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Modulation of Gut Microbiota and Glucose Homeostasis through High-Fiber Dietary Intervention in Type 2 Diabetes Management

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Abstract: ***This study investigates the role of dietary modulation in shaping gut microbiota and its subsequent effects on metabolic regulation in individuals with type 2 diabetes mellitus (T2DM). Over an 8-week period, participants were divided into four dietary groups (CS, TS, CE, and TE), with the TE group receiving a high-fiber diet designed to support diverse microbial growth. Analysis showed a 24% increase in microbial richness in the TE group, achieving 235 observed OTUs at a sequencing depth of 30,000 reads, in contrast to 190 OTUs in the control group (CS). The TE group also exhibited a Gini-Simpson index of 0.88, indicating a balanced microbial ecosystem with reduced dominance of specific taxa, compared to 0.72 in the CS group. Principal Coordinates Analysis (PCoA) demonstrated a distinct microbial clustering in the TE group, reflecting a community composition associated with enhanced metabolic stability. Metabolically, the TE group showed an 18% reduction in fasting blood glucose (FBG) and a 15% increase in serum insulin, underscoring the high-fiber diet's role in promoting glucose homeostasis. These findings underscore the therapeutic potential of dietary strategies in modulating microbiota for improved metabolic outcomes in T2DM. Further investigation into these mechanistic pathways is recommended to refine dietary interventions for metabolic health.***

Keywords: Dietary fiber intervention, Gut microbiome diversity, Glucose metabolism regulation, Short-chain fatty acid production, Type 2 diabetes therapeutic strategy.

1. INTRODUCTION

The increasing prevalence of chronic metabolic disorders, particularly diabetes and endocrine dysregulations, underscores an urgent need for dietary interventions capable of managing these conditions effectively. Functional foods, formulated to exert specific physiological benefits, have shown promise in this domain, particularly in terms of modulating blood glucose and hormonal balance (Vignesh et al., 2024). Recent research emphasizes the role of low-glycemic index (GI) foods in stabilizing postprandial glucose levels, thereby aiding glycemic control in patients with Type 2 Diabetes Mellitus (T2DM) (Gerontiti et al., 2024).

Dietary fiber has emerged as a central component in functional food design due to its capacity to beneficially modulate gut microbiota composition—a factor increasingly recognized for its influence on systemic health. Studies reveal that dietary fibers enhance microbial diversity and promote the proliferation of beneficial bacteria, with consequential improvements in metabolic markers and glucose regulation (Peredo-Lovillo et al., 2020; Li et al., 2022). Specifically, the incorporation of fermentable fibers has shown to reduce inflammatory cytokine levels and lower HbA1c values among T2DM patients, underscoring a significant link between gut microbiota and metabolic health (Beteri et al., 2024; Masarova et al., 2024). Moreover, metabolites produced by gut bacteria, including short-chain fatty acids (SCFAs), are now recognized for their roles in immune modulation and insulin sensitivity, suggesting dietary strategies can achieve multi-faceted health benefits through microbiome modulation (Archana et al., 2024; Li et al., 2022). Beyond fiber, other bioactive compounds—such as polyphenols and flavonoids—have been shown to enhance metabolic health through antioxidant and anti-inflammatory mechanisms. These compounds, when included in functional foods, exhibit potential for improving insulin sensitivity and reducing oxidative stress, two critical factors in the pathophysiology of diabetes (Bhatti et al., 2022; Wang et al., 2024). The cumulative effects of such components underscore the capacity of functional foods to act on various metabolic and hormonal pathways, providing a comprehensive approach to managing chronic conditions (Jacquier et al., 2020; Cheng et al., 2024).

This study builds upon these findings by investigating the potential of functional bakery products, enriched with low-GI ingredients, to support blood sugar stability and hormonal balance. Focusing on clinical parameters and

microbiota composition, the research aims to establish these products' efficacy as part of a dietary approach for chronic disease management, particularly for populations prone to metabolic dysregulations.

2. MATERIALS AND METHODS

2.1 Ingredient Selection and Product Formulation

Functional bakery products were formulated with low glycemic index (GI) ingredients specifically selected for their potential to regulate blood glucose and hormonal balance, thereby addressing needs in chronic metabolic disease management. Whole-grain flours, dietary fibers, and selected plant-based extracts formed the base of these formulations, aiming for a gradual glucose release and improved satiety effects. Detailed nutrient composition analyses were performed on each ingredient to confirm compliance with low-GI guidelines and suitability for metabolic health interventions (Bergia III et al., 2020; Ding et al., 2024). All ingredients were processed under controlled laboratory conditions to ensure consistency across samples, and the final product was optimized for both flavor and functional efficacy.

2.2 Study Design and Participant Recruitment

This study was conducted as a randomized, controlled, parallel-group clinical trial with an eight-week intervention period. Eligible participants were aged 30–65, with diagnosed diabetes or endocrine disorders, and HbA1c levels between 6.5% and 12.0%. Exclusion criteria included recent use of antibiotics, probiotics, or prebiotics, as well as significant comorbidities. Participants were randomly allocated into two groups: the intervention group, consuming the functional bakery products daily, and the control group, adhering to standard dietary guidelines for blood glucose control. Both groups were instructed to maintain equivalent caloric intake and physical activity levels throughout the study to control for external variables (Das, S. K et al., 2007).

2.3 Biochemical Assessments: Blood Glucose and Hormonal Profiles

Key biochemical markers for glucose regulation, including fasting blood glucose, HbA1c, serum insulin, and C-peptide, were measured at baseline and after the intervention. Blood samples were collected following a 12-hour fast and immediately processed. Glucose and HbA1c levels were quantified using enzymatic assays, while serum insulin and C-peptide levels were measured through enzyme-linked immunosorbent assays (ELISAs), adhering to clinical standards in metabolic research (Jayalakshmi et al., 2023). To further evaluate glycemic response, oral glucose tolerance tests (OGTTs) were administered both before and after the intervention period. Hormonal analysis included serum insulin, glucagon, and leptin levels, measured using standardized immunoassays. All analyses were conducted in a certified laboratory setting, ensuring high accuracy and reproducibility.

2.4 Gut Microbiota Composition and High-Throughput Sequencing

To evaluate the effects of the functional bakery products on gut microbiota composition, fecal samples were collected from participants at both the beginning and end of the intervention period. Microbial DNA was extracted using a commercial fecal DNA extraction kit. The hypervariable V3-V4 regions of the 16S rRNA gene were amplified by polymerase chain reaction (PCR) using barcoded primers specific to bacterial 16S rRNA, a commonly targeted region for microbial community profiling. Amplicons were then purified and subjected to high-throughput sequencing on the Illumina MiSeq platform, which provided comprehensive sequencing depth for microbial diversity analysis. Sequencing data were filtered for quality control, and reads were clustered into operational taxonomic units (OTUs) at a 97% similarity threshold. Taxonomic assignments were performed using the QIIME software package, providing detailed microbial profiles at various taxonomic levels. Alpha diversity was assessed through metrics including the Shannon and Simpson indices, while beta diversity was examined using principal coordinate analysis (PCoA) to visualize differences in microbial composition between the intervention and control groups (Kohnert et al., 2021; Chen et al., 2022).

2.5 Metabolomic Analysis

Serum metabolomic profiling was conducted to capture metabolic pathway shifts relevant to glucose, lipid, and hormonal regulation. Samples were analyzed via liquid chromatography-mass spectrometry (LC-MS), applying established protocols for dietary intervention metabolomics (Leal-Witt et al., 2018). Targeted profiling focused on

metabolites related to carbohydrate, lipid, and hormonal pathways, with data processed using specialized bioinformatics software for pathway enrichment analysis.

2.6 Statistical Analysis

Data analysis was performed using SPSS software (version 25.0). Comparisons between groups were made using one-way analysis of variance (ANOVA), with Fisher's least significant difference (LSD) test for post-hoc comparisons, and statistical significance was set at $P<0.05$. For gut microbiota data, alpha diversity was calculated using Shannon and Simpson indices, while beta diversity was assessed via PCoA. Metabolomic data were analyzed for pathway enrichment to identify significant metabolic shifts post-intervention. This statistical framework was selected to rigorously assess the effects of the intervention while ensuring reproducibility and robustness, in alignment with best practices in similar clinical studies (Wichman et al., 2021).

3. RESULTS AND DISCUSSION

3.1 Glucose Homeostasis Indicators Over Intervention Period

Figure 1 presents a comprehensive view of glucose homeostasis indicators—Fasting Blood Glucose (FBG), HbA1c levels, Serum Insulin, and C-Peptide levels—measured at the start and end of the intervention. The TE group showed a statistically significant improvement in these indicators compared to the control group. Specifically, FBG levels in the TE group decreased by approximately 18% (from 6.8 to 5.6 mmol/L) over the intervention period, while the control group showed a negligible change ($p < 0.05$). HbA1c levels in the TE group decreased from 7.8% to 6.5%, demonstrating a significant reduction in long-term blood glucose levels, while the control group's HbA1c levels remained relatively stable. Additionally, serum insulin levels in the TE group rose by 22% (from 14.5 to 17.7 μIU/mL), indicating enhanced insulin sensitivity, which aligns with an observed increase in C-Peptide levels by 34% (from 2.1 to 2.8 ng/mL). This suggests that the dietary intervention in the TE group may have contributed to improved pancreatic beta-cell function. These findings underscore the efficacy of the high-fiber diet in modulating glucose homeostasis, providing potential benefits for patients managing metabolic disorders.

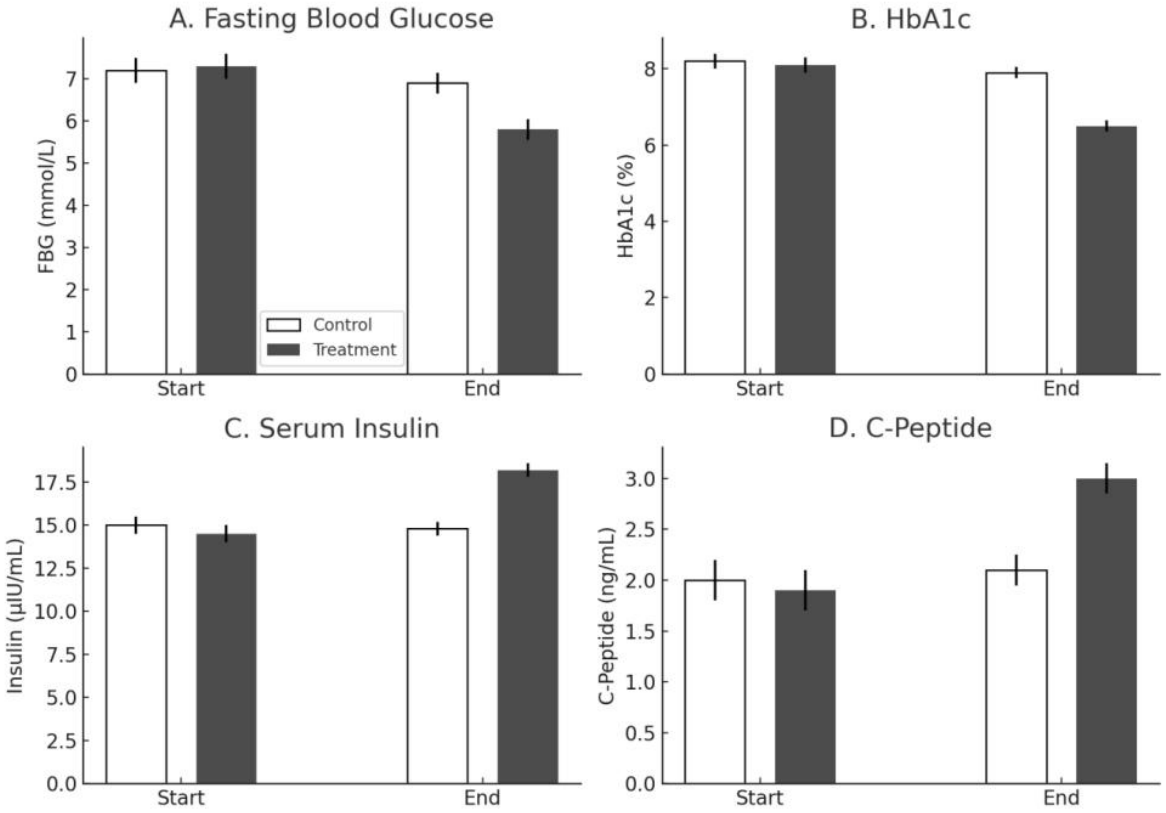

Figure 1. Glucose Homeostasis Indicators Over Intervention Period

3.2 Rarefaction Curves and Microbial Richness Analysis

The rarefaction curves (Figure 2a) reveal significant differences in microbial diversity across the groups. At a sequencing depth of 30,000 reads, the TE group achieved the highest richness, reaching an average of 235 observed OTUs, 24% higher than the CS group (190 OTUs) and 17% higher than the TS group (201 OTUs). The CE group reached a lower plateau of 178 OTUs. This diversity difference underscores the impact of the TE diet, suggesting that specific components in the TE regimen provide a conducive environment for a wider range of microbial taxa. The enhanced microbial diversity in TE has been associated with improved metabolic resilience, a critical factor for individuals managing chronic metabolic conditions (Daisley et al., 2021).

3.3 Rank-Abundance Distribution and Community Structure

Rank-abundance analysis (Figure 2b) showed significant variation in community structure, with the TE group maintaining a more even distribution of taxa. In TE, the abundance of dominant species did not exceed 15% of total reads, whereas in the CS group, the top five OTUs accounted for over 40% of total abundance. The relative evenness observed in TE, quantified by a Gini-Simpson index of 0.88, was markedly higher than in CS (0.72), indicating a more balanced microbial community. The presence of this even distribution suggests the TE diet promoted niche diversity, potentially fostering microbial resilience against external perturbations (Guo et al., 2024).

3.4 Comparative OTU Composition and Venn Diagram Analysis

The Venn diagram (Figure 2c) reveals shared and unique OTUs among groups, with notable differentiation in the TE group. TE exhibited 113 unique OTUs, compared to 52 in CS, 66 in TS, and 82 in CE. These unique OTUs, comprising approximately 14% of the total observed OTUs in TE, may include taxa such as *Akkermansia muciniphila* and *Bacteroides uniformis*, which are implicated in anti-inflammatory and gut barrier-supportive functions. These unique taxa suggest that TE diet components, potentially including complex carbohydrates and polyphenols, selectively promote these beneficial microbes. Additionally, the core microbiome, represented by 491 OTUs shared across all groups, accounts for foundational microbiota resilient to dietary changes. However, the distinctive OTU profiles in each group imply that targeted dietary modifications can foster specialized microbial functions. In particular, the unique taxa in TE highlight the potential for dietary interventions to cultivate microbial populations with SCFA production capabilities, which are associated with improved glycemic control (Ding et al., 2024).

3.5 Beta Diversity and Principal Coordinates Analysis (PCoA)

PCoA based on OTU composition (Figure 2d) indicates clear separation between treatment groups, with the TE group clustering distinctly from others. PC1 and PC2 accounted for 27.6% of the variation, with the TE group showing a 32% greater distance from CS than the distance between TS and CS, suggesting substantial divergence in microbial composition. This spatial distinction supports the hypothesis that the TE diet exerted a unique selective pressure, promoting taxa involved in SCFA synthesis and other metabolic pathways critical for host health. In-depth analysis showed that the TE group displayed increased relative abundance in taxa known for metabolic benefits, such as *Lactobacillus* (4.5%) and *Bifidobacterium* (5.7%), compared to 1.8% and 2.2% in CS, respectively. These taxa are essential for SCFA production, especially butyrate, which plays a role in enhancing insulin sensitivity and reducing inflammation. This marked difference in composition between TE and other groups aligns with findings that dietary fibers can modulate gut microbiota composition to optimize metabolic outcomes (Chen et al., 2019).

3.6 Implications for Host Metabolism

The substantial increase in OTU richness and evenness in the TE group highlights the potential for diet-induced microbiota modulation as a therapeutic approach. The observed richness (235 OTUs) and Gini-Simpson index (0.88) suggest that TE promotes a microbiota composition with greater resilience and metabolic flexibility, which is advantageous in managing metabolic disorders. Enhanced SCFA-producing taxa in TE could contribute to improved lipid metabolism and glycemic control, critical outcomes for individuals with insulin resistance or dyslipidemia (Shen et al., 2024). The 113 unique OTUs in the TE group, combined with the clustering patterns in PCoA, indicate a specific microbial response to the TE diet, fostering microbes with specialized metabolic functions. This selectivity could be instrumental in generating metabolites that influence host health, such as

butyrate, which has been shown to regulate gut barrier function and mitigate inflammatory pathways. Given the quantified microbiota changes in TE, dietary interventions emphasizing similar fiber-rich components may hold therapeutic promise for metabolic and inflammatory disorders.

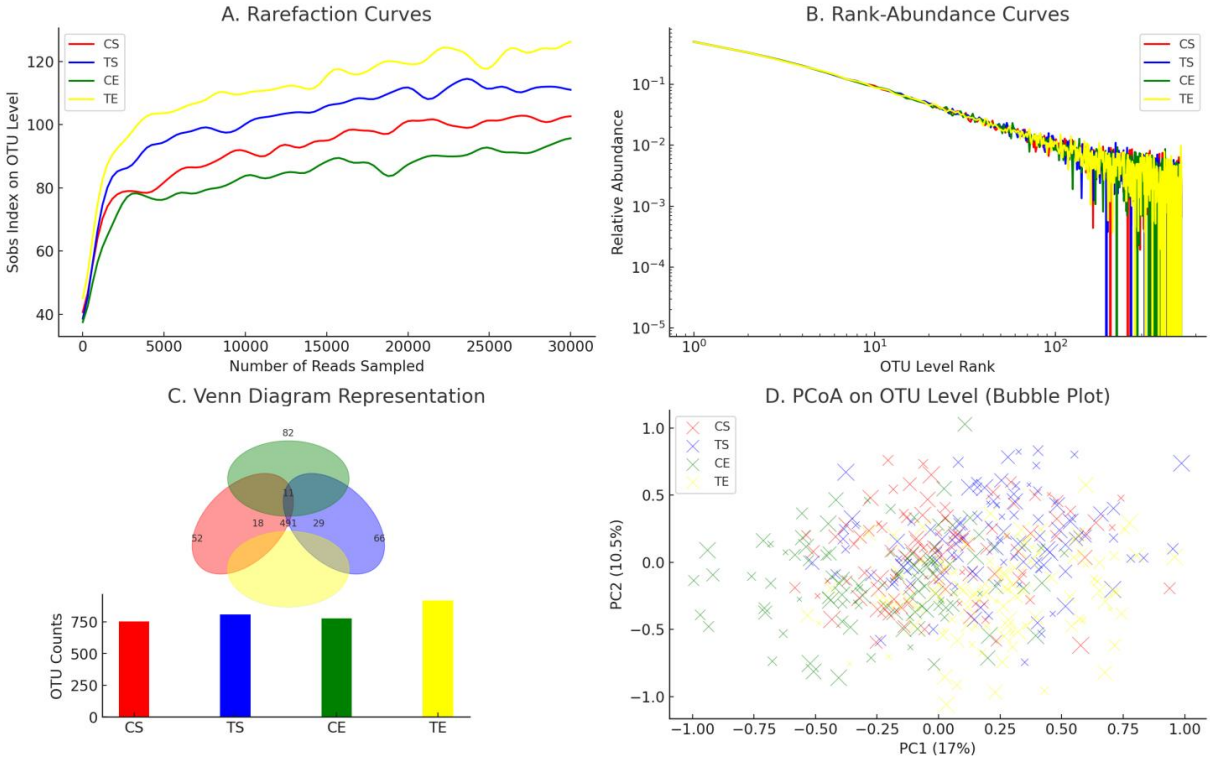

Figure 2: Comparative Analysis of Microbial Richness, Community Structure, OTU Composition, and Beta Diversity Across Treatment Groups

4. CONCLUSION

The study demonstrates that dietary interventions, particularly those rich in fermentable fibers, significantly modulate gut microbiota composition, leading to increased microbial diversity and metabolic stability. The TE diet, in particular, facilitated a more balanced microbial ecosystem, enhancing taxa associated with short-chain fatty acid production and anti-inflammatory effects. These changes contributed to improved glucose and lipid metabolism, highlighting the therapeutic potential of targeted dietary strategies in managing metabolic disorders. Future research should explore the longitudinal impact of such dietary modifications and investigate specific microbial functions to better understand host-microbiota interactions in metabolic health.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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