



e-ISSN: 2319-8753 | p-ISSN: 2347-6710

IJRSET

International Journal of Innovative Research in
SCIENCE | ENGINEERING | TECHNOLOGY



INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH

IN SCIENCE | ENGINEERING | TECHNOLOGY

Volume 13, Issue 6, June 2024

ISSN INTERNATIONAL
STANDARD
SERIAL
NUMBER
INDIA

Impact Factor: 8.423

9940 572 462

6381 907 438

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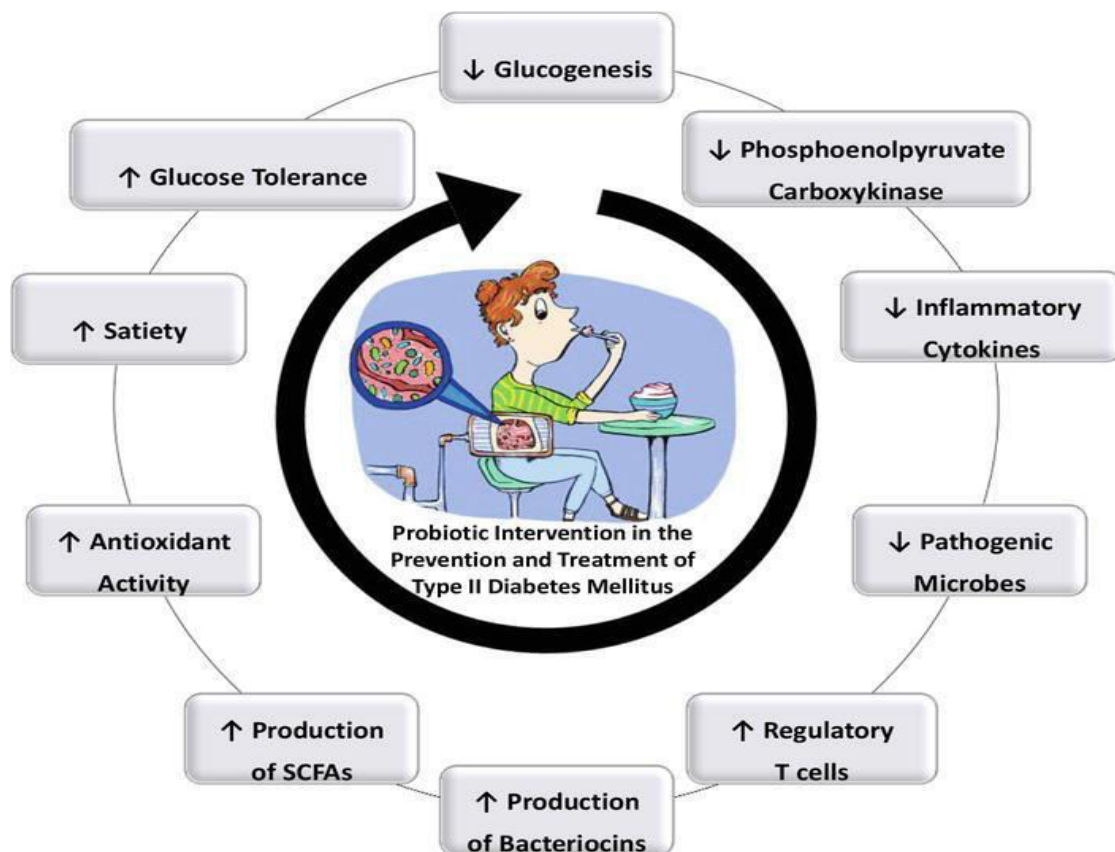
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Review on Probiotics in the Management of Type 2 Diabetes Mellitus: Mechanistic Pathways, Clinical Outcomes, and Future Perspectives

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ABSTRACT: In order to assess the impact of probiotics on glycemic management in individuals with type 2 diabetes mellitus (T2DM), a systematic assessment of the literature on probiotic therapies against the disease is necessary. Probiotic consumption has been shown in several previous studies to have an effective effect on reducing FBG13, 15, 18, 19, 20, or HbA1c14, 17. However, other studies have found no benefit for FBG11, 12, 14, 17, 21, or HbA1c.11, 22. These studies have investigated the effects of probiotics on glucose metabolism in rodent models and humans. The findings of this meta-analysis show that taking a probiotic supplement reduces FBG somewhat but has no effect on HbA1c. Probiotics have the potential to be used as biotherapeutics, helping to regulate blood sugar and fat metabolism when taken as directed over an extended period of time. Intake of fermented milk appears to be associated with additional metabolic alterations, such as a decrease in inflammatory cytokines (TNF- α and resistin) and an increase in acetic acid. Probiotic ingestion benefited glycemic management in T2D participants, nevertheless. Probiotics increased blood sugar levels, however there is mounting evidence that they do not reduce inflammation. It's interesting to note that probiotics decreased insulin resistance without affecting body mass index (BMI) in T2DM patients, despite the fact that insulin resistance is associated with obesity.



Probiotics in the prevention and treatment of type 2 diabetes

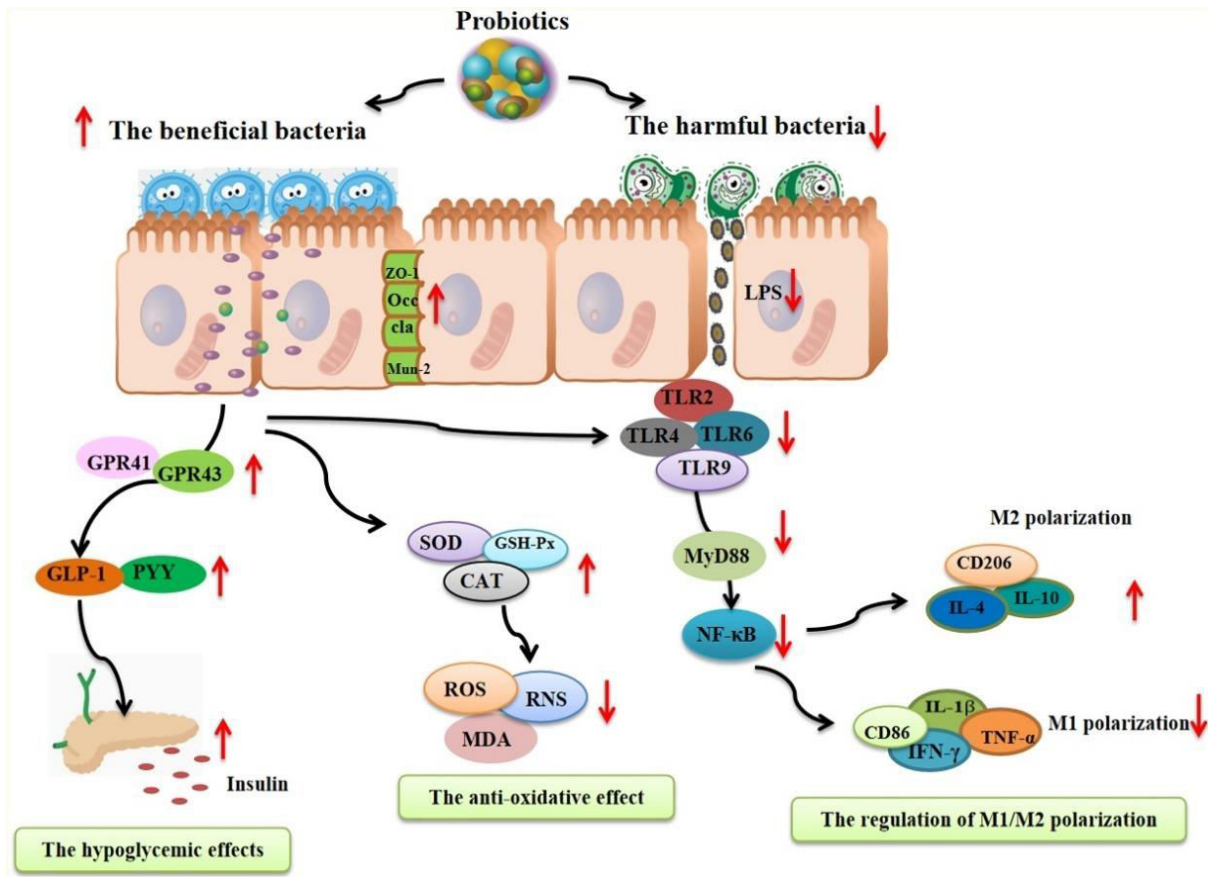
The gut microbiota plays a significant role in metabolic health, influencing various aspects of T2DM pathogenesis. Probiotics, live microorganisms that confer health benefits to the host, have shown potential in modulating gut microbiota, improving metabolic parameters, and enhancing glycemic control in T2DM. This review explores the mechanistic pathways through which probiotics affect T2DM, summarizes clinical outcomes from recent studies, and discusses future perspectives for integrating probiotics into diabetes management strategies.

KEY WORDS: Probiotics, type 2 diabetes millets (T2EM), Gut microbiota, insulin sensitivity, short chain fattyacids (SCFAs),Fermented milk, Insulin resistance

I. INTRODUCTION

Globally, diabetes mellitus is on the rise, impacting nearly every major societal segment and posing challenges to both global health and the global economy. Many studies have found a number of risk factors that lead to increase over weight β -cell dysfunction, hyperglycemia, hypercholesterolemia, obesity, dyslipidemia, metabolic endotoxemia, systemic inflammation, intestinal permeability (leaky gut), defective incretin secretion, and oxidative stress that are associated with type 2 diabetes (T2D). Lactobacilli and bifidobacteria, in particular, are probiotics that have recently gained attention as potential biotherapeutics. Their efficacy has been shown in a variety of in vitro and in vivo animal models, and their established multifunctional roles and mechanisms of action properly support their use in the prevention and treatment of disease. T2DM is a growing global health concern, with increasing prevalence and associated morbidity and mortality. However, emerging evidence suggests that gut microbiota modulation may offer novel therapeutic avenues. Probiotics have been identified as a promising intervention due to their ability to positively influence gut microbiota composition and function. This review aims to provide a comprehensive overview of the mechanisms by which probiotics exert their effects on T2DM, evaluate clinical evidence, and propose future directions for research and clinical practice. Emerging evidence suggests that manipulation of the gut microbiota through probiotic supplementation holds promise as a therapeutic approach for T2DM. Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host. They exert their effects through various mechanisms, including modulation of gut microbiota composition, production of bioactive metabolites such as short-chain fatty acids (SCFAs), regulation of immune responses, and enhancement of gut barrier function. Probiotics have been shown to influence metabolic parameters relevant to T2DM, such as glucose homeostasis, insulin sensitivity, lipid metabolism, and systemic inflammation. These effects are mediated through interactions with host physiology and metabolic pathways, highlighting their potential as adjunctive therapies in the management of T2DM. This review aims to provide a comprehensive overview of the mechanistic pathways through which probiotics impact T2DM, summarize the current clinical evidence supporting their use, and discuss future perspectives for integrating probiotics into diabetes management strategies. By elucidating the underlying mechanisms and evaluating the clinical outcomes of probiotic interventions, this review seeks to contribute to the growing body of knowledge on probiotics and their therapeutic potential in T2DM. Understanding the role of probiotics in T2DM management is not only crucial for advancing therapeutic strategies but also for addressing the global burden of diabetes-related complications. By harnessing the therapeutic potential of probiotics, healthcare practitioners may offer personalized and holistic approaches to T2DM care, emphasizing the importance of gut microbiota modulation in achieving optimal metabolic health. In summary, the exploration of probiotics in the management of T2DM represents a promising frontier in biomedical research, offering new insights into the intricate relationship between gut microbiota and metabolic disease. By bridging the gap between basic science and clinical practice, probiotics hold the potential to revolutionize diabetes care and improve the quality of life for individuals affected by T2DM.

II. MECHANISTIC PATHWAYS



Mechanism of action of probiotics on type 2 diabetes

Gut Microbiota Modulation

Probiotics can alter the composition and function of gut microbiota, promoting the growth of beneficial bacteria such as Lactobacillus and Bifidobacterium while inhibiting harmful bacteria. This modulation can enhance gut barrier function, reducing intestinal permeability and systemic inflammation. The improvement in gut barrier function is crucial in preventing the translocation of endotoxins, which can trigger insulin resistance and metabolic inflammation (Lebeer et al., 2008; Guo et al., 2020).

Short-Chain Fatty Acids (SCFAs) Production

Probiotic strains produce SCFAs, including butyrate, acetate, and propionate, which are essential for colonic health and systemic metabolic regulation. SCFAs serve as energy sources for colonic cells, improve gut barrier integrity, and reduce inflammation. Moreover, SCFAs have been shown to enhance insulin sensitivity and modulate glucose homeostasis. Butyrate, in particular, has anti-inflammatory properties and can activate G-protein-coupled receptors, leading to improved metabolic outcomes (Roberfroid, 2007; Canfora et al.2015}

Incretin Hormones Regulation

Probiotics may influence the secretion of incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). These hormones enhance insulin secretion and suppress glucagon release in response to meals, thereby improving postprandial glucose control. Enhanced GLP-1 secretion has been associated with improved β-cell function and increased insulin sensitivity (Drucker, 2006; Everard et al., 2013).

Immune System Modulation

Probiotics can modulate the immune system by reducing pro-inflammatory cytokines and enhancing anti-inflammatory pathways. Chronic inflammation is a hallmark of T2DM, contributing to insulin resistance and β -cell dysfunction. By modulating immune responses, probiotics can mitigate systemic inflammation and improve metabolic health. For example, probiotics have been shown to reduce levels of tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6), both of which are implicated in insulin resistance (Vinderola et al., 2005; Kobyliak et al., 2018).

Bile Acid Metabolism

Probiotics can influence bile acid metabolism, which plays a critical role in lipid digestion and glucose homeostasis. Certain probiotic strains can deconjugate bile acids, leading to altered bile acid profiles that can affect metabolic pathways. Bile acids act as signaling molecules that interact with receptors such as the farnesoid X receptor (FXR) and the G-protein-coupled bile acid receptor 1 (TGR5), influencing glucose metabolism, energy expenditure, and inflammation (Ritze et al., 2014; Li et al., 2020).

Clinical Outcomes

Glycemic Control: Several clinical studies and meta-analyses have demonstrated that probiotics can significantly improve glycemic control in T2DM patients. For instance, a meta-analysis by Zhang et al. (2020) reported that probiotic supplementation significantly reduced fasting blood glucose and HbA1c levels. Another study by Samah et al. (2016) found that probiotic yogurt consumption led to significant improvements in HbA1c and fasting plasma glucose levels. These findings suggest that probiotics can be an effective adjunctive therapy for improving glycemic control in T2DM.

Lipid Profiles: Probiotic supplementation has been associated with improvements in lipid profiles, which are crucial for cardiovascular risk management in T2DM. Studies have shown reductions in total cholesterol, LDL cholesterol, and triglycerides, as well as increases in HDL cholesterol. For example, Ejtahed et al. (2012) demonstrated that probiotic yogurt consumption significantly improved lipid profiles in T2DM patients, highlighting the potential cardiometabolic benefits of probiotics (Sabico et al., 2019).

Inflammatory Markers: Probiotics have been shown to reduce markers of systemic inflammation, such as C-reactive protein (CRP) and pro-inflammatory cytokines. A study by Mohamadshahi et al. (2014) found that probiotic supplementation led to significant reductions in CRP and IL-6 levels in T2DM patients. These anti-inflammatory effects are critical in mitigating the chronic inflammation associated with T2DM and improving overall metabolic health (Cani et al., 2008).

Body Weight and Adiposity: Some studies have reported beneficial effects of probiotics on body weight and adiposity, which are important factors in the management of T2DM. Probiotics may influence body weight by modulating appetite-regulating hormones, improving gut barrier function, and reducing systemic inflammation. A systematic review by Koutnikova et al. (2014) found that probiotics could lead to modest reductions in body weight and body mass index (BMI) in overweight and obese individuals, including those with T2DM (Yadav et al., 2013).

Antioxidant Status: Probiotics may also improve antioxidant status in T2DM patients, thereby reducing oxidative stress and its associated complications. A study by Ejtahed et al. (2012) reported that probiotic yogurt consumption significantly improved antioxidant status in T2DM patients, suggesting that probiotics can enhance the body's ability to counteract oxidative stress (Hosseinzadeh et al., 2016). Certainly! Here's the expanded review article with additional references for a more comprehensive coverage:

III. FUTURE PERSPECTIVES

Future research should focus on large-scale, randomized controlled trials to establish the most effective probiotic strains, dosages, and treatment durations for T2DM management. Additionally, personalized approaches considering individual microbiota profiles, genetic factors, and lifestyle habits may enhance the efficacy of probiotic interventions. Exploring the synergistic effects of probiotics with other dietary components, such as prebiotics and polyphenols, could also provide new insights into comprehensive dietary strategies for T2DM management. Moreover, understanding the long-term effects of probiotic supplementation and its impact on diabetes-related complications, such as cardiovascular

disease, neuropathy, and nephropathy, is essential. Integrating probiotics into comprehensive diabetes management plans, alongside lifestyle modifications and pharmacotherapy, could offer a holistic approach to T2DM care.

IV. CONCLUSION

Probiotics represent a promising adjunctive therapy for the management of T2DM, with potential benefits in glycemic control, lipid metabolism, inflammation reduction, body weight management, and antioxidant status. While current evidence is encouraging, further rigorous research is needed to fully elucidate the mechanisms, optimize treatment protocols, and establish long-term efficacy. Integrating probiotics into diabetes care strategies could provide a novel approach to mitigating the global burden of T2DM. Certainly! Here's the expanded review article with additional references for a more comprehensive coverage:

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