



## Gut Health and Diabetes: How Phytochemicals Can Help

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### Abstract

The role of gut microbiota in developing and managing diabetes has received significant attention in recent years. Phytochemicals, biologically active compounds found in plants, have been proposed as potential modulators of gut microbiota in diabetes. Studies suggest that phytochemicals may positively impact gut microbiota composition and function in diabetes and improve glucose metabolism and insulin sensitivity. Further investigation is required to comprehensively comprehend the mechanisms responsible for these impacts and establish the most effective quantities and origins of phytochemicals. Mechanisms of action for phytochemicals include acting as prebiotics, reducing inflammation and oxidative stress, and affecting the production of short-chain fatty acids. Limitations and challenges associated with clinical studies include heterogeneity of study populations, lack of standardized methods for assessing gut microbiota, and small sample sizes. Future research can focus on human clinical trials, mechanistic studies, identifying novel phytochemicals, and personalized medicine approaches.

**Keywords:** Diabetes, Microbiota, Phytochemicals, Prebiotics

### Introduction

Diabetes mellitus is a persistent condition that affects the body's ability to regulate glucose levels due to deficiencies in insulin secretion, insulin action, or both. According to estimates, around 463 million individuals globally suffer from diabetes, and this number is expected to grow to 700 million by 2045 (International Diabetes Federation, 2019).

In recent years, there has been growing interest in the role of gut microbiota in developing and managing diabetes. The gastrointestinal tract of humans and other animals is inhabited by a diverse and intricate ecosystem of microorganisms known as the gut microbiota. The gut microbiota comprises bacteria, fungi, viruses, and archaea and is estimated to contain up to 100 trillion microbial cells. Most of these microorganisms are bacteria, with over 1000 species identified in the human gut alone (Tremaroli and Bäckhed, 2012). One of the essential functions of the gut microbiota is its role in the digestion and absorption of dietary fibre. Fibre is a complex carbohydrate not digested by human enzymes but broken down by gut bacteria into short-chain fatty acids (SCFAs). SCFAs are essential energy sources for the colonocytes and have been shown to benefit gut health and immune function. In addition to its role in nutrient

metabolism, the gut microbiota also plays a crucial role in the development and maturation of the immune system. Gut bacteria interact with the immune system through various mechanisms, including producing metabolites and activating immune cells such as T and B cells. These interactions help to regulate the immune response and maintain immune homeostasis. There is growing interest in the potential of manipulating the gut microbiota as a therapeutic strategy for various diseases. This includes using prebiotics and probiotics, as well as fecal microbiota transplantation (FMT) for treating conditions such as *Clostridium difficile* infection.

Phytochemicals are biologically active compounds found in plants, which have been shown to have various health benefits, including anti-inflammatory, antioxidant, and antimicrobial properties. Several studies have investigated the potential role of phytochemicals as modulators of gut microbiota in diabetes.

### Specific Phytochemicals with the Potential to Modulate Gut Microbiota in Diabetes

#### Quercetin

A flavonoid found in many fruits and vegetables, including apples, onions, and citrus fruits. Quercetin has been shown

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to reduce inflammation and oxidative stress in the gut and modulate immune function. It has also been shown to increase the abundance of beneficial bacteria in the gut, such as *Bifidobacterium* spp. and *Lactobacillus* spp.

#### **Resveratrol**

Resveratrol, a type of polyphenol present in grapes, red wine, and peanuts, has been found to possess anti-inflammatory and antioxidant characteristics. Moreover, it is believed to regulate the immune system functioning in the gut. Additionally, Resveratrol has been found to promote the growth of helpful bacteria in the gut, including *Bifidobacterium* spp. and *Lactobacillus* spp.

#### **Epigallocatechingallate (EGCG)**

A polyphenol found in green tea. EGCG has been shown to have anti-inflammatory and antioxidant properties and may modulate immune function in the gut. It has also been shown to increase the abundance of beneficial bacteria in the gut, such as *Bifidobacterium* spp. and *Lactobacillus* spp.

#### **Curcumin**

A polyphenol found in turmeric. Curcumin has been shown to have anti-inflammatory and antioxidant properties and may modulate immune function in the gut. It has also been shown to increase the abundance of beneficial bacteria, such as *Bifidobacterium* spp. and *Lactobacillus* spp., in the gut.

#### **Impact of Phytochemicals on Gut Microbiota**

Phytochemicals are biologically active compounds found in plants and have been proposed as potential modulators of gut microbiota in diabetes. Several studies have investigated the impact of phytochemicals on gut microbiota in diabetes, and the results suggest that phytochemicals may positively impact gut microbiota composition and function.

Kim *et al.* (2016) conducted a research study to examine the effect of dietary fiber on the composition of gut microbiota in individuals with T2D. The results of the study revealed that dietary fiber intake led to an increase in gut microbiota diversity, along with a rise in the levels of beneficial bacteria, such as *Bifidobacterium* spp. and *Faecalibacterium prausnitzii*.

In addition to changes in gut microbiota composition, studies have also reported improvements in glucose metabolism and insulin sensitivity following phytochemical supplementation. Song *et al.* (2015) conducted a study to explore the effects of anthocyanin supplementation on glucose metabolism in individuals with T2D. The results indicated that such supplementation had a positive impact on glucose metabolism, including lowered fasting blood glucose levels and improved insulin sensitivity. Another study by Kim *et al.* (2015) investigated the impact of quercetin supplementation on insulin sensitivity in patients with T2D and found that quercetin supplementation improved insulin sensitivity, with a decrease in fasting insulin levels and an increase in glucose uptake.

The mechanisms underlying the impact of phytochemicals on gut microbiota in diabetes are not fully understood but may involve alterations in gut microbial diversity and

composition, as well as improvements in gut barrier function and immune system regulation. Studies have demonstrated that phytochemicals possess antimicrobial and anti-inflammatory characteristics that could potentially enhance gut microbial equilibrium and alleviate gut inflammation. Overall, the evidence suggests that phytochemicals may positively impact gut microbiota composition and function in diabetes and improve glucose metabolism and insulin sensitivity.

#### **Mechanism of Action**

One mechanism through which phytochemicals may modulate gut microbiota in diabetes is by acting as prebiotics. Prebiotics are substances that cannot be digested but aid in the proliferation of beneficial bacteria in the digestive tract. Multiple research studies indicate that prebiotic properties can be observed in phytochemicals such as polyphenols and flavonoids, thereby stimulating the growth of beneficial bacteria like *Bifidobacterium* spp. and *Lactobacillus* spp.

In addition to their prebiotic effects, phytochemicals may also modulate gut microbiota through their anti-inflammatory and antioxidant properties. Inflammation and oxidative stress are known to play a role in the pathogenesis of diabetes, and several studies have shown that phytochemicals can reduce inflammation and oxidative stress in the gut. For example, a study by Kim *et al.* (2015) found that quercetin, a flavonoid found in many fruits and vegetables, reduced inflammation and oxidative stress in the gut of mice with diabetes.

Phytochemicals may impact the gut microbiota in diabetes by altering the production of short-chain fatty acids (SCFAs), which are essential for regulating glucose metabolism and inflammation, and are synthesized by gut microbiota. Several studies have shown that phytochemicals, such as butyrate-producing polyphenols, can increase the production of SCFAs in the gut, which may have beneficial effects on glucose metabolism and inflammation.

#### **Limitations and Challenges Associated with Clinical Studies**

One major limitation is the heterogeneity of study populations, making it difficult to draw clear conclusions about the efficacy of phytochemicals. For example, different studies may use different doses or forms of phytochemicals or may include participants with varying degrees of diabetes severity, which can impact the results.

Another challenge is the lack of standardized methods for assessing gut microbiota composition and function. Different studies may use different techniques for analyzing gut microbiota, which can lead to inconsistent results. Additionally, there is a lack of consensus on what constitutes a “healthy” or “beneficial” gut microbiota composition, making it difficult to interpret the significance of changes in gut microbiota composition observed in clinical studies.

Finally, many clinical studies in this area have small sample sizes and relatively short study durations, which can limit the generalizability of the results and make it difficult to assess the long-term efficacy of phytochemical interventions.

Despite these challenges, clinical studies have provided

promising evidence for the potential of phytochemicals to modulate gut microbiota in diabetes. However, more rigorous and standardized studies with larger sample sizes and longer durations are needed to elucidate these compounds' efficacy and mechanisms of action fully.

### **Future Research Directions for Exploring the Role of Phytochemicals in Modulating Gut Microbiota in Diabetes Can Focus on the Following Areas**

#### **Human Clinical Trials**

More human clinical trials are needed to establish the efficacy and safety of phytochemicals in managing diabetes. These studies should use rigorous study designs, larger sample sizes, and long-term follow-up to determine the effects of phytochemicals on gut microbiota composition and function.

#### **Mechanistic Studies**

Additional investigations are required to clarify the pathways by which phytochemicals impact the gut microbiota in individuals with diabetes. These studies can use in vitro models, animal models, and human clinical samples to determine the effects of phytochemicals on gut microbiota metabolites, gene expression, and protein levels.

#### **Identification of Novel Phytochemicals**

There is a need to identify novel phytochemicals with the potential to modulate gut microbiota in diabetes. This can be achieved by screening natural products, synthesizing novel compounds, and high-throughput screening of phytochemical libraries.

#### **Personalized Medicine**

Future research can focus on identifying biomarkers that predict response to phytochemicals in individuals with diabetes. This can enable personalized medicine approaches that consider individual differences in gut microbiota composition and function.

#### **Conclusion**

In conclusion, diabetes is a significant global health concern with long-term complications affecting multiple organ systems. Phytochemicals, biologically active compounds

found in plants, have been shown to positively impact gut microbiota composition and function in diabetes, potentially improving glucose metabolism and insulin sensitivity. Mechanisms through which phytochemicals modulate gut microbiota include acting as prebiotics, reducing inflammation and oxidative stress, and affecting the production of SCFAs. However, limitations and challenges associated with clinical studies, such as heterogeneity of study populations and lack of standardized methods for assessing gut microbiota, suggest that more rigorous and standardized studies are needed to fully elucidate the efficacy and mechanisms of action of phytochemicals in diabetes management. Future research directions can focus on human clinical trials, mechanistic studies, identification of novel phytochemicals, and personalized medicine approaches to improve the understanding of the role of phytochemicals in modulating gut microbiota in diabetes.

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