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Review Article

The Effects of Probiotics, Prebiotics and Synbiotics on Glycemic Control in Diabetic Patients: A Narrative and Meta-Analysis Study

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ABSTRACT

One of the most important therapeutic fields in management of persistent and progressive illnesses that substantially affects global health burden is glycemic control. Recently, probiotics and prebiotics have emerged as complementary therapies in diabetes, aiming the composition and function of gut microbiota. These microbiome-modulating agents can improve metabolic health through an enhanced glucose homeostasis and the insulin sensitivity. The key focus of the present review is a research into the effect of probiotics, prebiotics, and synbiotics on metabolic health in diabetic patients, concerning glucose metabolism, inflammation, and insulin sensitivity. A literature review was conducted between 2010 and 2024 using databases of Science Direct, Springer, Google Scholar, and PubMed. Based on findings, such interventions were shown to provide new strategies to improve glycemic control in patients with diabetes through inflammatory mechanisms, gut-derived metabolites, and other metabolic pathways. In addition, these nutraceuticals can present broader benefits beyond simple glycemia control, such as modifying lipid level and reducing systemic inflammation; while both of which are crucial for management of metabolic syndrome and the prevention of complications from diabetes. While the evidence seems promising at this point, this review is a call to the need for further long-term studies to establish the sustained efficacy and safety of such microbiome-targeting therapies. Therefore, more researches would be needed to fully establish the therapeutic potential of these therapies and to further develop their clinical use for treatment of diabetes.

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by prolonged elevation of blood glucose level that is mainly caused by an increased insulin resistance or inadequate secretion of insulin (1, 2). The most common form, type 2 diabetes mellitus (T2DM), arises from insulin resistance and can lead to serious complications, which include cardiovascular diseases, hypertension, renal failure, and obesity (3, 4). In United States, over 8.5% of adults suffer from T2DM, especially those with a high body mass index (BMI) and among older

adults (5). The worldwide burden of T2DM is high showing that over one million deaths happen annually due to diabetes. The prevalence varies in different populations and requires population-based public health measures to keep the burden low (5). The prediabetes entails an impaired glucose metabolism and is considered as a precursor to T2DM and contributes to a pro-inflammatory state and increases healthcare costs (6). Gestational diabetes mellitus (GDM) is an emerging problem that is associated with obesity and insulin resistance and involves the risk for both mothers and offspring if not appropriately managed (7, 8).

Recent studies have stressed the role of gut microbiota in several diseases including metabolic diseases such as T2DM and GDM presenting probiotics and prebiotics as potential adjuvant therapies in diabetes (9). Probiotics are living beneficial microorganisms that can act by enhancing insulin sensitivity, reducing inflammation, and increasing the intestinal barrier (10, 11). Prebiotics are undigested food ingredients that allow the good bacteria of the gut to grow and possibly regulate glucose metabolism, thereby reducing complications of the disease (12, 13). Synbiotics, a combination of probiotics and prebiotics, have been studied as means to return the balance of the gut microbiome to normal in an effort to enhance metabolic outcomes for improved management of many diseases such as diabetes (10, 14, 15). This review discussed the effect of such microbiome-modulating therapies on glycemic control in diabetic patients with standard treatments. It is a comprehensive analysis of the current state of research that aimed to provide a deeper understanding of the potential of microbiome-modulating nutraceuticals in improving glycemic control, and thereby contributes to managing this global health issue.

Probiotics

Probiotics, encompassing various species from the Lactobacillus and Bifidobacterium genera as well as yeasts such as *Saccharomyces cerevisiae* to provide substantial health advantages when utilized properly (10, 16, 17). The gastrointestinal tract, commonly termed the "second brain," is essential for metabolic well-being, and disturbances in gut microbiota can aggravate disorders such as type 1 diabetes mellitus (T1DM), T2DM and GDM (10, 18). Probiotic therapy along with a controlled diet and prebiotics can help restore gut microbiota balance, improve insulin resistance, enhance gut barrier integrity and reduce inflammation (17, 18). In T1DM, gut microbial shift may influence autoimmune responses, while in T2DM, gut dysbiosis can worsen insulin resistance through an increased gut permeability and a chronic inflammation (17, 18). Probiotics have been shown to improve T2DM outcome by reducing systemic lipopolysaccharide (LPS) level, decreasing endoplasmic reticulum stress, and improving insulin sensitivity that make them a promising therapeutic option for diabetes management (17). Additionally, prebiotic fermentation produces short-chain fatty acids, and further supports the metabolic regulation (17, 19).

Prebiotics

Prebiotics are consisted of non-digestible dietary elements that are mainly carbohydrates to facilitate the proliferation of advantageous gut microbes, including Bifidobacterium and *Faecalibacterium prausnitzii*, by acting as substrates within the colon (20). Examples include inulin, oligofructose, and high amylose maize starch (HAMS), which are fermented by gut bacteria to produce short-chain fatty acids (SCFAs) like butyrate and acetate, known for their anti-inflammatory properties and role in enhancing gut barrier integrity, insulin sensitivity, and glycemic control (20, 21). It was shown that prebiotics can reduce the incidence of T1DM by modulating gut microbiota and lowering autoimmunity, while in T2DM and obesity, prebiotics can lower blood glucose, reduce insulin resistance and decrease systemic inflammation through SCFAs and other metabolites affecting glucose and lipid metabolism (20, 21). Furthermore, prebiotics like inulin and fructooligosaccharides modulate lipid metabolism and regulate the appetite and glucose tolerance and improve fat mass and enteroendocrine peptide production, which further help regulate appetite and insulin resistance and contribute to anti-obesity effects and metabolic health benefits (10).

Synbiotics

Synbiotics as synergistic interaction of probiotics and prebiotics can accentuate health benefits through the promotion of gut health and metabolic outcomes more than when given individually (18). Probiotics benefit from the nutritional support provided by prebiotics, which in turn can enhance the survival and residence time in the gut, and thereby improve the glycemic control and lessen the severity of metabolic disorders such as T1DM and T2DM (14). In T1DM, gut microbiota alteration is associated with autoimmune responses, while in T2DM, gut dysbiosis promotes intestinal permeability and inflammation, and further exacerbates insulin resistance (18). Synbiotics target these issues by restoring gut balance, hence can potentially offer a holistic therapeutic approach to manage diabetes

through dietary interventions (18, 21). Although some researchers showed significant improvements in glycemic parameters related to synbiotics, disparate results from meta-analysis suggest that further studies are still needed to establish the efficacy over a broad range of clinical applications (21).

Probiotics and Inflammation

Probiotics can significantly improve glycemic control in T2DM by reducing inflammation and oxidative stress and enhancing insulin sensitivity. They modulate the gut microbiota, decrease the level of lipopolysaccharides as a pro-inflammatory component linked to systemic inflammation. By reducing the level of LPS and strengthening the intestinal barrier, probiotics prevent harmful substances from entering the bloodstream, which help lower inflammation. It is important in management of T2DM because poor gut integrity may cause increased translocation of LPS, and precipitate chronic disorders such as obesity and atherosclerosis. Probiotics also decrease inflammation by downregulating pro-inflammatory markers such as Tumor Necrosis Factor alpha (TNF-α), Interleukin-6 (IL-6), and IL-1β; while increasing anti-inflammatory markers like IL-10. So it decreases chronic low-grade inflammation that usually characterizes diabetes. Among the strains of probiotics, *Bifidobacterium animalis* (subsp. Lactis 420) has been shown to improve overall metabolism and reduce metabolic endotoxemia (6). Moreover, probiotics can improve metabolic markers by decreasing low-density lipoprotein (LDL) cholesterol and C-reactive protein (CRP), fasting blood glucose (FBG), and increasing high-density lipoprotein (HDL) cholesterol, all of which are very useful in managing diabetes. Probiotics also enhance the production of SCFAs from dietary fibers, which increases the secretion of glucagon-like peptide-1 (GLP-1) which plays an important role in regulating appetite, enhancing insulin sensitivity, and maintaining gut barrier integrity, which further leads to reduced bacterial translocation, reduction in pro-inflammatory markers, and an improvement in glycemic control revealing the potential for probiotics to become a valuable tool in managing T2DM (10).

Probiotics and Oxidative Stress

Probiotics have been stated to play an essential role in reducing oxidative stress, improving insulin sensitivity, and enhancing general glycemic control, especially in patients with T2DM. One of the mechanisms behind these changes induced by probiotics is increasing SCFAs, particularly butyrate, which has antioxidant properties. Consequently, an increase in the antioxidant potential can reduce oxidative stress that is one of the most critical factors in development and progression of diabetes and its complications. More than their antioxidant activities, probiotics can increase intestinal barrier function which impairs the passage of substances and leads to generalized oxidative stress and inflammation. This is because of the preservation of integrity in the intestinal barrier by probiotics that can further reduce the level of bacterial endotoxins, such as LPS, that is responsible for induction of inflammation and oxidative damages. A reduction in oxidative stress can play a dual role in cellular protection by enhancing glucose metabolism and by promoting insulin sensitivity. Some studies presented promising results with different probiotic strains including *Lactobacillus casei*, *Bifidobacterium lactis* and *Lactobacillus acidophilus* to induce marked improvements in metabolic vital parameters. These studies demonstrated that antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase activities are increased due to supplementation of probiotics that can enhance the total antioxidant capacity. This is usually accompanied by decrease in FBG, HbA1c and insulin resistance markers illustrating the comprehensive metabolic benefits of probiotics (16, 17).

Probiotics and Insulin Sensitivity

Probiotics were shown to play an important role in modulating insulin sensitivity through regulating gut hormones such as GLP-1 which is involved in glucose metabolism. GLP-1 increases insulin secretion, delays gastric emptying and as a result decreases appetite and improves glucose level. Also, probiotics can contribute to a decrease in oxidative stress, improvement of intestinal barrier function, and modulation of gut-derived hormones and metabolites that turn them into useful tools to manage T2DM. The probiotic strains displayed the potential to lower harmful lipids, to reduce FBG, glycated hemoglobin (HbA1c), and insulin levels, together with a reduction in pro-inflammatory markers such as TNF-α, IL-6, and IL-1β to enhance the production of SCFAs that are beneficial in metabolic health (16, 17).

Indeed, several studies have shown that multi-strain probiotics consisted of *Lactobacillus rhamnosus*, *L. acidop*hilus, and *Bifidobacterium bifidum* have the ability to alter gut microbiota by increasing benevolent bacteria like Bacteroidetes and reducing harmful Firmicutes, which are valuable in individuals on high-caloric diets. This shift can improve the intestinal permeability, reduce the systemic inflammation, and enhance the glucose tolerance. Moreover, probiotics

play a crucial role in maintaining lipid metabolism by reducing LDL cholesterol level, increasing HDL cholesterol level, and normalizing overall cholesterol level. They also decrease inflammation markers like CRP and improve glycemic control by reducing FBG, HbA1c, and insulin levels. SCFAs, especially butyrate, formed through the process of saccharolytic fermentation, increase insulin sensitivity and promote the integrity of the intestinal barrier, and further can support their potential therapeutic role in treatment of diabetes (17, 18).

Probiotics can help decrease inflammation and oxidative stress with an improvement in the integrity of the intestinal lining. This is vital in prevention of formation of harmful substances such as LPS passing through the gut wall into the bloodstream and as a result reduces the inflammation and improves the insulin sensitivity. Probiotics can also modulate the gut microbiome, reduce the pro-inflammatory cytokines that are involved in the insulin resistance and lower the autoimmune responses related to hyperglycemia. Further, prebiotics promote the proliferation of the gut-friendly bacteria that produce SCFAs, which in turn, regulate glucose homeostasis and adipogenesis. There is a growing interest in the modulation of the gut microbiome by nutraceuticals-probiotics, prebiotics, and synbiotics that are considered to be capable of correcting gut dysbiosis and improving metabolic control in T2DM patients (5, 17).

Probiotics, Prebiotics and Glycemic Control

The effect of prebiotics and probiotics on glycemic control is high since they influence gut microbiota composition and further affect metabolic health. Prebiotics are non-digestible carbohydrates that include substances like inulin and oligofructose and stimulate the growth of gut bacteria like Bifidobacterium and Lactobacillus. This specific mechanism of fermentation leads to the production of SCFAs, particularly acetate and butyrate, which are involved in increasing insulin sensitivity and lowering blood glucose levels. SCFAs bind to G-protein-coupled receptors on intestinal L-cells and stimulate them to secrete hormones such as GLP-1 and peptide YY (PYY). These hormones have several roles in glucose homeostasis. They enhance insulin secretion, inhibit glucagon secretion and promote better control of hyperglycemia. In addition, prebiotics may change the gut microbiota composition, which is important for a healthy gut and contributes to metabolic health (20, 22).

Animal study of diabetes-prone BioBreeding rats and non-obese diabetic mice has shown that metabolic disease is very much influenced by interventions aimed at gut dysbiosis correction. Prebiotic intervention, with inulin or oligofructose supplementation, seems to restore gut microbial balance, increase the SCFA production and improve insulin sensitivity; while lowering systemic inflammation. SCFAs can also foster the decrease in intestinal permeability, reduce the circulating endotoxins that may drive chronic inflammation, and support their role in metabolic health (22). Indeed, clinical trials were reported to support these findings by documenting that prebiotic supplementation is associated with an improvement in glycemic outcome in patients with T2DM, including reduction in HbA1c, postprandial blood glucose excursions, and level of inflammatory markers. The randomized controlled trial by Mirmiranpour *et al.* demonstrated that probiotic and symbiotic supplementation resulted in significant reductions of FBG level among patients with T2DM over a three-month period (20, 22).

HAMS can be identified as one of the prebiotics showing a lot of promise regarding the management of diabetes through gut microbiota modulation and SCFA production. HAMS is resistant to digestion in the small intestine and, upon its fermentation in the large intestine, shifts the profile of the gut microbiome toward those that produce SCFAs in great abundance. HAMS feeding has been associated with high blood and fecal levels of acetate and butyrate and lower rates of progression toward T1DM in nude mice. Preliminary results with non-diabetic subjects indicated that HAMS can improve insulin sensitivity and lower postprandial glucose levels (20). In general, inulin, oligofructose, and HAMS represented good prebiotic strategies to improve metabolic health through the stimulation of gut microbiota, insulin sensitivity, and lowering of inflammation. With these promising results, further investigations, especially extensive and longer-term studies, are required to confirm these benefits and allow for decisions on prebiotics application in the management of diabetes and related metabolic disorders (23).

Materials and Methods

The current review as a meta-analysis presented an overview of the effect of probiotics, prebiotics and synbiotics on glycemic control in diabetic patients. An extensive literature search was conducted through Science Direct, Springer, Google Scholar, and PubMed databases between 2010 and 2024. The keywords of probiotics, prebiotics, synbiotics, glycemic control, diabetes, gut microbiome, and glucose homeostasis were used. Articles were selected based on the inclusion criteria of (i) they were published in English, (ii) investigating on diabetes, glycemic control and probiotics,

prebiotics and synbiotics and (iii) focused on vital glycemic markers such as FBG, HbA1c, and insulin sensitivity. Exclusion criteria were (i) Articles not to be directly related to glycemic outcomes in diabetic populations and (ii) those focusing on metabolic conditions other than diabetes. The review enrolled original research articles, clinical trials, meta-analyses, and review articles. Selected articles were based on their relevance to the topic, their methodological quality, and the importance of their findings to contribute to knowledge on the relationship between probiotics, prebiotics, synbiotics and glycemic control. The collected information was demonstrated in Figure 1.

Probiotics and Lipopolysaccharides

Probiotic mechanisms to control the level of glycemia are numerous. The main one involves taking part in the decrease of bacterial lipopolysaccharides. Actually, by increasing the integrity of the gut barriers, probiotics decrease LPS translocation into the blood circulation. A lower level of LPS demonstrated less systemic inflammation, which is crucial to an increase in insulin sensitivity. Such action of probiotics reveals that T2DM is one of the most widespread chronic disorders that exhibit the role of gut microbiota in T2DM pathology. Also, selected probiotic strains of Lactobacillus and Bifidobacterium have already been reported to improve parameters related to T2DM, which underlines the importance of continuing research in this area (17).

Probiotics and Pro-inflammatory Cytokines

Probiotics have an immunomodulatory effect by downregulating pro-inflammatory cytokines such as TNF-α and IL-6; while upregulating anti-inflammatory markers such as IL-10. Such a decrease in inflammation could also improve insulin sensitivity and improve glycemic control (17, 18).

Probiotics and Short-chain Fatty Acids

It was shown that supplementation of *Saccharomyces boulardii* may be associated with an improvement in glycemic control, protection of the cardiovascular system, and anti-inflammatory impact on a rat model. This was also repeated in our meta-analyses, where the effect of probiotics on FBG and serum insulin was significant; but with inconsistent amplitude, suggesting that probiotics can serve as modulators for the secretion of insulin (18). Probiotics can modulate the synthesis of anti-inflammatory short-chain fatty acids such as butyrate that can enhance an increase in both insulin sensitivity and secretion (17, 24, 25). The gut microbiota in a significant way aids production of short-chain fatty acids through anaerobic fermentation of dietary fibers; while SCFA is created from acetate, propionate, and butyrate. These molecules take part in energy homeostasis and gut health maintenance. Butyrate, in particular, increases insulin sensitivity by stimulating the secretion of GLP-1 and reducing adipocyte inflammation. It was shown that the Chinese population with T2DM had a reduction in butyrate-producing bacteria; thus resulted in an

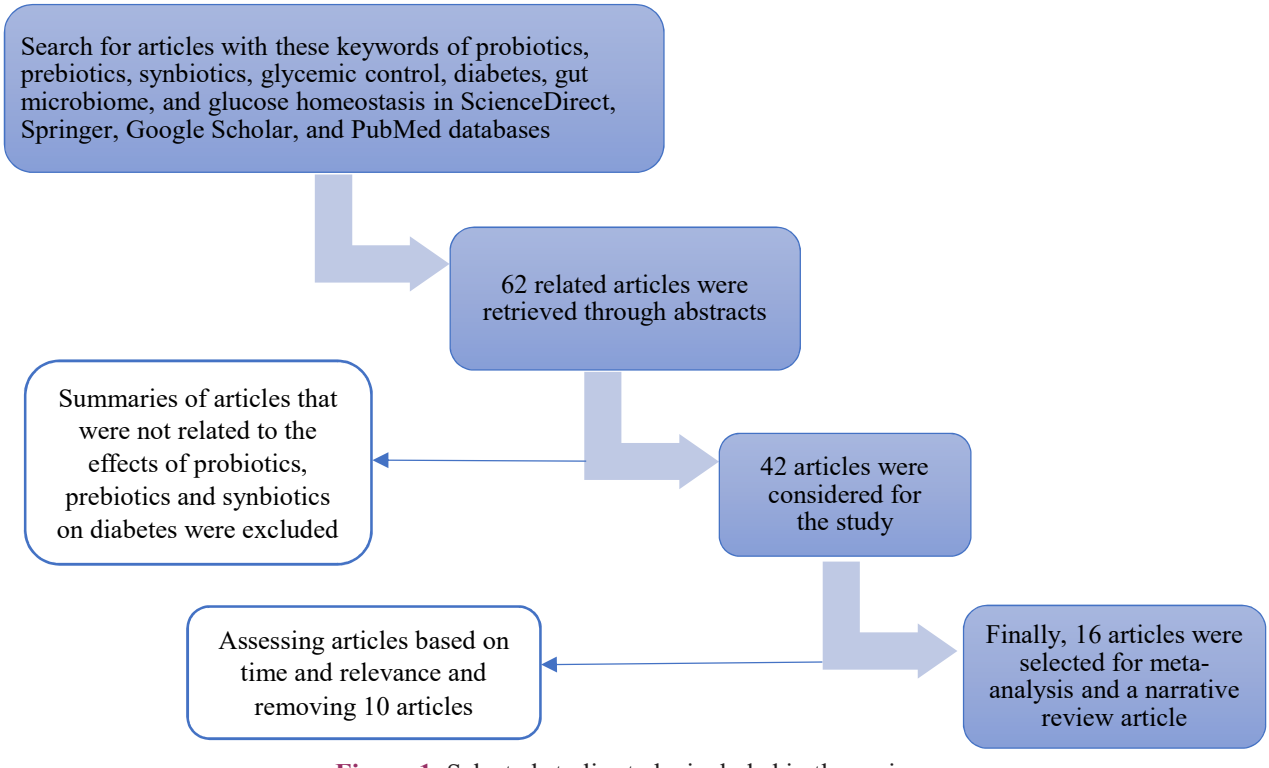

Figure 1: Selected studies to be included in the review.

increase in SCFA level, especially butyrate that plays a vital role in managing the symptoms of T2DM (25).

Apart from reducing endotoxemia, which can promote insulin resistance, butyrate can increase intestinal barrier integrity, which is critical in preventing gut permeability. Indeed, oral butyrate consumption was found to substantially lower the plasma HbA1c concentration, decrease cytokine levels, and decrease LPS level in experimental diabetic models. Such findings suggest that butyrate might be essential in increasing insulin sensitivity by protecting the intestinal epithelial barrier (25).

Probiotics in Previous Studies

The current study evaluated FBG and HbA1c values at baseline and after 4-month intervention. Results indicated no significant differences in FBG, insulin and HbA1c levels between the probiotic-treated and the control group. Although there was some improvement in glycemic control at one month in the probiotic group, this was transient, and there was no difference by the end of the study. Overall, this study revealed that probiotics did not have a meaningful impact on glycemic control in prediabetic adolescents, highlighting the need for larger and longer-duration trials to clarify the role of probiotics in managing glycemic control (16-18).

However, some publications have been more encouraging regarding the impact of probiotics on glycemic control. A meta-analysis performed among nine RCTs revealed a significant decline in FBG and HbA1c levels in cases of T2DM and obesity by consumption of probiotic yogurt (26). Another meta-analysis showed that probiotic supplementation could significantly reduce fasting insulin and FBG levels and insulin resistance in patients with T2DM suggesting that probiotics may be a beneficial adjunct therapy in managing glycemic control, particularly when combined with conventional pharmacological treatments (26).

The main differences between the previous study and our research might be related to population characteristics, probiotic strains and the study duration. Indeed, in that study, patients with T2DM or obesity were predominantly included, who might be more responsive to probiotic intervention than adolescents with prediabetes. Moreover, the mentioned study included extended intervention periods and used specific probiotic formulations that may have been more effective in modulating the gut microbiome and improving metabolic outcomes (26). This highlights the need for further research to determine the optimal probiotic strains and intervention lengths required to achieve sustained improvements in glycemic control.

Discussion

Probiotics and Interpretation of Findings

No significant changes were reported in glycemic control markers such as FBG, insulin and HbA1c levels between the probiotic and the control groups throughout an intervention period of 4 months (24). Several factors were mentioned to impact the finding of this study (24) such as insufficient sample size, individuals with variation in responses from probiotic treatment, and the short duration of the study. So a larger sample size would increase statistical power and improve the ability to detect meaningful differences between groups. Besides, tracking changes during four months was shown to be too short since most metabolic adaptations require extended interventions (22). Another important factor could be the participants' adherence to the probiotic supplementation regimen. Low compliance may have masked potential benefits that highlight the need for future studies with longer durations and stricter adherence monitoring (22). Our intervention group showed some improvement when compared to the baseline measurements. It is recommended that future investigations increase both sample size and the duration of intervention to ensure the compliance monitoring (22, 24).

Our meta-analysis had some geographical scope limitations. Most of the studies in the meta-analysis focused on Iran alone, and the applicability of findings would be limited to populations with other genetic and environmental backgrounds. As such regional concentration would lead to a bias; future studies should focus more on a broader geographic scope. Moreover, variations in research design, demographic characteristics, and probiotic strains across studies may contribute to outcome differences (24). Our study results are in contrast with a previous meta-analysis that reported significant reductions in FBG and HbA1c levels following probiotic supplementation (22). The presence of publication bias, though few, can also suggest that caution should be exercised when interpreting the pooled findings (24); so more extensive studies are needed to understand the full impact of probiotics on glycemic control.

Probiotics Practical Application

Incorporating probiotic and prebiotic-rich food into the diet may have a particular value in addition to regular management in patients with diabetes and prediabetes. The positive effect of probiotics on gut health, together with fiber-rich vegetables and whole grains or legumes that are rich in prebiotic fiber can further influence the glycemic control. Therefore, the

dietary intervention can eventually lead to changes in the gut microbiome and, in return, can affect other metabolic processes involved in glucose homeostasis.

Probiotics and Future Endeavors

These findings are put into perspective within the general understanding of the global diabetes pandemic and the increasing need for new strategies to improve the current pharmacological armamentarium. Nutrients capable of modulating the microbiome including prebiotics and probiotics with the capability of metabolic and floral balance restoration can offer a promising perspective. This approach is consistent with the growing recognition of the gut microbiota as an essential player in metabolic health. As our understanding of the role of the gut microbiota in diabetes and metabolic disorders improves, it promises to enable more effective and personalized therapeutic interventions. Such findings call for further researches into how these nutrients can be developed for use in comprehensive diabetes management programs and can potentially reduce the impact of the disease and improve the lives of millions of people worldwide (26).

Table 1: Intervention, duration, participants, key Findings, and mechanisms of seven studies.

Intervention	Duration	Participants	Key findings	Mechanisms	Reference	
Probiotics	Four months	Prediabetic adolescent patients	No significant differences in glycemic control markers between groups after 4 months; minor effects at 1 month	Reduction in bacterial LPS and pro-inflammatory cytokines, improved insulin sensitivity	(5)	
Probiotics	Varied across studies	Gestational diabetic patients	Lower fasting serum glucose, fasting serum insulin, HOMA-IR, triglycerides, total cholesterol, and VLDL levels	Production of SCFAs, regulation of hormones like leptin and ghrelin, increased expression of GLP-1 and GLP-2	(7)	
Probiotics, Prebiotics	Varied across studies	Obese and diabetic patients	Improved insulin resistance, gut barrier function, and immune modulation	Production of SCFAs, activation of GLP-1 and PYY, reduction in gut permeability	(10)	
Probiotic yogurt	Varied across studies	Type 2 diabetic and obese patients	No significant improvement in glycemic markers compared to control	Potential minimal differences in active bacteria between probiotic and conventional yogurt	(26)	Probiotic yogurt
Probiotics, Prebiotics, Synbiotics	Varied across studies	Type 2 diabetes patients	Significant reductions in fasting plasma glucose, HbA1c, fasting insulin, HOMA-IR, and QUICKI	Modulation of gut microbiota, reduction in chronic low-grade inflammation, improved gut barrier function	(27)	
Probiotics, Prebiotics, Synbiotics	Varied across studies	Type 1 and Type 2 diabetes patients	Reduced fasting blood glucose, total cholesterol, triglycerides, and insulinemia; increased HDL-cholesterol	Changes in microbiota composition, inhibition of intestinal α-glucosidase enzymes, improved gut barrier integrity	(28)	
Probiotics, Synbiotics	6 months	Prediabetic adults	Decreased triglyceride level; no significant effect on HDL, total cholesterol, and LDL	Lipolysis of triglycerides, suppression of NF-κB pathway, gut microbiota-SCFA-hormone axis	(29)	

GLP-1: Glucagon-like peptide-1, GLP-2: Glucagon-like peptide-2, HbA1c: Glycated hemoglobin, HDL: High-density lipoprotein, HOMA-IR: Homeostatic model assessment for insulin resistance, LPS: LDL: Low-density lipoprotein, LPS: Lipopolysaccharide, NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cells PYY: Peptide YY, QUICK: Quantitative insulin sensitivity check index, SCFAs: Short-chain fatty acids, VLDL: Very-low-density lipoprotein.

Conclusion

Even though substantial findings stated notable results in our study such as reduction in FBG, fasting insulin, and HbA1c levels, but they were not significant and also, the change between two and four months from baseline was not statistically significant for both the probiotic and placebo groups including the substantial reduction in HbA1c and FBG. It is necessary to mention that further beneficial effects of the probiotics during a longer period of time in glycemic control of patients with T2DM is needed. Some possible ways by which probiotics could affect glycemic control are a reduction in bacterial LPS and pro-inflammatory cytokines, together with an increase in SCFA production and improved integrity of the gut wall. These differences might reflect the complexity of the relationship between gut microbiota and metabolic health, and there is a further need to characterize the most valuable use of probiotics and prebiotics in management of diabetes (5, 26). Future researches are needed to be targeted towards long-term studies with larger and more diverse cohorts for better insight into the role of probiotics and prebiotics in management of diabetes. It may be related to the most effective strains, dosing, or combination of probiotics and prebiotics, along with their long-term use. Future researches should also be directed toward an individual approach, differing in gut microbiota, genetic background, and other lifestyle variables that can influence responses to probiotic and prebiotic treatments. Intervention, duration, participants, key findings, and mechanism were summarized in Table 1.

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Authors' Contribution

D.G has contributed to all aspects of the manuscript.

Conflict of Interest

None declared.

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