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ROLE OF PROBIOTICS IN DIABETES MELLITUS

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ABSTRACT

Diabetes has emerged as a predominant global epidemic, profoundly affecting both economic stability and individual health. Diabetes is linked to various problems, including obesity, hyperglycaemia, hypercholesterolaemia, dyslipidaemia, metabolic endotoxemia, intestinal barrier impairment, insulin secretion deficiencies, heightened oxidative stress, and chronic low-grade systemic inflammation. Diabetes is incurable; hence, contemporary research has concentrated on devising diverse strategies for diabetes management. Utilising probiotics is a viable technique for diabetes intervention. The pathophysiology of diabetes mellitus is intricate, involving variables such as oxidative stress and inflammation. Certain probiotics have been documented to diminish oxidative stress and inhibit the effector capabilities of CD4+ T cells while simultaneously lowering pro-inflammatory chemicals and exhibiting antioxidant, immunomodulatory, and antidiabetic properties. Moreover, probiotics may enhance the lipid profile, a primary risk factor for cardiovascular diseases (CVD), and may increase insulin sensitivity by mitigating systemic inflammation. This study consolidates information from scientific literature indicating that yoghurt is a functional food with potential antidiabetic and antioxidant effects. Interest in human microflora has lately emerged, demonstrating that it likely plays a significant role in maintaining metabolic homeostasis, and the administration of probiotics is a beneficial strategy for modulating human microbiota.

KEYWORDS: Diabetes mellitus, oxidative stress, inflammation, probiotics.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterised by elevated blood glucose levels and impaired insulin circulation, which results in considerable morbidity and mortality globally.[1] According to the 9th edition of the International Diabetes Federation Diabetes Atlas, approximately 463 million individuals worldwide suffer from

diabetes. The figure is anticipated to increase to 578 million (10.2% of the global population) by 2030,[2] positioning diabetes as a significant danger to human health in the 21st century. Diabetes mellitus is defined by increased blood glucose levels resulting from impairments in insulin secretion and function.[3] Diabetes is categorised as type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM) according to genetic factors, aetiology, and diagnostic standards. Type 2 diabetes mellitus (T2DM) constitutes the predominant variant of diabetes, accounting for 90% of global cases. Consequently, T2DM is the primary focus of diabetes prevention and management.[4] This review aims to examine the effects of probiotics on type 2 diabetes mellitus and the associated processes.

Insulin injections, oral hypoglycaemic agents, and lifestyle modifications are the primary treatments for diabetes.[5] Nonetheless, prolonged insulin injection therapy may result in insulin resistance, potentially exacerbating symptoms of type 2 diabetes mellitus (T2DM).[6] Additionally, T2DM frequently correlates with insulin resistance, rendering direct insulin injections less efficacious.[7] Hypoglycaemic medications may induce side effects, such as gastrointestinal distress and allergy responses, in addition to potentially causing tissue damage to the liver, kidneys, and nervous system.[8] Consequently, numerous researchers have been pursuing medicines that have low side effects and can rapidly and efficiently manage or potentially cure diabetes.

In addition to inherent genetic factors, other detrimental lifestyles are significantly associated with diabetes, such as insufficient physical activity, regular consumption of a high-sugar and high-fat diet, tobacco use, and alcohol misuse.[9,10] Overnutrition resulting from the consumption of a diet high in sugar and fat is the primary cause of diabetes development. Intestinal microbes act as a vital connection between nutrition and human health. Research indicates that the chemicals generated by the host's intestinal microbiota are significantly associated with diabetes risk.[11] Consequently, probiotics can be utilised to modulate the composition and metabolism of intestinal flora when consumed as dietary supplements, thus regulating and impeding the progression of diabetes.

Gut Microbiota

The gut microbiota is crucial in overseeing and modulating various physiological processes. The ecological architecture of microflora can modify several processes in the human body due to the impact of internal and external stimuli,[12] such as antibiotics, prebiotics, and probiotics. The gut microbiota is fundamentally a vital element in connecting genes, the environment, and the immune system.[13] The microbiome, a microbial organ of the human genome, is twice the size of the human nuclear genome and carries out essential metabolic and biological tasks. Bacteria such as *Bacteroidetes and Firmicutes* dominate the gut microbiome.[14] It is noted that in the baby stomach, levels are normally quite low.[15] The microbiota undergoes alterations along the progression from birth to old age.[16] Babies are colonised by various bacteria by chance, depending on their transmission method in different surroundings.[17]

The composition of gut microbiome species in adulthood is influenced by early-life antibiotic therapy, dietary patterns, luminal pH and osmolality, as well as environmental influences.[18] Despite significant variations in gut microbial composition and inter-individual differences, it has been proposed that the majority of individuals possess microbiota that may be categorised into one of three predominant genera: *Bacteroides, Prevotella,* or *Ruminococcus*.[19] To alter the composition of gut microbiota, the consumption of probiotics "live microorganisms that, when ingested in adequate quantities, confer health benefits to the host"[20] is recommended. Diverse compositions of probiotic cultures are present

in dairy products such as fermented meals, yoghurts, and some cheeses. It remains unclear at what level dietary sources alter gut microbiota and confer beneficial biological effects beyond research findings.[21]

Probiotics

Probiotics are living bacteria that confer health advantages to the host when consumed as dietary supplements. Probiotics can diminish the prevalence of pathogenic bacteria in the gut microbiota and enhance the presence of good bacteria; therefore, they modulate intestinal metabolism. Additionally, probiotics strengthen the intestinal barrier, which helps reduce inflammation in the gut and lowers the risk of infections from harmful germs.[22] Recently, probiotics have been employed to positively influence the composition of gut microbiota. A new categorisation of the genus formerly known as *Lactobacillus* was proposed for 2020.[23,24] Frequently cited probiotics encompass lactic acid bacteria (e.g., *lactobacilli, Bifidobacterium,* and *Streptococcus*), non-lactic acid-producing bacteria (e.g., Bacillus and Propionibacterium), and non-pathogenic yeasts (e.g., *Saccharomyces cerevisiae*), as well as non-spore-forming and non-flagellated cocci.[25] *Lactobacilli* and *Bifidobacterium* have been the most thoroughly researched among them. The efficacy of various probiotics for performing their biological functions *in vivo* is contingent upon their distinct characteristics, including tolerance to acidic pH, resistance to degradation by bile and pancreatic secretions, and high colonisation effectiveness in the intestine.[26] Probiotics are known to provide several advantageous biological actions within the human intestine. Probiotic supplementation may fortify the junctions of intestinal epithelial cells and promote the integrity of the gastric mucosal barrier, hence improving intestinal barrier function.[22,27] Furthermore, probiotics can modulate intestinal motility through reciprocal interactions between the intestinal probiotic flora and the enteric nervous system, therefore influencing intestinal motility.[28,29] Probiotics interact with other intestinal microbiota through cross-feeding and other interactions, thereby influencing the metabolic capacity of the host's intestinal microbiota.

Probiotics and Diabetes Mellitus

Diabetes, a chronic disease affecting several systems and characterised by various problems linked to several molecular processes, is associated with the intestinal microbiota.[30] The primary risk factors for the development of Type 2 Diabetes (T2D) include ageing over 40 years, obesity, familial susceptibility, chronic stress, insufficient physical exercise, and an inadequate diet.[31]

Oxidative stress is a contributing factor to the pathophysiology of diabetes mellitus. It is inhibited by a diet containing probiotics. *Lactobacillus acidophilus* and *Lactobacillus casei* mitigate oxidative stress and have antidiabetic properties. *Lactobacillus* casei has been shown to diminish oxidative stress and eliminate the effector activities of CD4+ T cells, accompanied by a reduction in pro-inflammatory chemicals[32], thereby exhibiting antioxidant, immunomodulatory, and antidiabetic properties.

Probiotics may enhance the lipid profile, a primary risk factor for cardiovascular diseases (CVD). Probiotic microorganisms enhance insulin sensitivity by reducing systemic inflammation. Chronic low-grade inflammation, characterised by consistently increased circulating pro-inflammatory cytokines, is regarded as a primary pathogenic factor for insulin resistance and type 2 diabetes. Probiotics exhibit immunological modulatory effects. Probiotic supplementation enhances insulin resistance and hepatic steatosis caused by a high-fat diet.

Multiple reports have experimentally and clinically validated that oxidative stress plays a role in the pathogenesis and progression of diabetes mellitus, along with its subsequent complications.[33] The generation of oxygen-free radicals resulting from non-enzymatic protein glycosylation, the auto-oxidation of glucose, and compromised antioxidant defence enzymes are the predominant consequences of diabetes.[34] The disrupted equilibrium of oxidants and antioxidants may result in cellular damage, the onset of insulin resistance, enzyme malfunction, inflammation, and lipid peroxidation.[33,35] Probiotic diets have been shown to mitigate oxidative stress. *L. acidophilus* and *L. casei* mitigate oxidative stress and exhibit antidiabetic properties. The antioxidative actions of probiotics may be attributed to the scavenging of reactive oxygen species, chelation of metal ions, inhibition of pro-oxidant enzymes, and the decrease and inhibition of ascorbate oxidation.[36]

CONCLUSION

Literature indicates that intestinal microbiota is a factor influencing metabolic disorders, including obesity[37] and diabetes.[38] These disorders are linked to substantial alterations in the composition and metabolic processes of gut microbiota.[39] Research indicates that a gain in body weight correlates with a higher prevalence of *Firmicutes* bacteria and a lower prevalence of *Bacteroidetes.*[38] Furthermore, antibiotic administration, which alters intestinal microflora in obese mice, results in weight reduction and enhanced glucose tolerance.[40] This indicates that intestinal microflora could serve as a significant target for the treatment of metabolic disorders.[39,41] In summary, probiotics exhibit a wide range of advantageous effects on health and disease, alleviating external disturbances, inhibiting inflammation, and possessing antioxidant properties by diminishing and preventing the formation of reactive free radicals, thereby enhancing antioxidant defences in diabetic patients.

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