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**Gut microbiome supplementation: As therapy for metabolic syndrome**

Gut microbiome supplementation: As therapy for metabolic syndrome

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**Abstract**

+ADw-html+AD4APA-p+AD4-This letter to the editor discusses the publication on gut microbiome supplementation as therapy for metabolic syndrome. Gut microbiome dysbiosis disrupts intestinal bacterial homeostasis and is related to chronic inflammation, insulin resistance, cardiovascular diseases (CVDs), type 2 diabetes mellitus (T2DM), and obesity. Previous research has found that increasing the abundance of beneficial microbiota in the gut modulates metabolic syndrome by reducing chronic inflammation and insulin resistance. Prebiotics, probiotics, synbiotics, and postbiotics are often used as supplements to increase the number of beneficial microbes and thus the production of short-chain fatty acids, which have positive effects on the gut microbiome and metabolic syndrome. In this review article, the author summarizes the available supplements to increase the abundance of beneficial gut microbiota and reduce the abundance of harmful microbiota in patients with metabolic disorders. Our group is also researching the role of the gut microbiota in chronic liver disease. This article will be of great help to our research. At the end of the letter, the mechanism of the gut microbiota in chronic liver disease is discussed.+ADw-/p+AD4APA-/html+AD4-

**Key Words:** Gut microbiome; Metabolic syndrome; Diabetes mellitus; Short-chain fatty acids; Chronic liver disease.

Xu YW, Tian J, Song Y, Zhang B, Wang J. <sup>1</sup> Gut microbiome supplementation: As therapy for metabolic syndrome. *World J Diabetes* 2024; In press

**Core Tip:** I am writing to express my appreciation for the enlightening study titled "Gut microbiome supplementation as therapy for metabolic syndrome" recently published in your esteemed journal. <sup>10</sup> The findings presented in this research shed light on the pivotal role of the gut microbiome in modulating metabolic syndrome, emphasizing the potential therapeutic impact of supplementation. The paper delves into the diverse array of supplements, including <sup>1</sup> probiotics, synbiotics and postbiotics, and their distinct effects on the gut microbiome and its association with metabolic syndrome. I believe that this study will further investigations, inspire clinical trials, and foster the development of targeted interventions to enhance metabolic health through the modulation of the gut microbiome. Our research group is also researching the <sup>8</sup> role of the gut microbiota in chronic liver disease. This article will be of great help to our research.

<sup>1</sup>  
**TO THE EDITOR**

Dear Editor, we read with great interest the recently published review paper by Mc Anto Antony, entitled "Gut microbiome supplementation as therapy for metabolic syndrome", in *World Journal of Diabetes* 2023 <sup>[1]</sup>. The gut microbiota may have a significant role in controlling the host's health. Even though gut microbes have been studied for several decades, the investigation into the purposes of those microorganisms has attracted significant interest outside of the realm of traditional diseases associated with infection. This systematic review of recent evidence from some mice and human model experiments concluded that microbiome supplementation improves people's gut microbiomes that suffer from metabolic syndrome. They <sup>4</sup> produce

beneficial metabolites, such as short-chain fatty acids (SCFAs), including butyrate, acetate, and, propionate which can improve insulin sensitivity and the patient's body weight [2]. Acetate, butyrate, and propionate are formed because of the intestinal microflora's fermentative action on fibre from the diet. The microbiota in the gut transforms the primary bile acids into bile acids, which may further increase the synthesis of cyclic adenosine monophosphate and enhance insulin sensitivity [3].

We agree with that opinion in this review. Previous studies similarly reported that microbiome supplementation increases the gut microbes' abundance of benefits and reduces the prevalence of dangerous bacteria in people with metabolic syndrome and diabetes. Endotoxemia and chronic inflammation can result from type 2 diabetes mellitus (T2DM) weakening the barrier between the intestines and allowing gram-negative microbes to get into the circulatory system [4]. Gut microbiome supplements, for example, probiotics, synbiotics, or postbiotics, affect the gut microbiome and metabolic syndrome by increasing the abundance of beneficial microbiota; therefore, these supplements could reduce insulin resistance and chronic inflammation to modify the metabolic syndrome [3].

Prebiotics provide a multitude of health effects, one of which is immunological regulation *via* the creation of more immune globulin and interleukins and a decrease in inflammatory interleukins [5]. Additionally, the SCFAs may lower gut pH, which will stop harmful bacteria from growing. These elements can enhance insulin sensitivity, enhance the condition of the gut, as well as decrease the generation of cytokines that are associated with inflammation. [6]. Among probiotics, the two most associated bacteria are *Lactobacillus* and *Bifidobacterium*. It has been discovered that probiotics affect the expression of genes and proteins linked to inflammation [7]. Among the beneficial bacteria crucial in preserving this barrier in the intestine are *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*. *Faecalibacterium prausnitzii* is linked to decreased inflammation and creates SCFA butyrate. Bifidobacteria enhance insulin sensitivity, enhance gut health, and reduce the generation of cytokines associated with inflammation. [8]. From previous research, we found that probiotics, synbiotics, or

postbiotics are three substances that can lead to the production of SCFAs, in the gastrointestinal tract improve health and promote intestinal barrier integrity.

Three SCFAs possess an impact on energy homeostasis and metabolic processes, and they may positively influence the functioning of muscle in the skeleton, the tissue of the liver, and fatty tissue. These SCFAs not only are of importance in gut health and as signaling molecules but also might directly affect metabolism <sup>[9]</sup>. SCFAs in the gut, maybe they can improve the health of the gastrointestinal tract, and then they also can protect against inflammation and most importantly promote intestinal barrier integrity.

SCFAs are produced in the distal intestine during the fermentation of indigestible meals. In the caecum, ileum, and colon, the ratio of acetate to propionate to butyrate is around 3:1:1<sup>[10]</sup>. Since the liver and colon are normally where butyrate and propionate are processed, they primarily impact the functioning of the local gastrointestinal tract and liver <sup>[11]</sup>. such as GPR41 and GPR43 were G-protein-coupled receptors (GPRs), in the distal gut are bound by SCFAs, influencing satiety and glucose homeostasis, and producing the gut hormones peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) <sup>[12]</sup>. High concentrations of acetate and low levels of propionate and butyrate enter the bloodstream and can have an immediate impact on the function and metabolism of substrates in the muscles, liver, and peripheral fat tissue. Acetate and butyrate might influence skeletal muscle glucose metabolism in an adenosine monophosphate-activated protein kinase (AMPK)-dependent manner, this could promote the uptake of glucose (via the glucose transporter type 4; GLUT4) and the subsequent retention of glycogen (perhaps through a process that involves GPR41/GPR43) <sup>[13]</sup>. Through elevated systemic levels of gut-derived PYY and GLP-1, SCFAs may also indirectly influence muscle insulin susceptibility and the breakdown of glucose. This could impact the muscle's response to insulin and absorption of glucose, improving tissue insulin tolerance and glucose management <sup>[14]</sup>.

Some proinflammatory cytokines such as IL-6, IL-1 $\beta$ , IL-8, and TNF $\alpha$  may be affected by SCFAs in epithelial cells and they are also promoted by enhancing nuclear factor kappa-B (NF- $\kappa$ B) activation in Toll-like receptors (TLR) ligand responses <sup>[15]</sup>. SCFAs can

also inhibit the production of proinflammatory cytokines, such as TNF $\alpha$ , in neutrophils [16]. SCFAs regulate dendritic cell activities, which in turn control the immunological response by influencing T-cell interaction as well as cytokine secretion.

Butyrate and propionate inhibit the activation of bone marrow-derived stem cells by suppressing the LPS-induced expression of the costimulatory molecule CD40 and the secretion of interleukin 6 (IL-6) and IL-12p40 [16]. They can inhibit proinflammatory mediators, including nitric oxide (NO), IL-6, and interleukin 12 (IL-12), but they do not affect the production of tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) or monocyte chemotactic protein 1 (MCP1). Growing evidence points to SCFAs' regulatory role in both adaptive and innate immune cells, among other immune system cell types.

The potential role of increasing SCFAs as a metabolic tool to prevent insulin resistance and associated cardiometabolic risk factors is increasing. It is still unknown how these findings may affect human metabolism and clinical relevance because most of the data come from *in vitro* and animal research. This may be important for future research. Ingesting complex carbs stimulates the microbiota to produce SCFAs, a helpful strategy to stop glucose metabolism and potentially delay the onset of insulin resistance. Long-term well-controlled human intervention studies are needed to clarify the role of SCFAs in the control of body weight and insulin sensitivity and to define the mechanism of action of SCFAs in organisms. Supplementing with gut microbiota can help treat the metabolic syndrome.

When probiotics are supplemented, side effects may be caused. Probiotics are not released in the stomach but play a role in the intestine. When excessive probiotics are supplemented, it will cause intestinal dysfunction. In addition, in some patients with severely damaged intestinal barrier, bacteria easily break through the intestinal barrier into the blood, causing infection. However, randomised, large-scale, high-quality research and clinical trials should be developed to evaluate the use of SCFAs to alter the gut microbiome and affect different metabolic illnesses. The side effects of bacteria also need to be considered, which will be another focus of research. Moreover, additional

beneficial strains with effects on the gut microbiome need to be identified for the treatment of other diseases.

According to this review, gut-healthy bacteria enhance insulin sensitivity and reduce the release of cytokines associated with inflammation. Therefore, in our research centre, we consider that SCFAs may affect the composition of the gut microbiome and its functions can affect chronic liver disease most likely by regulating innate and adaptive cells; however, further investigation is needed.



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