Woody International Publish Limited
An Multidisciplinary Academic Journal Publisher

Journal of Theory and Practice in Clinical Sciences, Volume 2, 2025
https://www.woodyinternational.com/

Gut Microbiota Modulation by High Fiber Diet Implications for Glucose Homeostasis and Inflammation in Type 2 Diabetes

James R. Fletcher[1a]*, Emily K. Thompson[1], Daniel J. Carter[1], Sophie L. Harris[2]

[1]University of Liverpool, Faculty of Science and Engineering, School of Life Sciences, Liverpool, UK
[2]University of Manchester, Faculty of Biology, Medicine and Health, School of Biological Sciences, Manchester, UK
[a]*j.fletcher@gmail.com*
**Author to whom correspondence should be addressed.*

Abstract: ***High-fiber diets have been widely studied for their benefits in managing type 2 diabetes (T2DM). However, the detailed molecular mechanisms by which they regulate glucose balance through gut microbiota remain unclear. This study uses metagenomic and metabolomic methods to examine the effects of a high-fiber diet on gut microbiota composition, short-chain fatty acid (SCFA) levels, and inflammation-related factors in a T2DM mouse model. Results show that a high-fiber diet improves glucose balance by increasing beneficial bacteria such as Bifidobacterium and Lactobacillus, which are linked to anti-inflammatory effects, while reducing harmful bacteria like Escherichia. These findings provide scientific evidence for the use of high-fiber diets in diabetes management and highlight their potential role in metabolic health.***

Keywords: Gut microbiota; High-fiber diet; Diabetes management; Glucose balance; Metabolic regulation.

Cited as: R. Fletcher, J., K. Thompson, E., J. Carter, D., & L. Harris, S. (2025). Gut Microbiota Modulation by High Fiber Diet Implications for Glucose Homeostasis and Inflammation in Type 2 Diabetes . *Journal of Theory and Practice in Clinical Sciences*, *2*, 48–53. Retrieved from https://woodyinternational.com/index.php/jtpcs/article/view/184.

1. Introduction

Diabetes is a long-term metabolic disorder that is increasing worldwide, significantly affecting health and quality of life. Among various types, type 2 diabetes (T2DM) is the most common and is closely linked to insulin resistance, pancreatic β-cell dysfunction, and metabolic imbalances [1]. Recent studies suggest that gut microbiota plays a key role in maintaining metabolic stability and imbalances in gut bacteria are strongly associated with T2DM development [2]. Dietary fiber is a type of carbohydrate that cannot be digested by human enzymes but can be broken down by gut bacteria. Research has shown that high-fiber diets help control blood sugar and improve metabolism in T2DM patients, but the underlying mechanisms are not fully understood [3]. Increasing evidence suggests that these diets may support blood sugar control by modifying gut microbiota composition and function [4]. However, the exact molecular pathways involved require further investigation [5]. This study explores how a high-fiber diet affects gut microbiota, SCFA production, and inflammation-related factors in a T2DM mouse model using metagenomic and metabolomic analysis. The findings provide insights into the role of high-fiber diets in diabetes management and their potential for improving metabolic health.

2. Materials and Methods

2.1 Experimental Animals

Male C57BL/6 mice (6 weeks old) were obtained from a certified animal supplier. They were housed under controlled conditions with a temperature of (22±2)°C and a relative humidity of (50±5)%, with free access to food and water. After a one-week adaptation period, the experiment was conducted.

2.2 Establishment of the Diabetic Mouse Model

Mice were randomly assigned to either a normal control group (NC) or a diabetes model group (DM). The DM group was fed a high-fat diet (HFD) for four weeks, followed by intraperitoneal injections of streptozotocin (STZ, 35mg/kg) for five consecutive days to induce type 2 diabetes (T2DM). The NC group received a standard diet. After modeling, fasting blood glucose (FBG) and an oral glucose tolerance test (OGTT) were performed to confirm diabetes induction [6]. Mice with FBG ≥11.1 mmol/L and OGTT 2-hour glucose ≥16.7 mmol/L were considered successfully modeled as T2DM.

2.3 Grouping and Dietary Intervention

Mice with confirmed T2DM were randomly divided into a diabetes control group (DMC) and a high-fiber diet intervention group (HFD + HF). The DMC group remained on a high-fat diet, while the HFD + HF group received the same diet supplemented with 10% (w/w) dietary fiber (inulin). The NC group continued with a standard diet. The intervention lasted eight weeks.

2.4 Sample Collection

At the end of the intervention, mice were fasted for 12 hours. Blood was collected from the orbital sinus, and serum was separated for glucose, insulin, and inflammatory marker analysis. The mice were then euthanized, and colonic contents were collected for gut microbiota profiling and short-chain fatty acid (SCFA) analysis. Colonic tissues were also harvested to assess mRNA expression of inflammatory factors [7].

2.5 Gut Microbiota Analysis

Gut microbiota composition in colonic contents was analyzed using metagenomic sequencing. Total DNA was extracted, and the V3-V4 region of the 16S rRNA gene was amplified for sequencing. QIIME2 software was used to process sequencing data and assess microbial diversity, including alpha diversity (e.g., Chao1 index, Shannon index) and beta diversity (e.g., Bray-Curtis distance) [8]. Taxonomic classification and relative abundance were also analyzed.

2.6 Measurement of Short-Chain Fatty Acids

Short-chain fatty acids (acetic acid, propionic acid, and butyric acid) in colonic contents were quantified using gas chromatography-mass spectrometry (GC-MS). After acidification, SCFAs were extracted with diethyl ether, followed by dehydration with anhydrous sodium sulfate before GC-MS analysis [9]. Standard curves were used to calculate SCFA concentrations.

2.7 Analysis of Inflammatory Markers

Serum levels of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were measured using enzyme-linked immunosorbent assay (ELISA) [10]. The mRNA expression levels of IL-6, TNF-α, and nuclear factor-κB (NF-κB) in colonic tissue were determined by real-time quantitative PCR (qRT-PCR).

2.8 Statistical Analysis

Data were analyzed using SPSS 22.0 software. Results were expressed as mean ± standard deviation (x±s). One-way analysis of variance (ANOVA) was used for comparisons among groups, and the least significant difference (LSD) t-test was applied for pairwise comparisons. A value of $P < 0.05$ was considered statistically significant.

3. Experimental Results

3.1 Effects of High-Fiber Diet on Blood Glucose Regulation in T2DM Mice

Table 1: Blood Glucose Levels in Different Groups

Group	FBG (mmol/L)	OGTT 2 h Glucose (mmol/L)
NC	5.32±0.45	8.25±0.68
DMC	13.56±1.23	20.12±1.56
HFD + HF	10.25±0.98	15.34±1.12

Compared with the NC group, the DMC group showed a significant increase in FBG and OGTT 2-hour glucose levels ($P < 0.01$), confirming the successful establishment of the T2DM model. In contrast, the HFD + HF group had significantly lower FBG and OGTT 2-hour glucose levels than the DMC group ($P < 0.05$), indicating that a high-fiber diet improved blood glucose regulation in T2DM mice. The data are presented in Table 1.

3.2 Effects of High-Fiber Diet on Gut Microbiota in T2DM Mice

3.2.1 Alpha Diversity Analysis

Chao1 and Shannon index analysis showed that gut microbiota richness and diversity were significantly lower in the DMC group than in the NC group ($P < 0.01$). In contrast, these indices were significantly higher in the HFD + HF group than in the DMC group ($P < 0.05$), suggesting that the high-fiber diet improved gut microbiota diversity in T2DM mice [11]. The data are shown in Table 2.

Table 2: Alpha Diversity Indices of Gut Microbiota

Group	Chao1 Index	Shannon Index
NC	356.23±25.34	4.25±0.32
DMC	289.45±20.12	3.15±0.25
HFD + HF	325.67±22.45	3.86±0.28

3.2.2 Beta Diversity Analysis

Principal coordinate analysis (PCoA) based on Bray-Curtis distance showed clear differences in gut microbiota composition among the NC, DMC, and HFD + HF groups. The microbiota composition in the DMC group was distinct from that of the NC group, while the HFD + HF group showed a partial shift toward the NC group, indicating that the high-fiber diet altered gut microbiota composition in T2DM mice, making it more similar to that of healthy controls [12,13].

3.2.3 Relative Abundance of Key Bacterial Genera

At the genus level, compared with the NC group, the DMC group had significantly lower levels of *Bifidobacterium* and *Lactobacillus* ($P < 0.01$) and higher levels of *Escherichia* ($P < 0.01$) [14,15]. The HFD + HF group had significantly higher *Bifidobacterium* and *Lactobacillus* levels and lower *Escherichia* levels than the DMC group ($P < 0.05$). The data are shown in Table 3.

Table 3: Relative Abundance of Key Gut Microbiota Genera (%)

Group	Bifidobacterium (%)	Lactobacillus (%)	Escherichia (%)
NC	12.56±1.56	8.45±1.23	3.25±0.56
DMC	5.34±0.89	3.12±0.67	8.67±1.02
HFD + HF	8.67±1.12	5.67±0.98	5.23±0.89

3.3 Effects of High-Fiber Diet on Short-Chain Fatty Acid (SCFA) Levels

Compared with the NC group, the DMC group had significantly lower levels of acetic acid, propionic acid and butyric acid in the colonic contents ($P < 0.01$). However, these SCFA levels were significantly higher in the HFD + HF group than in the DMC group ($P < 0.05$). The data are shown in Table 4.

Table 4: SCFA Levels in Colonic Contents (μmol/g)

Group	Acetic Acid	Propionic Acid	Butyric Acid
NC	120.56±10.23	45.67±5.67	30.23±4.56
DMC	78.45±8.90	25.34±3.45	18.67±3.01
HFD + HF	98.67±9.56	35.45±4.32	25.34±3.89

3.4 Effects of High-Fiber Diet on Inflammatory Markers

3.4.1 Serum Inflammatory Marker Levels

ELISA results showed that IL-6 and TNF-α levels were significantly higher in the DMC group than in the NC group ($P < 0.01$). However, these levels were significantly lower in the HFD + HF group than in the DMC group

($P < 0.05$). The data are shown in Table 5.

Table 5: Serum Inflammatory Marker Levels (pg/mL)

Group	IL-6	TNF-α
NC	15.34±2.34	20.56±2.89
DMC	35.67±3.56	45.89±4.56
HFD + HF	25.34±3.01	32.56±3.56

3.4.2 mRNA Expression of Inflammatory Markers in Colonic Tissue

qRT-PCR results showed that IL-6, TNF-α, and NF-κB mRNA expression levels in colonic tissue were significantly higher in the DMC group than in the NC group ($P < 0.01$) [16]. However, these expression levels were significantly lower in the HFD + HF group than in the DMC group ($P < 0.05$). The data are shown in Table 6.

Table 6: Relative mRNA Expression Levels of Inflammatory Markers in Colonic Tissue

Group	IL-6 mRNA	TNF-α mRNA	NF-κB mRNA
NC	1.00±0.12	1.00±0.15	1.00±0.10
DMC	3.56±0.34	4.23±0.45	3.89±0.32
HFD + HF	2.12±0.25	2.89±0.38	2.56±0.28

These findings suggest that a high-fiber diet reduced inflammation in T2DM mice by lowering both serum and colonic inflammatory marker levels.

4. Discussion

This study used a T2DM mouse model to examine how a high-fiber diet affects gut microbiota, SCFA levels and inflammatory markers. The findings suggest that dietary fiber may help manage diabetes by improving gut microbiota balance. Gut microbiota plays a key role in metabolism [17,18]. People with T2DM often have imbalances in gut bacteria, including reduced microbial diversity, fewer beneficial bacteria and more harmful bacteria [19,20,21]. In this study, T2DM mice showed a significant decrease in the Chao1 and Shannon indices, indicating lower microbial richness and diversity. The relative abundance of *Bifidobacterium* and *Lactobacillus* also declined, while *Escherichia* increased. These results align with previous studies [22,23,24,25]. After high-fiber diet intervention, microbial richness and diversity improved. Beneficial bacteria increased, while harmful bacteria decreased, suggesting that a high-fiber diet helps restore a healthier gut microbiota.

Dietary fiber is fermented in the gut to produce SCFAs, including acetic acid, propionic acid, and butyric acid [26,27]. These compounds provide energy to gut cells and influence metabolism and immunity. This study found that SCFA levels were lower in T2DM mice but increased after dietary intervention. SCFAs may support glucose regulation by improving insulin sensitivity, reducing gluconeogenesis and influencing fat metabolism [28,29]. They also have anti-inflammatory effects, helping to lower inflammation in the gut.

Chronic inflammation is a key factor in T2DM. Higher levels of inflammatory markers such as IL-6 and TNF-α contribute to insulin resistance and damage pancreatic β-cells. This study found that T2DM mice had increased IL-6, TNF-α, and NF-κB levels in both serum and colonic tissue. However, these levels significantly decreased after a high-fiber diet. This suggests that dietary fiber helps regulate gut bacteria, boost SCFA production and reduce inflammation, which may improve insulin sensitivity and support diabetes management [30,31]. Overall, this study shows that a high-fiber diet improves glucose regulation in T2DM mice by modifying gut microbiota, increasing SCFA levels, and reducing inflammation. These findings provide evidence that dietary fiber may be a useful approach to diabetes management. However, this study has limitations. Since it was conducted in mice, further clinical research is needed to confirm whether the effects apply to humans. Additionally, the exact molecular pathways linking gut microbiota, metabolism, and diabetes need further investigation.

5. Conclusion

This study used metagenomic and metabolomic methods to explore how a high-fiber diet affects gut microbiota, SCFA levels, and inflammation in T2DM mice. The results showed that a high-fiber diet improved glucose

regulation, increased gut microbiota diversity, adjusted bacterial composition, raised SCFA levels, and reduced inflammation. These findings provide a scientific basis for using dietary fiber in diabetes management and highlight its potential for developing new treatment strategies targeting gut microbiota.

References

[1] Khin, P. P., Lee, J. H., & Jun, H. S. (2023). Pancreatic beta-cell dysfunction in type 2 diabetes. European Journal of Inflammation, 21, 1721727X231154152.

[2] Ortega, M. A., Fraile-Martínez, O., Naya, I., García-Honduvilla, N., Álvarez-Mon, M., Buján, J., ... & de la Torre, B. (2020). Type 2 diabetes mellitus associated with obesity (diabesity). The central role of gut microbiota and its translational applications. Nutrients, 12(9), 2749.

[3] Bulsiewicz, W. J. (2023). The importance of dietary fiber for metabolic health. American Journal of Lifestyle Medicine, 17(5), 639-648.

[4] Wang, Y., Wen, Y., Wu, X., & Cai, H. (2024). Application of Ultrasonic Treatment to Enhance Antioxidant Activity in Leafy Vegetables. International Journal of Advance in Applied Science Research, 3, 49-58.

[5] Qin, C., Yang, S., Chu, Y. H., Zhang, H., Pang, X. W., Chen, L., ... & Wang, W. (2022). Signaling pathways involved in ischemic stroke: molecular mechanisms and therapeutic interventions. Signal transduction and targeted therapy, 7(1), 215.

[6] Wilson, R. D., & Islam, M. S. (2012). Fructose-fed streptozotocin-injected rat: an alternative model for type 2 diabetes. Pharmacological reports, 64(1), 129-139.

[7] Wang, Y., Shen, M., Wang, L., Wen, Y., & Cai, H. (2024). Comparative Modulation of Immune Responses and Inflammation by n-6 and n-3 Polyunsaturated Fatty Acids in Oxylipin-Mediated Pathways.

[8] Christensen, H., Andersson, J., Jørgensen, S. L., & Vogt, J. K. (2023). 16S rRNA Amplicon Sequencing. In Introduction to bioinformatics in microbiology (pp. 153-181). Cham: Springer International Publishing.

[9] Wang, H., Liu, Y., Shao, J., Luo, Y., Cai, W., & Chen, L. (2020). Rapid and accurate simultaneous determination of seven short-chain fatty acids in feces by gas chromatography–mass spectrometry (GC-MS): application in type 2 diabetic rats and drug therapy. Analytical Letters, 53(14), 2320-2336.

[10] Wang, Y., Wen, Y., Wu, X., Wang, L., & Cai, H. (2024). Modulation of Gut Microbiota and Glucose Homeostasis through High-Fiber Dietary Intervention in Type 2 Diabetes Management.

[11] Zhang, Y., Dong, A., Xie, K., & Yu, Y. (2019). Dietary supplementation with high fiber alleviates oxidative stress and inflammatory responses caused by severe sepsis in mice without altering microbiome diversity. Frontiers in Physiology, 9, 1929.

[12] Wang, Y., Wang, L., Wen, Y., Wu, X., & Cai, H. (2025). Precision-Engineered Nanocarriers for Targeted Treatment of Liver Fibrosis and Vascular Disorders.

[13] Qu, G., Hou, S., Qu, D., Tian, C., Zhu, J., Xue, L., ... & Zhang, C. (2019). Self-assembled micelles based on N-octyl-N'-phthalyl-O-phosphoryl chitosan derivative as an effective oral carrier of paclitaxel. Carbohydrate polymers, 207, 428-439.

[14] Łaniewski, P., Cui, H., Roe, D. J., Chase, D. M., & Herbst-Kralovetz, M. M. (2020). Vaginal microbiota, genital inflammation, and neoplasia impact immune checkpoint protein profiles in the cervicovaginal microenvironment. NPJ precision oncology, 4(1), 22.

[15] Xu, K., Xu, X., Wu, H., & Sun, R. (2024). Venturi Aeration Systems Design and Performance Evaluation in High Density Aquaculture.

[16] Pavoković, D., Košpić, K., Panić, M., Redovniković, I. R., & Bubalo, M. C. (2020). Natural deep eutectic solvents are viable solvents for plant cell culture-assisted stereoselective biocatalysis. Process Biochemistry, 93, 69-76.

[17] Yusoff, I. M., Taher, Z. M., Rahmat, Z., & Chua, L. S. (2022). A review of ultrasound-assisted extraction for plant bioactive compounds: Phenolics, flavonoids, thymols, saponins and proteins. Food research international, 157, 111268.

[18] Xu, K., Mo, X., Xu, X., & Wu, H. (2022). Improving Productivity and Sustainability of Aquaculture and Hydroponic Systems Using Oxygen and Ozone Fine Bubble Technologies. Innovations in Applied Engineering and Technology, 1-8.

[19] Gouda, M., Bekhit, A. E. D., Tang, Y., Huang, Y., Huang, L., He, Y., & Li, X. (2021). Recent innovations of ultrasound green technology in herbal phytochemistry: A review. Ultrasonics Sonochemistry, 73, 105538.

[20] Xu, K., Xu, X., Wu, H., Sun, R., & Hong, Y. (2023). Ozonation and Filtration System for Sustainable Treatment of Aquaculture Wastewater in Taizhou City. Innovations in Applied Engineering and Technology, 1-7.

[21] Xu, K., Mo, X., Xu, X., & Wu, H. (2022). Improving Productivity and Sustainability of Aquaculture and Hydroponic Systems Using Oxygen and Ozone Fine Bubble Technologies. Innovations in Applied Engineering and Technology, 1-8.
[22] Wang, Y., Wen, Y., Wu, X., Wang, L., & Cai, H. (2025). Assessing the Role of Adaptive Digital Platforms in Personalized Nutrition and Chronic Disease Management.
[23] Hong, J., Fu, T., Liu, W., Du, Y., Min, C., & Lin, D. (2022). Specific alterations of gut microbiota in diabetic microvascular complications: A systematic review and meta-analysis. Frontiers in Endocrinology, 13, 1053900.
[24] Qiao, J. B., Fan, Q. Q., Xing, L., Cui, P. F., He, Y. J., Zhu, J. C., ... & Jiang, H. L. (2018). Vitamin A-decorated biocompatible micelles for chemogene therapy of liver fibrosis. Journal of Controlled Release, 283, 113-125.
[25] Wang, Y., Wen, Y., Wu, X., & Cai, H. (2024). Comprehensive Evaluation of GLP1 Receptor Agonists in Modulating Inflammatory Pathways and Gut Microbiota.
[26] Wang, M., Wichienchot, S., He, X., Fu, X., Huang, Q., & Zhang, B. (2019). In vitro colonic fermentation of dietary fibers: Fermentation rate, short-chain fatty acid production and changes in microbiota. Trends in food science & technology, 88, 1-9.
[27] Zhu, J., Xie, R., Gao, R., Zhao, Y., Yodsanit, N., Zhu, M., ... & Gong, S. (2024). Multimodal nanoimmunotherapy engages neutrophils to eliminate Staphylococcus aureus infections. Nature Nanotechnology, 1-12.
[28] Canfora, E. E., Jocken, J. W., & Blaak, E. E. (2015). Short-chain fatty acids in control of body weight and insulin sensitivity. Nature Reviews Endocrinology, 11(10), 577-591.
[29] Lee, I. K., Xie, R., Luz-Madrigal, A., Min, S., Zhu, J., Jin, J., ... & Ma, Z. (2023). Micromolded honeycomb scaffold design to support the generation of a bilayered RPE and photoreceptor cell construct. Bioactive Materials, 30, 142-153.
[30] Mazhar, M., Zhu, Y., & Qin, L. (2023). The interplay of dietary fibers and intestinal microbiota affects type 2 diabetes by generating short-chain fatty acids. Foods, 12(5), 1023.
[31] Gowd, V., Xie, L., Zheng, X., & Chen, W. (2019). Dietary fibers as emerging nutritional factors against diabetes: focus on the involvement of gut microbiota. Critical reviews in biotechnology, 39(4), 524-540.