to the observed disparities.

2.9 Total RNA Extraction, Reverse Transcription-Quantitative Polymerase Chain Reaction Analysis (RT-qPCR) of Gene Expression Levels

Total RNA was extracted from rat liver and adipose tissue using the RNA extraction kit (Shanghai Sangon Biotech Co., Ltd., China) in accordance with the manufacturer's instructions. First-strand cDNA was synthesized with the EasyScript® One-Step gDNA Removal and cDNA Synthesis SuperMix (Beijing TransGen Biotech Co., Ltd., China). RT-qPCR was carried out using the SYBR Primescript™ Real-Time PCR Kit (Beijing Solarbio Science & Technology Co., Ltd., China) following the recommended protocol. Complete details of the PCR amplification procedure and the primer sequences are available in the **Supplementary Materials** and **Supplementary Table 2**.

2.10 Statistical Analyses

All experiments were repeated five times (three replicates were used for gene expression validation experiments), and the results are expressed as the mean ± standard deviation (SD). Statistical analysis was performed using GraphPad Prism version 11.0.0 (GraphPad Software, San Diego, CA, USA). Comparisons among multiple groups were evaluated by one-way analysis of variance (ANOVA), followed by Tukey's post hoc test for multiple comparisons. The effects of body weight and time were assessed using two-way ANOVA with Geisser-Greenhouse correction, followed by Šidák's multiple comparisons test. Pairwise comparisons between the two groups at the same time point were analysed using the Mann-Whitney test. Nonparametric statistical tests were applied to the microbial community data. Specifically, the Kruskal-Wallis rank-sum test was used to compare differences among multiple groups, while the Wilcoxon rank-sum test was used to compare two groups. A p-value of <0.05 was set as the threshold for statistical significance.

3. Results

3.1 Main Substance Components of FSNF

Non-targeted metabolomics was employed to profile the major chemical constituents of FSNF. A total of 338 compounds were detected, of which 277 were structurally identified. The identified compounds comprised 1 alkaloid or derivative, 18 benzenoids, 62 lipids and lipid-like molecules, 1 mixed metal/non-metal compound, 9 nucleosides, nucleotides and analogues, 52 organic acids and derivatives, 9 organic nitrogen compounds, 45 organic oxygen compounds, 34 organoheterocyclic compounds, and 46 phenylpropanoids and polyketides. Among these, the most abundant constituent was erythronolactone, followed by choline, oleamide, α,α-trehalose, and palmitic acid, which represented the top five compounds in terms of concentration (see **Supplementary Table 3** for the complete list).

In our analysis of the active components and their concentrations in FSNF, we found that this beverage contains: total sugars: 9.75 ± 0.60 mg/mL; total acids: 2.31 ± 0.13 mg/mL; total polyphenols: 0.33 ± 0.009 mg/mL; total flavonoids: 1.08 ± 0.04 mg/mL; pH: 3.24 ± 0.03.

3.2 Effects of FSNF on Physiological Characteristics in a High-Fat Diet-Induced Obese Rat Model

3.2.1 Establishment of a High-Fat Diet-Induced Obesity Model in Rats

After four weeks of continuous high-fat diet feeding, body weight in the HFD group was significantly higher than that in the Con group ($p = 0.0079$), and the FSNF group also exhibited a significant increase relative to Con ($p = 0.0159$), whereas no significant difference was observed between the HFD and FSNF groups ($p = 0.0952$, Fig. 2A). Lee's index, a commonly used indicator of obesity in rats, was also markedly elevated in the HFD group ($p < 0.0001$, Fig. 2B). Obesity induced adipocyte hypertrophy (**Supplementary Fig. 1B**), leading to fat accumulation and the formation of adipose deposits, as reflected by a significant increase in white fat mass (Con vs. HFD, $p = 0.002$, Fig. 2C). In addition, high-fat diet consumption resulted in substantial white fat deposition in the liver (Con vs. HFD, $p = 0.0002$; **Supplementary Fig. 2A**) and kidneys (Con vs. HFD, $p = 0.0084$, **Supplementary Fig. 2B**). Taken together, these data confirm the successful establishment of the rat obesity model after four weeks of high-fat diet intervention (Fig. 2).

3.2.2 Effects of FSNF on Physiological Characteristics

Starting in the fourth week, an FSNF gavage intervention was administered to treat obesity. After four weeks, about the time factor, provided that there was no significant change in the rats' food intake (**Supplementary Fig. 3**). However, there was a significant effect of treatment ($p = 0.0193$, **Supplementary Fig. 3**); this may be related to differences in the dietary composition or intervention components across the different groups. The rate of weight gain in the rats slowed, though it remained significantly higher

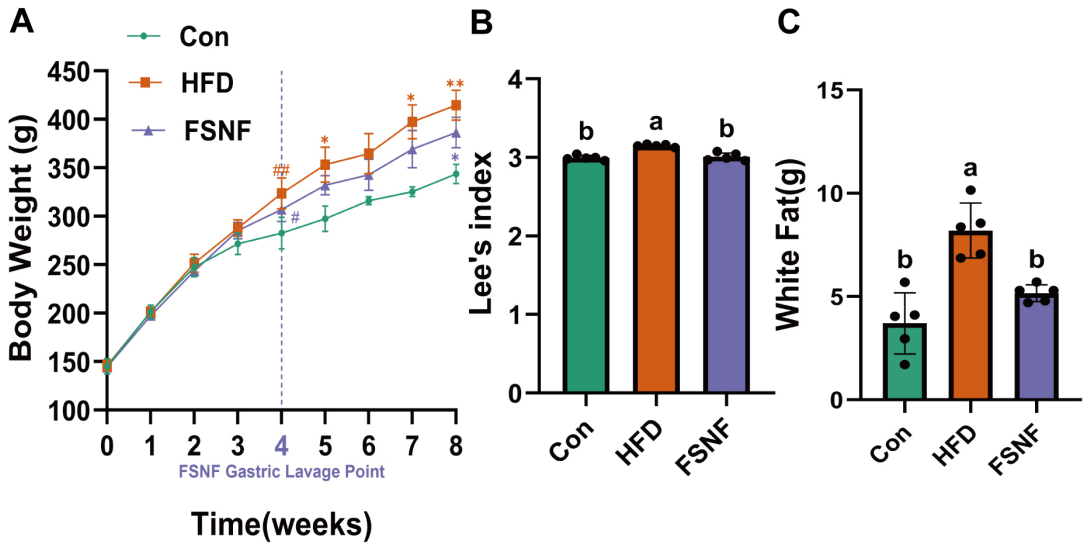


Fig. 2. Effects of FSNF administration on physiological parameters. (A) Body weight progression in rats. Statistical comparisons among the three groups at each time point were performed using two-way ANOVA with Geisser-Greenhouse correction, followed by Šidák's multiple comparisons test. Significance levels are denoted as *$p < 0.05$, **$p < 0.01$. Pairwise comparisons between two groups at the same time point were analysed using the Mann-Whitney test, with significance indicated as #$p < 0.05$, ##$p < 0.01$. (B) Lee's index, calculated as [cube root of body weight (g) × 10] / body length (cm), where body length is the distance from the tip of the nose to the anus. One-way ANOVA with Tukey's multiple comparisons test was applied for intergroup comparisons; different letters above the bars denote statistically significant differences ($p < 0.05$). (C) White fat mass. One-way ANOVA with Tukey's multiple comparisons test was used for group comparisons; means with different letters are significantly different ($p < 0.05$). Data were presented in the figure as the mean ± SD from five independent experiments (N = 5 per group). ANOVA, analysis of variance; SD, standard deviation.

than that in the Con group (p = 0.0428, Fig. 2A); however, there was no significant difference in weight between the FSNF and the HFD group (p = 0.4394, Fig. 2A), with only a downward trend observed. At the same time, Lee's index showed a significant reduction in the degree of obesity (Fig. 2B). There was a significant reduction in white fat mass (HFD vs. FSNF, p = 0.0039, Fig. 2C, **Supplementary Fig. 1C**), and fat accumulation in the liver (HFD vs. FSNF, p = 0.0137, **Supplementary Fig. 2A** and **Supplementary Fig. 9**). There has also been a reduction in kidneys weight (HFD vs. FSNF, p = 0.0068, **Supplementary Fig. 2B**), which may be related to the metabolism of fat within the kidneys. This indicates that after four weeks of FSNF intervention, the trend toward obesity had been mitigated.

3.3 Anti-inflammatory, Antioxidant, and Hormone-regulating Effects of FSNF in an Obese Rat Model

Increased adiposity was associated with elevated circulating pro-inflammatory cytokines and altered levels of obesity-related hormones. Accordingly, we measured the serum concentrations of representative pro-inflammatory cytokines and obesity-related hormonal markers to evaluate the effects of FSNF on systemic inflammation and endocrine status in obese rats.

Compared with the Con group, the HFD group exhibited significantly higher serum levels of interleukin-6 (IL-6, p = 0.0001) and tumor necrosis factor-α (TNF-α, p = 0.0009; Fig. 3A,B). In contrast, the FSNF group showed substantial reductions in both IL-6 (p = 0.0128) and TNF-α (p = 0.0092), indicating that FSNF effectively attenuated the inflammatory response induced by the high-fat diet. Furthermore, hepatic oxidative stress was assessed by measuring malondialdehyde (MDA), a terminal product of lipid peroxidation and an indicator of oxidative damage. MDA content was significantly suppressed in the FSNF group (p = 0.0202, Fig. 3C). Collectively, these findings demonstrate that FSNF intervention not only reduces systemic pro-inflammatory cytokine levels but also improves hepatic antioxidant capacity, thereby effectively mitigating oxidative stress in the obese rat model.

Adiponectin (ADPN) is an endogenous active peptide or protein secreted by fat cells and serves as a key regulator in the body's network for regulating lipid metabolism and blood glucose homeostasis [32]. In the FSNF group, serum ADPN levels were markedly elevated (p = 0.0003) and recovered to values comparable to those of the Con group (p = 0.1534), suggesting that FSNF treatment enhances adiponectin secretion, thereby modulating lipid metabolism and suppressing gluconeogenesis (Fig. 3D). Glucose metabolism was further evaluated using the homeostatic model assessment of insulin resistance (HOMA-IR), a surrogate marker derived from fasting serum glucose and insulin levels that reflects the dynamic interplay be-

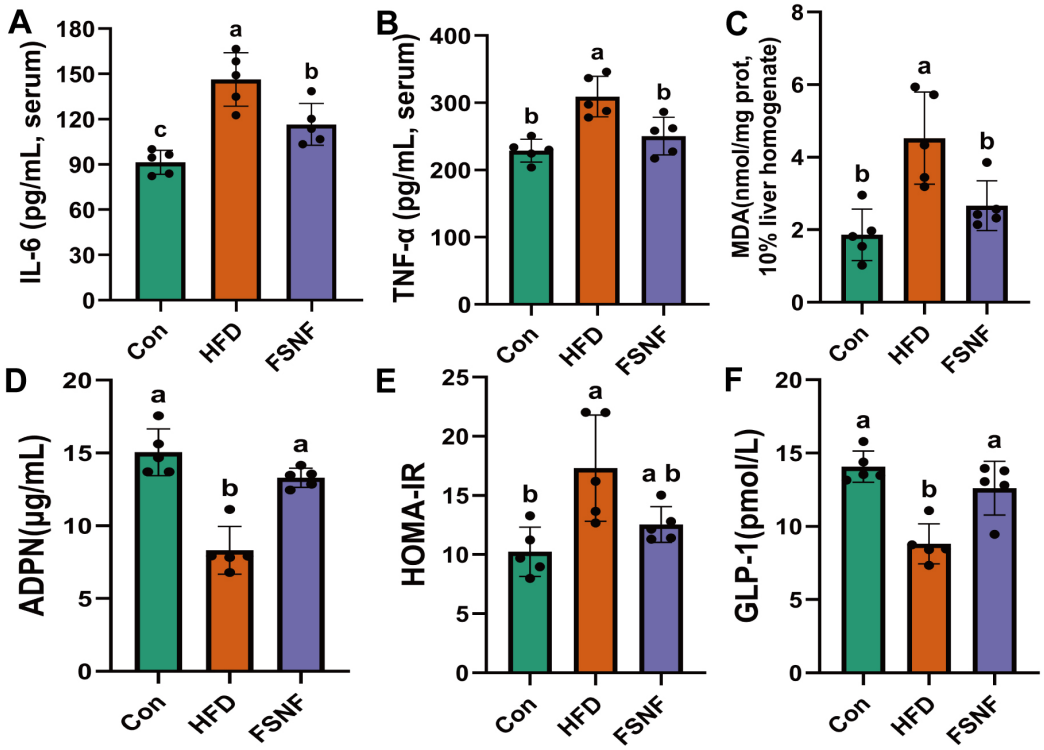


Fig. 3. Effects of FSNF on changes in inflammatory factors, antioxidant factors, and hormone levels. (A) IL-6 level in serum. (B) TNF-α level in serum. (C) MDA level in liver. (D) ADPN level in serum. (E) HOMA-IR (homeostatic model assessment of insulin resistance, calculated as [fasting blood glucose (mmol/L) × fasting insulin (mU/L)] / 22.5). (F) GLP-1 level in serum. Data were presented in the figure as the mean ± SD from five independent experiments (N = 5 per group). Data were compared among the three groups using one-way ANOVA with Tukey's multiple comparisons test. Different letters indicate statistically significant differences ($p < 0.05$). IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; MDA, malondialdehyde; ADPN, adiponectin; GLP-1, glucagon-like peptide-1.

tween glycaemia and insulin responsiveness. In the FSNF group, HOMA-IR values exhibited a decreasing trend relative to the HFD group, although the differences did not reach statistical significance (p = 0.0639 vs. HFD; p = 0.4639 vs. Con), indicating a gradual improvement in insulin sensitivity (Fig. 3E). Consistent with this trend, serum insulin levels were also reduced in the FSNF group, suggesting improved glycaemic control (**Supplementary Fig. 4**). Glucagon-like peptide-1 (GLP-1) suppresses appetite, delays gastric emptying, reduces calorie intake, and modulates metabolic pathways, thereby promoting weight loss, and is recognised as a key therapeutic agent in obesity management [33,34,35,36]. Subsequent GLP-1 revealed a marked increase in serum GLP-1 levels in the FSNF group (p = 0.0037), approaching the levels observed in the Con group (p = 0.2898; Fig. 3F). This elevation in GLP-1 likely contributes to glycaemic regulation in response to blood glucose fluctuations, thereby reinforcing effective and stable glycaemic control.

3.4 The Effects of FSNF on Lipid Metabolism in an Obese Rat Model

Given the modulatory effects of FSNF on ADPN-mediated fat metabolism, we evaluated several key lipid parameters in both liver and serum samples to assess the influence of FSNF on lipid homeostasis. The measured indicators included cholesterol (CHOl), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C).

Relative to the HFD group, hepatic CHOl levels in the FSNF group were significantly reduced (p = 0.0088) and approached those of the Con group (p = 0.9392), whereas serum CHOl levels remained largely unchanged (p = 0.7093), suggesting restoration of hepatic capacity to regulate CHOl metabolism (Fig. 4A, **Supplementary Fig. 5**). Furthermore, TG levels were significantly decreased in both liver tissue (p = 0.0458) and serum (p = 0.0334) in the FSNF group, indicative of enhanced hepatic TG catabolism, which contributed to the alleviation of lipid accumulation and the amelioration of hepatic impairment (Fig. 4B,C). In addition, HDL-C levels were markedly elevated in both the liver (p = 0.0009) and serum (p = 0.0405), further confirming the restoration of hepatic regulation of reverse cholesterol transport from peripheral tissues to the liver for subsequent metabolism (Fig. 4D,E).

3.5 Changes in Gut Microbiome Diversity, Interrelationships, and Functional Predictions in FSNF

To evaluate whether FSNF modulates the gut microbiota, faecal samples from rats were analysed. Across the experimental groups, the Shannon index exhibited an in-

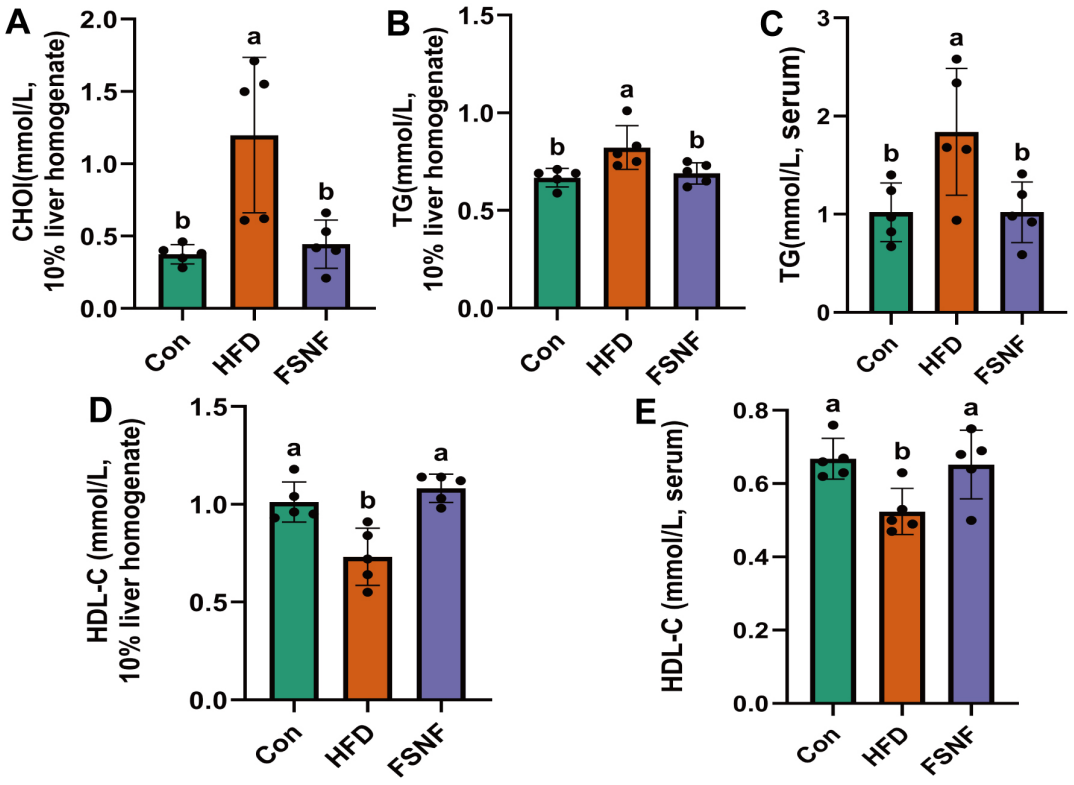


Fig. 4. Effects of FSNF on biochemical parameters in serum and liver tissue. (A) CHOl level in liver. (B) TG level in liver. (C) TG level in serum. (D) HDL-C level in liver. (E) HDL-C level in serum. Data were presented in the figure as the mean ± SD from five independent experiments (N = 5 per group). Data were compared among the three groups using one-way ANOVA with Tukey's multiple comparisons test. Different letters above the bars denote statistically significant differences ($p < 0.05$). CHOl, cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.

creasing trend in the HFD group, whereas the Con and FSNF groups showed similar values (Fig. 5A). This observation suggests that the high-fat diet may slightly perturb the evenness of microbial communities; however, no statistically significant differences were detected ($p = 0.0750$). For β-diversity, principal coordinate analysis (PCoA) revealed a clear separation between the Con and HFD groups ($p = 0.004$, ANOSIM), while the FSNF group clustered in an intermediate position, indicating that FSNF exerted a certain modulatory effect on gut microbiota composition, with a tendency toward recovery towards the Con group, although not fully separated from the HFD cluster (Fig. 5B).

At the genus level, comparative analysis of microbial composition and relative abundance revealed that the high-fat diet led to a fluctuating decline in the levels of certain indigenous beneficial microorganisms. Specifically, genera such as *Ligilactobacillus*, *Lactobacillus*, *Romboutsia*, and *Limosilactobacillus* exhibited this decreasing trend (Fig. 5C). Following FSNF intervention, the abundance of all these genera was restored to higher levels. In contrast, several genera, including *Clostridia_UCG-014 Incertae Sedis*, *Lachnospiraceae_NK4A136 group*, *[Eubacterium]_coprostanoligenes group Incertae Sedis*, *Treponema*, and *Oscillospiraceae_NK4A214 group*, showed a sustained increase in both the HFD and FSNF groups (Fig. 5C). Meanwhile, *unclassified Lachnospiraceae*, *Turicibacter*, and *Oscillospiraceae_UCG-005 group* demonstrated increased abundance in the HFD group but decreased abundance in the FSNF group (Fig. 5C).

Subsequent LEfSe identified several genera with significantly differential abundance in the FSNF group, including *Limosilactobacillus*, *Allobaculum*, *Oscillospiraceae_NK4A214 group*, *Lachnospiraceae_UCG-006*, and *Bacillus*, which collectively contributed prominently to the separation of the FSNF group (Fig. 5D).

Among these, *Limosilactobacillus*, which exhibited relatively high abundance, showed a negative correlation with *Turicibacter*, *Erysipelotrichaceae Incertae Sedis*, and *Staphylococcus*; *Ligilactobacillus*, which had a high abundance, showed negative correlations with *Erysipelotrichaceae Incertae Sedis*, *Staphylococcus*, *Candidatus Saccharimonas*, *Lactobacillus*, and *Clostridia vadin BB60 group Incertae Sedis* (**Supplementary Fig. 6**).

Collectively, these findings indicate that a high-fat diet suppresses the abundance of beneficial bacterial genera, whereas FSNF intervention alters the gut microbial community structure, leading to distinct functional consequences. Changes in the relative abundance of specific genera appear to induce correlated shifts in other members, forming

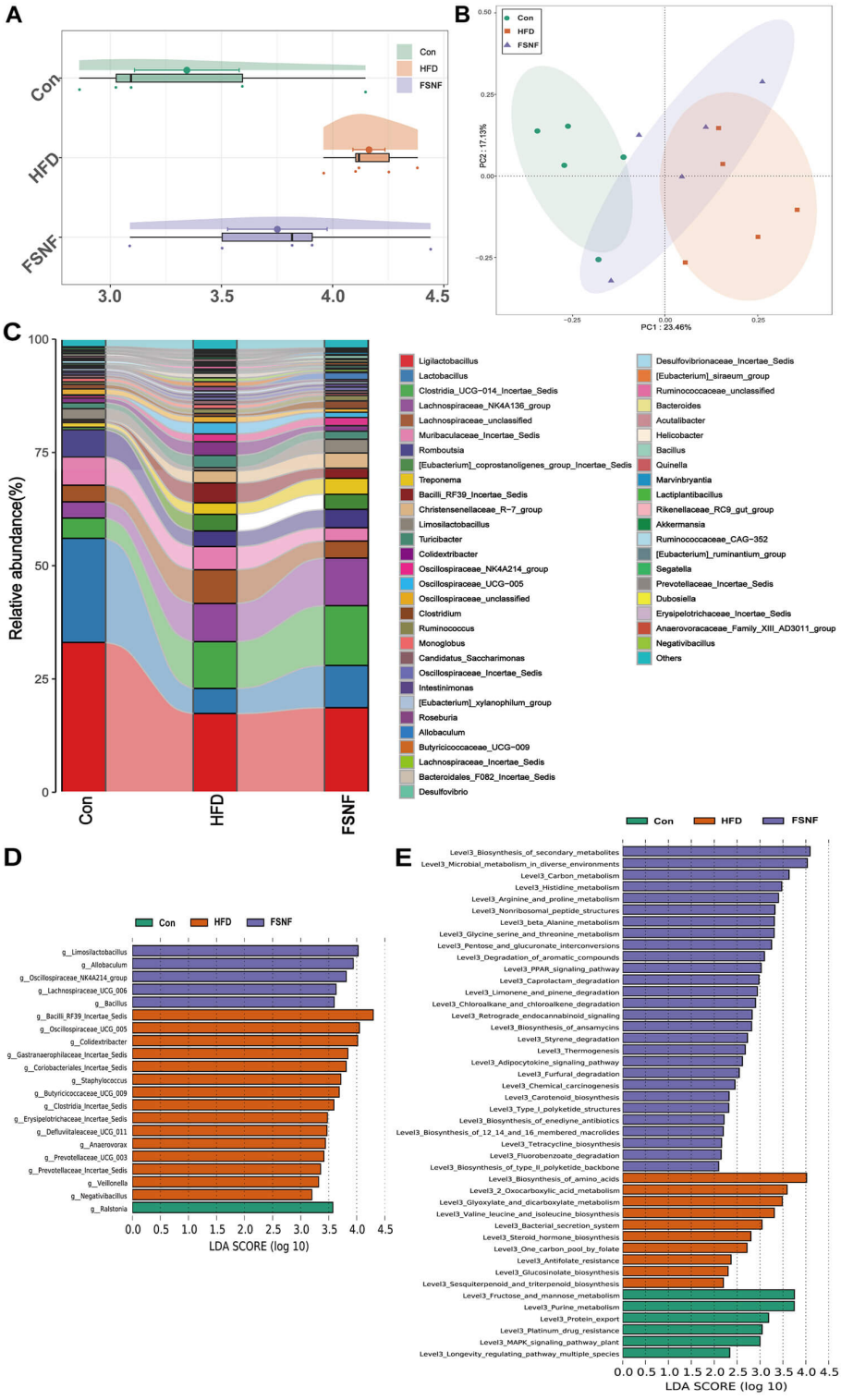


Fig. 5. Gut microbiome analysis. (A) Shannon diversity index. Boxes represent the interquartile range (IQR, 25th to 75th percentiles), with the horizontal line inside each box indicating the median. The whiskers extend from the quartiles to the most extreme data points within 1.5 times the IQR. Little dots beyond the boxes represent outliers. Dots with error bars in different colors represent the mean ± SD. Data were obtained from N = 5 independent experiments per group. (B) PCoA. (C) Bar plot depicting microbial composition and relative abundance at genus level. (D) LEfSe at the genus level. (E) LEfSe analysis of functional pathways annotated at Kyoto Encyclopedia of Genes and Genomes (KEGG) Level 3. Intergroup differences were assessed using the Kruskal-Wallis rank-sum test, with $p < 0.05$ considered statistically significant. In PCoA, the overall similarity between groups was assessed using the ANOSIM analysis, with $p < 0.05$ considered statistically significant. PCoA, principal coordinate analysis; ANOSIM, Analysis of Similarities; LEfSe, Linear Discriminant Analysis Effect Size.

a complex interaction network. This suggests that gut microorganisms do not operate in isolation but rather exert their biological effects through interconnected ecological relationships.

To explore the potential functional repertoire of the gut microbiota, we employed Tax4Fun2 (version 2) for functional prediction based on 16S rRNA gene data. At Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway Level 2, there was a suggestive trend of enrichment: the "Lipid metabolism" category showed a trend toward significant enrichment in the FSNF group compared with the Con group ($p = 0.0079$, $q = 0.0317$), while the "Xenobiotics biodegradation and metabolism" pathway showed a trend toward enrichment in the FSNF group relative to the HFD group ($p = 0.0317$, $q = 0.0874$, **Supplementary Fig. 7**). Further analysis at the more detailed KEGG Level 3 revealed several pathways with notable contributions in the FSNF group, including the peroxisome proliferator-activated receptor (PPAR) signaling pathway (associated with lipid metabolism), the retrograde endocannabinoid signaling pathway (linked to mood regulation), thermogenesis and the adipocytokine signaling pathway (involved in fat metabolism), as well as biosynthesis pathways for 12-, 14-, and 16-membered macrolides and tetracyclines (related to anti-infective properties). Additionally, pathways supporting anti-inflammatory and anti-infective functions, such as Type I polyketide structures and Type II polyketide backbone biosynthesis, were also prominent in the FSNF group (Fig. 5E). Functional predictions suggest that, within the FSNF group, the gut microbiota exhibits enhanced functions related to lipid metabolism and anti-inflammation.

3.6 Effects and Validation of FSNF on the Expression of Lipid-Related Metabolic Genes

Analysis of the gut microbiota revealed changes in fat-related metabolic functions. Subsequently, relevant functional genes were tested in the rats subjected to the FSNF intervention to determine whether similar changes had occurred in their bodies and to verify whether the changes in the microbiota and host functions were consistent.

Fatty acid β-oxidation is a metabolic pathway that breaks down fats to provide energy for the body. In this process, AMP-activated protein kinase (AMPK) and carnitine palmitoyltransferase-1 (CPT-1) participate in the β-oxidation process to promote fat utilization. RT-qPCR analysis revealed that FSNF intervention significantly upregulated the expression of CPT-1 ($p = 0.0002$, Fig. 6A) and AMPK ($p = 0.0070$, Fig. 6B), thereby promoting fat consumption. AMPKα2 is a subunit of AMPK and forms the core responsible for its kinase catalytic function, enabling it to play a role in glucose and lipid metabolism. Notably, AMPKα2 expression was significantly elevated following FSNF treatment ($p = 0.0026$, Fig. 6E), indicating enhanced activation of the AMPK signalling pathway.

In contrast, sterol regulatory element-binding protein 1C (SREBP-1C) is a master regulator of de novo fatty acid synthesis, contributing to lipid formation and accumulation. The expression of SREBP-1C was significantly decreased ($p = 0.0138$, Fig. 6C), suggesting that FSNF intervention suppressed fatty acid synthesis and thereby reduced lipid storage.

Utilizing thermogenic capacity to burn fat is another approach to addressing obesity. The peroxisome proliferator-activated receptor gamma coactivator 1α (PGC-1α) gene promotes mitochondrial oxidative capacity, thereby reducing fat accumulation. Our results showed a marked upregulation of PGC-1α expression ($p < 0.0001$, Fig. 6D). However, this thermogenic enhancement occurred without significant changes in brown adipose tissue mass ($p = 0.0751$, **Supplementary Fig. 8**). Interestingly, functional prediction of the gut microbiota had previously identified significant enrichment of thermogenesis-related pathways in the FSNF group, suggesting that microbial functional shifts may influence host thermogenic responses, although the precise mechanisms and signalling routes remain to be elucidated. Furthermore, PGC-1α is known to activate peroxisome proliferator-activated receptor alpha (PPARα), thereby modulating the PPAR signalling pathway. This observation is consistent with the microbiota functional predictions, supporting the notion that gut microbiota-host interactions contribute to increased fat oxidation, reduced lipid accumulation, and enhanced thermogenic energy expenditure.

4. Discussion

In this study, we used the probiotic *Lactiplantibacillus plantarum* HW 006 to ferment *Solanum nigrum* L. fruit to produce a beverage, which we then administered to obese rats. The results demonstrated that this intervention exerted a significant anti-obesity effect.

In this preliminary exploratory study, we designed the experiment and assigned groups based on the minimum sample size required to meet statistical criteria. In existing comparative studies, particularly in omics research comparing disease and health states, sample size is the fundamental basis for determining the extent to which a given effect is supported in the study [37]. Although the small sample size constitutes a limitation of the present study, it nevertheless represents the first preliminary investigation into the effects of FSNF intervention. It will help us conduct more in-depth mechanistic studies-including, but not limited to, large-scale animal model studies and population cohort studies-while ensuring the validity of our findings.

Using non-targeted metabolomics, we conducted a preliminary profiling of the major constituents in the fermented beverage. Several compounds of relatively high abundance were identified, some of which are known to exert beneficial effects against obesity and may even confer protective functions on the host. Among the top five most abundant compounds, choline has well-established

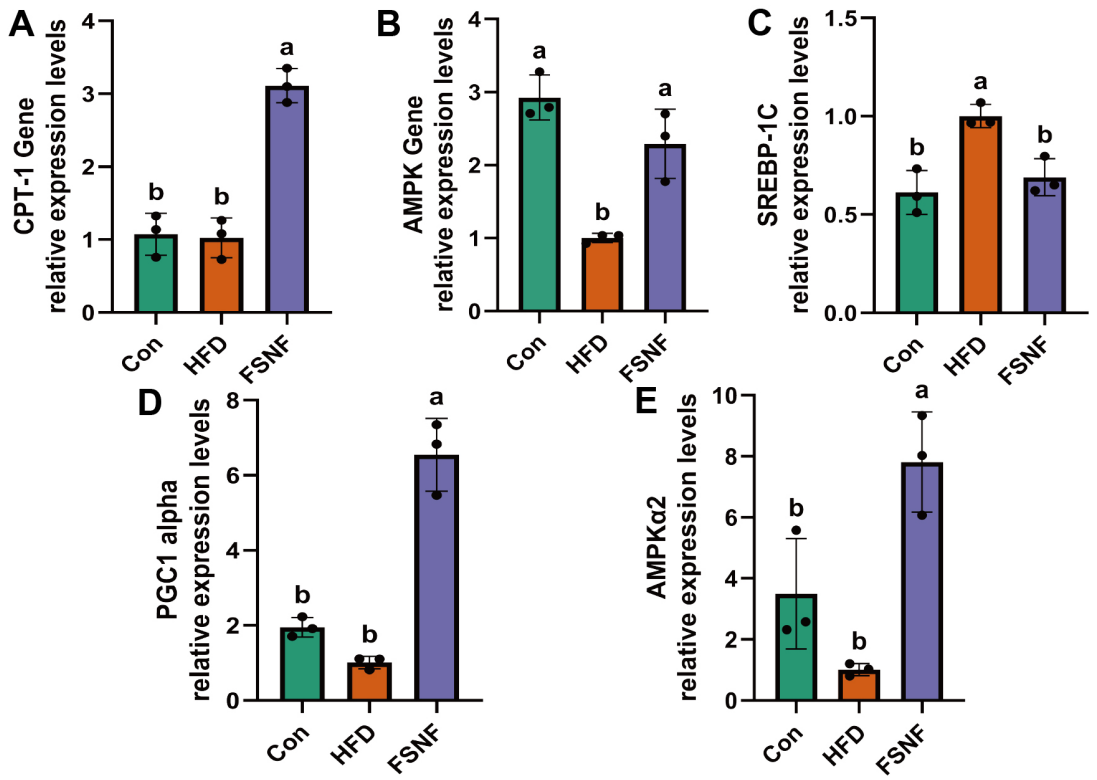


Fig. 6. Relative mRNA expression of lipid-related metabolic genes. (A) CPT-1 level in liver tissue. (B) AMPK level in adipose tissue. (C) SREBP-1C level in liver tissue. (D) PGC-1α level in liver tissue. (E) AMPKα2 level in adipose tissue. Data were compared among the three groups using one-way ANOVA with Tukey's multiple comparisons test. Different letters indicate statistically significant differences ($p < 0.05$). Data were presented in the figure as the mean ± SD from three independent experiments (N = 3 per group). CPT-1, carnitine palmitoyltransferase-1; AMPK, AMP-activated protein kinase; SREBP-1C, sterol reg-ulatory element binding protein-1c; PGC-1α, peroxisome proliferator-activated receptor gamma coactivator 1α; AMPKα2, protein kinase AMP-activated catalytic subunit Alpha 2.

physiological roles, including the maintenance of cell membrane integrity and function [38], as well as participation in lipid metabolism and the support of hepatic health [39]. These properties help preserve cellular barriers and reduce the likelihood of inflammation arising from cell damage. Moreover, choline facilitates hepatic triglyceride transport, regulates cholesterol homeostasis in the liver, and ameliorates oxidative stress and inflammation [39]-findings that are corroborated by the physiological parameters measured in the present study. Similarly, oleamide possesses antioxidant activity and supports cholinergic system function [40]; it may mitigate cellular membrane injury by reducing lipid peroxidation, thereby limiting damage to nerves, tissues, and organs. α,α-Trehalose is regarded as a protective agent capable of directly scavenging reactive oxygen species and protecting cells against oxidative stress [41]. Palmitic acid exhibits dual functionality. On the one hand, it is a critical component of pulmonary surfactant, essential for reducing alveolar surface tension and maintaining normal respiratory function; it also participates in protein modification, influencing protein localisation, stability, and function, and modulating multiple cellular signalling pathways. Furthermore, it serves as a precursor to palmitoylethanolamide, a bioactive lipid with anti-inflammatory, analgesic, and neuroprotective properties [42]. On the other hand, elevated concentrations of palmitic acid may induce inflammation and insulin resistance, and its accumulation can lead to lipotoxicity, impairing cellular function and survival [42]. Although several potentially beneficial substances were detected in the beverage, many other constituents remain unidentified. Moreover, it is currently unclear how these detected compounds exert their effects following oral administration—whether a single compound acts independently, whether they function synergistically, and how their respective concentrations contribute to the observed beneficial outcomes. These questions warrant further investigation.

Some studies have reported that medicine and food homology can be used to intervene in rat disease models over a longer period [43,44]. Our objective was to achieve a rapid therapeutic effect through a short-term intervention.

At four weeks post-FSNF administration, while some physiological, biochemical, and genetic parameters exhibited significant improvements, other indicators displayed a clear downward trend that did not reach statistical significance. This observation may be attributable to the

relatively brief duration of the intervention. Although the present study does not provide a conclusive explanation for this phenomenon, the intervention period remains a factor worthy of consideration in future investigations, and well-designed comparative studies with extended time frames could help elucidate the underlying reasons.

Excessive lipid accumulation in the liver triggers lipid peroxidation and subsequent oxidative stress [45,46], which in turn promotes the production and release of pro-inflammatory cytokines such as TNF-α and IL-6, contributing to the progression of hepatic disease [47]. In the present rat model, four weeks of FSNF intervention resulted in significant improvements in several physiological and biochemical parameters. Specifically, the levels of inflammatory cytokines (IL-6 and TNF-α) were reduced; the oxidative stress marker MDA was decreased; hepatic CHOl and TG were lowered, while HDL-C was elevated. Collectively, these findings demonstrate that FSNF exerts beneficial effects on inflammation, oxidative stress, and lipid metabolism. Moreover, the observed trends are largely consistent with those reported in previous studies [29,43,44], further supporting the comparable efficacy of FSNF.

Analysis of the gut microbiota in rats revealed no significant differences in the α-diversity index, which is consistent with previously reported findings [48,49]. Previous studies have shown that the α-diversity index does not undergo significant changes under disease [48] or intervention conditions [49], suggesting that disease or intervention is not caused by an increase or decrease in the number of microbial species, but may instead result from changes in the abundance of dysbiotic species.

Additionally, we examined genus-level variations in microbial abundance. Under a high-fat diet (HFD), the abundance of several beneficial bacterial genera in the rat gut declined, whereas FSNF intervention effectively restored their levels. Notably, *Ligilactobacillus*, *Lactobacillus*, and *Limosilactobacillus*—members of the traditional lactic acid bacteria (LAB) group, which were reclassified as distinct genera in 2020 [50]—are primarily implicated in mitigating intestinal barrier disruption, restoring epithelial integrity, and suppressing the production of pro-inflammatory cytokines [51]. In addition, *Romboutsia*, a short-chain fatty acid (SCFA)-producing genus, acts synergistically with probiotics to ameliorate metabolic disorders [52]. In the HFD and FSNF groups, the sustained increase in *Clostridia UCG−014 Incertae Sedis* and *[Eubacterium] coprostanoligenes group Incertae Sedis* indicates enhanced capacity for lipid metabolism [53,54]. The sustained increase in *Lachnospiraceae NK4A136 group*, *Treponema*, and *Oscillospiraceae NK4A214 group* indicates that the gut's ability to process carbohydrates, particularly dietary fiber, has been effectively restored [55,56]. Conversely, *unclassified Lachnospiraceae*, *Turicibacter*, and *Oscillospiraceae_UCG-005 group* exhibited increased abundance under HFD conditions but showed a decreasing trend following FSNF treatment. Although *unclassified Lachnospiraceae* and *Oscillospiraceae_UCG-005* are known to ferment dietary fibre into SCFAs [57,58], and *Turicibacter* is involved in lipid metabolism [59], their post-intervention decline may reflect functional redundancy, whereby other genera compensate for SCFA production. The reduction in *Turicibacter* abundance could also be attributable to inhibitory effects of palmitic acid present in the beverage [60]. While our observations are broadly consistent with these interpretations, they do not definitively elucidate the underlying mechanisms; nonetheless, they provide valuable directions for future mechanistic investigations.

Correlation analysis revealed that alterations in beneficial gut microbiota were associated with changes in the abundance of other genera, consistent with the prevailing view that microorganisms function not in isolation but through coordinated community networks [61]. Nevertheless, the precise mechanisms governing these interspecies interactions remain elusive and merit further investigation.

Functional predictions for the gut microbiome suggest a possible significant enrichment of components associated with lipid metabolism. Subsequent gene expression analyses demonstrated that FSNF, in synergy with the gut microbiota, downregulates SREBP-1C to suppress lipid synthesis, upregulates AMPKα2 expression to enhance energy metabolism, and promotes lipid metabolism. Concurrently, the AMPK and CPT-1 genes reside at key nodes of the regulatory pathway governing fatty acid β-oxidation, and the expression of both genes can promote fatty acid β-oxidation, thereby reducing fat accumulation. Collectively, these findings provide a molecular rationale for the effective attenuation of obesity in rats following FSNF intervention.

5. Limitations

In this study, a beverage was formulated by fermenting *Solanum nigrum* L. fruit with probiotics and evaluated for its therapeutic potential against obesity. Owing to the exploratory nature of this initial investigation, the sample size was determined to satisfy the minimum statistical requirements, intending to detect any preliminary phenotypic effects.

The FSNF intervention exhibited measurable anti-obesity effects as early as four weeks post-administration. However, whether long-term FSNF treatment yields sustained benefits remains to be validated through further research.

We acknowledge that subsequent studies involving large-scale rat models and population-based cohort analyses are warranted. Such endeavors would not only corroborate the present findings but also enable the elucidation of underlying mechanisms through comprehensive data analyses, thereby establishing a robust theoretical basis for the development of novel strategies in obesity management.

It is widely acknowledged that next-generation high-throughput sequencing predominantly relies on short-read data, which provide the highest reliability for

genus-level taxonomic assignments. Accordingly, our current interpretation is primarily confined to the genus level. Nevertheless, individual genera may encompass a broad spectrum of species with diverse functional roles. Therefore, the dataset generated in this study serves as a valuable resource for future investigations targeting species-level resolution, potentially offering deeper insights into the specific functional contributions of distinct taxa.

6. Conclusions

In this study, a beverage was produced by fermenting *Solanum nigrum* L. fruit with *Lactiplantibacillus plantarum* HW 006, resulting in a product rich in beneficial compounds. In a rat model of obesity, following a four-week intervention with the beverage, pro-inflammatory cytokines (IL-6 and TNF-α) were significantly attenuated, lipid peroxidation (MDA) was reduced, obesity-related metabolic parameters (ADPN, GLP-1) were restored toward normal levels, HOMA-IR was showing signs of recovery, and lipid profile markers (CHOl, TG, HDL-C) were substantially improved. Although gut microbiota profiling did not detect significant changes in species richness, the observed increases and decreases in the relative abundance of specific genera, in conjunction with FSNF, appeared to facilitate the amelioration of obesity in the host. Through gut microbiota functional prediction, potential metabolic pathways (SREBP-1C/AMPKα2/AMPK/CPT-1) involved in these microbial changes were identified. By subsequently detecting the expression of host-related genes to identify potential intervention pathways, the preliminary mechanism by which FSNF improves obesity was partially elucidated.

Availability of Data and Materials

Due to the ongoing nature of the project, the raw data have not yet been made public; however, relevant data can be obtained from the corresponding author upon request.

Author Contributions

JRS and XTY designed the research study. JRS, RXW, and XTY performed the research. RXW provided help and advice on the research. JRS analyzed the data. JRS, RXW, and XTY wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The animal study protocol was approved by the Experimental Animal Welfare and Ethics Committee, Guilin Tourism University (protocol code GTU2023003, December 3, 2023). The research process in this study followed the ARRIVE (Animal Research: Reporting of *In Vivo* Experiments) guidelines.

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Conflicts of Interest

Jiarui Sun is an employee of Shanghai MoBio Biomedical Technology Co., Ltd. The company has no financial or commercial conflicts of interest in relation to this study. Jiarui Sun confirms that this employment relationship does not compromise the objectivity of the research. The remaining authors declare that they have no competing interests.

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

During the manuscript revision process, the authors used AI and AI-related technologies to revise the article's grammar and writing. The authors have personally reviewed and revised the content as required and assume full responsibility for the content of this publication.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJVNR54420.

References

[1] Busebee B, Ghusn W, Cifuentes L, Acosta A. Obesity: A Review of Pathophysiology and Classification. Mayo Clinic Proceedings. 2023; 98: 1842–1857. https://doi.org/10.1016/j.mayocp.2023.05.026

[2] Suren Garg S, Kushwaha K, Dubey R, Gupta J. Association between obesity, inflammation and insulin resistance: Insights into signaling pathways and therapeutic interventions. Diabetes Research and Clinical Practice. 2023; 200: 110691. https://doi.org/10.1016/j.diabres.2023.110691

[3] Christensen S, Nelson C. Chronicity of obesity and the importance of early treatment to reduce cardiometabolic risk and improve body composition. Obesity Pillars. 2025; 15: 100175. https://doi.org/10.1016/j.obpill.2025.100175

[4] Kushner RF, Shapiro M. Obesity: assessment and treatment across the care continuum. Annals of Medicine. 2025; 57: 2521433. https://doi.org/10.1080/07853890.2025.2521433

[5] World Obesity Federation. World Obesity Atlas 2025. 2025.

Available at: https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2025 (Accessed: 30 May 2026).
[6] World Obesity Federation. Prevalence of Obesity. 2025. Available at: https://www.worldobesity.org/about/about-obesity/prevalence-of-obesity (Accessed: 30 May 2026).
[7] Shaikh SR, Beck MA, Alwarawrah Y, MacIver NJ. Emerging mechanisms of obesity-associated immune dysfunction. Nature Reviews. Endocrinology. 2024; 20: 136–148. https://doi.org/10.1038/s41574-023-00932-2
[8] Bojórquez-González AY, Gómez-Sánchez E, Suarez-Rico DO, Beltrán-Ramírez A, Balleza-Alejandri LR, López-Murillo LD, et al. Biomarkers and Endothelial Damage in Obesity: An Insight into the Pharmacological Modulation. International Journal of Molecular Sciences. 2026; 27: 3694. https://doi.org/10.3390/ijms27083694
[9] Park C, Kim Y, Raygani S, Grunvald E. A glimpse into the pipeline of anti-obesity medication development: combining multiple receptor pathways. Frontiers in Endocrinology. 2025; 16: 1630199. https://doi.org/10.3389/fendo.2025.1630199
[10] Steenackers N, Toumazia J, Deleus E, Mertens A, Lannoo M, Pazmino S, et al. Pharmacotherapy for obesity: are we ready to select, tailor and combine pharmacotherapy to achieve more ambitious goals? Frontiers in Endocrinology. 2025; 16: 1569468. https://doi.org/10.3389/fendo.2025.1569468
[11] Cifuentes L, Hurtado A MD, Eckel-Passow J, Acosta A. Precision Medicine for Obesity. Digestive Disease Interventions. 2021; 05: 239–248. https://doi.org/10.1055/s-0041-1729945
[12] Sun-Waterhouse DX, Chen XY, Liu ZH, I.N. Waterhouse G, Kang WY. Transformation from traditional medicine-food homology to modern food-medicine homology. Food & Medicine Homology. 2024; 1: 9420014. https://doi.org/10.26599/fmh.2024.9420014
[13] Wang R, Chen YQ. Consanguinity of edibles and medicinals (食药同源). Food Bioscience. 2025; 73: 107691. https://doi.org/10.1016/j.fbio.2025.107691
[14] Das M, Yagnik U, Raninga I, Banerjee D. Metabolic regulation of obesity by naturally occurring compounds: mechanisms and therapeutic potential. Frontiers in Endocrinology. 2025; 16: 1655875. https://doi.org/10.3389/fendo.2025.1655875
[15] Yi Y, Qin S, Ding S, Fang J. Polysaccharides in the medicine and food homology to combat obesity via gut-liver axis: A review of possible mechanisms. International Journal of Biological Macromolecules. 2025; 312: 144044. https://doi.org/10.1016/j.ijbiomac.2025.144044
[16] Pillay D, Kuppusamy UR, Arumugam B. Role of terpenes and terpenoids in cross-talk between adipocyte browning and gut microbiome in obesity. Fitoterapia. 2026; 190: 107113. https://doi.org/10.1016/j.fitote.2026.107113
[17] Asante JO, Oduro I, Wireko-Manu F, Larbie C. Assessment of the antioxidant and nutritive profile of the leaves and berries of Solanum nigrum and Solanum torvum Swart. Applied Food Research. 2024; 4: 100438. https://doi.org/10.1016/j.afres.2024.100438
[18] Gul B, Anwar R, Saleem M, Ahmad M, Ullah MI, Kamran S. Attenuation of CFA-induced arthritis through regulation of inflammatory cytokines and antioxidant mechanisms by Solanum nigrum L. leaves extracts. Inflammopharmacology. 2023; 31: 3281–3301. https://doi.org/10.1007/s10787-023-01357-z
[19] Wang J, Pan J, Luan F, Shi H, Xie Y, Zhao C, et al. Progress in Solanum nigrum L. research: Traditional uses, phytochemistry, pharmacological activities, quality control, and clinical applications. Journal of Ethnopharmacology. 2025; 352: 120271. https://doi.org/10.1016/j.jep.2025.120271
[20] Wang X, Sun Z, Wang X, Li M, Zhou B, Zhang X. Solanum nigrum L. berries extract ameliorated the alcoholic liver injury by regulating gut microbiota, lipid metabolism, inflammation, and oxidative stress. Food Research International (Ottawa, Ont.). 2024; 188: 114489. https://doi.org/10.1016/j.foodres.2024.114489
[21] Zhang YM, Huang FW, Zhai JH, Zhang SX. Research progress on hepatoprotective effect and mechanism of Solanum nigrum. China Pharmacy. 2025; 36: 891–896. https://doi.org/10.6039/j.issn.1001-0408.2025.07.22
[22] Kang H, Jeong HD, Choi HY. The chloroform fraction of Solanum nigrum suppresses nitric oxide and tumor necrosis factor-α in LPS-stimulated mouse peritoneal macrophages through inhibition of p38, JNK and ERK1/2. The American Journal of Chinese Medicine. 2011; 39: 1261–1273. https://doi.org/10.1142/S0192415X11009548
[23] Aouadi A, Saoud DH, Rebiai A, Ibrahim MH, Messaoudi M, Alia K, et al. Chemical composition's effect on Solanum nigrum Linn.'s antioxidant capacity and erythrocyte protection: Bioactive components and molecular docking analysis. Open Life Sciences. 2024; 19: 20220944. https://doi.org/10.1515/biol-2022-0944
[24] Setiarto RHB, Anshory L. Bacteriocin, Plantaricin and Pediocin Biosynthesis in Lactic Acid Bacteria, Antimicrobial Mechanism and Applications as Food Preservatives: Review. CURRENT APPLIED SCIENCE and TECHNOLOGY. 2024; 24: e0258161. https://doi.org/10.55003/cast.2023.258161
[25] Coelho-Rocha ND, de Jesus LCL, Barroso FAL, da Silva TF, Ferreira E, Gonçalves JE, et al. Evaluation of Probiotic Properties of Novel Brazilian Lactiplantibacillus plantarum Strains. Probiotics and Antimicrobial Proteins. 2023; 15: 160–174. https://doi.org/10.1007/s12602-022-09978-6
[26] Grigore-Gurgu L, Cotârleț M, Pihurov M, Păcularu-Burada B, Vasile AM, Enachi E, et al. Lactiplantibacillus plantarum and Lactiplantibacillus paraplantarum postbiotics: Assessment of the biotic-derived metabolites with cytocompatibility and antitumoral potential. Food Bioscience. 2024; 59: 103863. https://doi.org/10.1016/j.fbio.2024.103863
[27] Varada VV, Kumar S, Balaga S, Thanippilly AJ, Pushpadass HA, M RH, et al. Oral delivery of electrohydrodynamically encapsulated Lactiplantibacillus plantarum CRD7 modulates gut health, antioxidant activity, and cytokines-related inflammation and immunity in mice. Food & Function. 2024; 15: 10761–10781. https://doi.org/10.1039/d4fo02732a
[28] Chen S, Shi M, Chen X, Le Q, He J. Lactiplantibacillus Plantarum YDJ-03 and Limosilactobacillus fermentum YDJ-6 Alleviate Metabolic Syndrome in Mice. International Journal for Vitamin and Nutrition Research. 2025; 95: 31275. https://doi.org/10.31083/IJVNR31275
[29] Sun JR, Liu RH, Yu YY, Zhang LF, Yan XT. Orange Peel Compound Plant Beverage improving nonalcoholic fatty liver disease through anti-inflammatory and antioxidant factors and gut microbiota in rat model. Applied Biological Chemistry. 2026; 69: 9. https://doi.org/10.1186/s13765-026-01080-7
[30] Wemheuer F, Taylor JA, Daniel R, Johnston E, Meinicke P, Thomas T, et al. Tax4Fun2: prediction of habitat-specific functional profiles and functional redundancy based on 16S rRNA gene sequences. Environmental Microbiome. 2020; 15: 11. https://doi.org/10.1186/s40793-020-00358-7
[31] Segata N, Izard J, Waldron L, Gevers D, Miropolsky L, Garrett WS, et al. Metagenomic biomarker discovery and explanation. Genome Biology. 2011; 12: R60. https://doi.org/10.1186/gb-2011-12-6-r60
[32] Ghadge AA, Khaire AA, Kuvalekar AA. Adiponectin: A potential therapeutic target for metabolic syndrome. Cytokine & Growth Factor Reviews. 2018; 39: 151–158. https://doi.org/10.1016/j.cytogfr.2018.01.004
[33] Lotosky J, Jean X, Altankhuyag A, Khan S, Bernotas A, Sharafshah A, et al. GLP-1 and Its Role in Glycogen Production: A Narrative Review. Biomedicines. 2025; 13: 1610. https://doi.org/10.3390/biomedicines13071610
[34] Wong HJ, Sim B, Teo YH, Teo YN, Chan MY, Yeo LLL, et al.

Efficacy of GLP-1 Receptor Agonists on Weight Loss, BMI, and Waist Circumference for Patients With Obesity or Overweight: A Systematic Review, Meta-analysis, and Meta-regression of 47 Randomized Controlled Trials. Diabetes Care. 2025; 48: 292–300. https://doi.org/10.2337/dc24-1678

[35] Aldawsari M, Almadani FA, Almuhammadi N, Algabsani S, Alamro Y, Aldhwayan M. The Efficacy of GLP-1 Analogues on Appetite Parameters, Gastric Emptying, Food Preference and Taste Among Adults with Obesity: Systematic Review of Randomized Controlled Trials. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2023; 16: 575–595. https://doi.org/10.2147/DMSO.S387116

[36] Beauregard N, McInnis K, Goldfield GS, Doucet É. Energy balance and obesity: the emerging role of glucagon like peptide-1 receptor agonists. Current Opinion in Clinical Nutrition and Metabolic Care. 2024; 27: 472–478. https://doi.org/10.1097/MCO.0000000000001064

[37] Li CI, Samuels DC, Zhao YY, Shyr Y, Guo Y. Power and sample size calculations for high-throughput sequencing-based experiments. Briefings in Bioinformatics. 2018; 19: 1247–1255. https://doi.org/10.1093/bib/bbx061

[38] Kenny TC, Scharenberg S, Abu-Remaileh M, Birsoy K. Cellular and organismal function of choline metabolism. Nature Metabolism. 2025; 7: 35–52. https://doi.org/10.1038/s42255-024-01203-8

[39] Burns BC, Belani JD, Wittorf HN, Brailoiu E, Brailoiu GC. Choline-An Essential Nutrient with Health Benefits and a Signaling Molecule. International Journal of Molecular Sciences. 2025; 26: 7159. https://doi.org/10.3390/ijms26157159

[40] Park CK, Choi SJ, Kim CR, Shin HR, Shin EC, Kim YJ, et al. Ethanolic Extract of Rosa rugosa Roots and Its Bioactive Compound, Oleamide, Prevented Amyloid β-Induced Oxidative Stress and Improved Behavioral Tests in Mice. International Journal of Molecular Sciences. 2025; 26: 4214. https://doi.org/10.3390/ijms26094214

[41] Furuki T, Oku K, Sakurai M. Thermodynamic, hydration and structural characteristics of alpha,alpha-trehalose. Frontiers in Bioscience (Landmark Edition). 2009; 14: 3523–3535. https://doi.org/10.2741/3468

[42] Carta G, Murru E, Banni S, Manca C. Palmitic Acid: Physiological Role, Metabolism and Nutritional Implications. Frontiers in Physiology. 2017; 8: 902. https://doi.org/10.3389/fphys.2017.00902

[43] Hu M, Zhang L, Ruan Z, Han P, Yu Y. The Regulatory Effects of Citrus Peel Powder on Liver Metabolites and Gut Flora in Mice with Non-Alcoholic Fatty Liver Disease (NAFLD). Foods (Basel, Switzerland). 2021; 10: 3022. https://doi.org/10.3390/foods10123022

[44] Wang W, Zhu E, Yang Y, Huang Q, Xiao X, Piao S. An analysis of the intestinal microbiome combined with metabolomics to explore the mechanism of how Pangxiejiao tea improves metabolic disorders in HFFD-treated rats. Frontiers in Nutrition. 2025; 12: 1653855. https://doi.org/10.3389/fnut.2025.1653855

[45] El-Sehrawy AAMA, Mohammed AN, Gupta J, Mohammed JS, Roopashree R, Kashyap A, et al. Combating oxidative stress in non-alcoholic fatty liver disease: From mechanisms to therapeutic strategies. Pathology, Research and Practice. 2025; 272: 156053. https://doi.org/10.1016/j.prp.2025.156053

[46] Svobodová G, Horní M, Velecká E, Boušová I. Metabolic dysfunction-associated steatotic liver disease-induced changes in the antioxidant system: a review. Archives of Toxicology. 2025; 99: 1–22. https://doi.org/10.1007/s00204-024-03889-x

[47] Sutti S, Albano E. Oxidative stress in nonalcoholic fatty liver disease: a reappraisal of the role in supporting inflammatory mechanisms. Redox Experimental Medicine. 2022; 2022: R57–R68. https://doi.org/10.1530/rem-22-0002

[48] Butler MI, Bastiaanssen TFS, Long-Smith C, Morkl S, Berding K, Ritz NL, et al. The gut microbiome in social anxiety disorder: evidence of altered composition and function. Translational Psychiatry. 2023; 13: 95. https://doi.org/10.1038/s41398-023-02325-5

[49] Loomba R, Ling L, Dinh DM, DePaoli AM, Lieu HD, Harrison SA, et al. The Commensal Microbe Veillonella as a Marker for Response to an FGF19 Analog in NASH. Hepatology (Baltimore, Md.). 2021; 73: 126–143. https://doi.org/10.1002/hep.31523

[50] Lemos Junior WJ, Sant'Ana AS, Di Cagno R, Campanaro S, Gobbetti M. Five years after the lactobacillus reclassification: genomic and functional insights into Levilactobacillus, Lacticaseibacillus, Limosilactobacillus, Lactiplantibacillus, and Ligilactobacillus in fermented foods. Trends in Food Science & Technology. 2025; 163: 105118. https://doi.org/10.1016/j.tifs.2025.105118

[51] Li L, Qiu X, Lu S, Yu H, Lu P, Zeng S, et al. The Role of Probiotics Limosilactobacillus reuteri, Ligilactobacillus salivarius, and Lactobacillus johnsonii in Inhibziting Pathogens, Maintaining Gut Health, and Improving Disease Outcomes. International Journal of Molecular Sciences. 2026; 27: 1545. https://doi.org/10.3390/ijms27031545

[52] Dai Z, Lin Y, Chen G, Yu P, Wu H, Ning M, et al. Novel approach for ameliorating high-fat diet-induced syndromes via probiotic-fermented oyster mushroom: from metabolites and microbiota to regulation mechanisms. Food & Function. 2024; 15: 10472–10489. https://doi.org/10.1039/d4fo02142h

[53] Wang Z, Yao W, Sun Y, Han Y, Chen X, Gong P, et al. Eucommia Bark/Leaf Extract Improves Lipid Metabolism Disorders by Affecting Intestinal Microbiota and Microbiome-Host Interaction in HFD Mice. Journal of Agricultural and Food Chemistry. 2023; 71: 3297–3314. https://doi.org/10.1021/acs.jafc.2c07239

[54] Arp G, Levy S, Jiang AK, Dufault-Thompson K, Zhong A, Grant M, et al. SpiR is a gut microbial enzyme that drives cholesterol conversion. Nature Communications. 2026; 17: 3495. https://doi.org/10.1038/s41467-026-70820-6

[55] Yu C, Ahmadi S, Hu X, Wu J, Wu D, Hou Z, et al. Individual Difference in the Capacity of Gut Microbiota to Ferment Four Complex Carbohydrates from Normal to Overweight People: An In Vitro Study. Journal of Agricultural and Food Chemistry. 2024; 72: 20513–20526. https://doi.org/10.1021/acs.jafc.4c05864

[56] Li Y, Gao J, Xue Y, Sun R, Sun X, Sun Z, et al. Nutrient availability of roughages in isocaloric and isonitrogenous diets alters the bacterial networks in the whole gastrointestinal tract of Hu sheep. BMC Microbiology. 2023; 23: 70. https://doi.org/10.1186/s12866-023-02814-z

[57] Lin X, Hu T, Wu Z, Li L, Wang Y, Wen D, et al. Isolation of potentially novel species expands the genomic and functional diversity of Lachnospiraceae. IMeta. 2024; 3: e174. https://doi.org/10.1002/imt2.174

[58] Li H, Ma L, Li Z, Yin J, Tan B, Chen J, et al. Evolution of the Gut Microbiota and Its Fermentation Characteristics of Ningxiang Pigs at the Young Stage. Animals. 2021; 11: 638. https://doi.org/10.3390/ani11030638

[59] Lynch JB, Gonzalez EL, Choy K, Faull KF, Jewell T, Arellano A, et al. Gut microbiota Turicibacter strains differentially modify bile acids and host lipids. Nature Communications. 2023; 14: 3669. https://doi.org/10.1038/s41467-023-39403-7

[60] Klag K, Ott D, Tippetts TS, Nicolson RJ, Tatum SM, Bauer KM, et al. Dietary fat disrupts a commensal-host lipid network that promotes metabolic health. Cell Metabolism. 2026; 38: 157–173.e9. https://doi.org/10.1016/j.cmet.2025.10.007

[61] Wu G, Zhao N, Zhang C, Lam YY, Zhao L. Guild-based analysis for understanding gut microbiome in human health and diseases. Genome Medicine. 2021; 13: 22. https://doi.org/10.1186/s13073-021-00840-y