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Macronutrients, Microbiota, and Metabolism: Dietary Strategies Against Obesity and Diabetes

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Abstract

Obesity and type 2 diabetes (T2D) are escalating global health crises, driven by metabolic dysfunctions such as insulin resistance (IR), chronic inflammation, and dyslipidemia. Conventional dietary recommendations have shown limited success in halting these conditions, emphasizing the urgent need for targeted, mechanistically informed strategies. Recent research underscores the pivotal role of gut microbiota in mediating host metabolism, providing a new frontier for nutritional interventions. This review synthesizes current evidence on how dietary macronutrients influence gut microbiota composition and function, ultimately affecting metabolic outcomes. It highlights the central role of microbial metabolites, particularly short-chain fatty acids (SCFAs), in modulating glucose homeostasis, adiposity, and inflammation. The review discusses how diets rich in fiber and polyphenols enhance microbial diversity and SCFAs production, improving insulin sensitivity and weight regulation. Conversely, excessive intake of saturated fats and refined sugars is shown to disrupt gut microbial balance, promoting dysbiosis and metabolic derangements. Evidence from clinical and preclinical studies on dietary strategies, including Mediterranean, low-carbohydrate, and intermittent fasting (IF) approaches is critically evaluated for their microbiota-mediated effects. Finally, the review advocates personalized nutrition, integrating gut microbial profiles to optimize dietary interventions in obesity and diabetes management. Future research should prioritize the identification of precise microbial signatures and metabolites that predict individual responses to dietary interventions. Advances will enable the development of personalized, microbiota-targeted nutritional therapies. Integrating dietary modulation with gut microbiome profiling holds the promise of transforming obesity and diabetes care into a more precise and effective discipline.

Keywords: Dietary fiber, Gut microbiota, Insulin resistance, Macronutrients, Metabolic health, Obesity, Type 2 diabetes

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Introduction

Obesity and diabetes have become pervasive health concerns globally, with significant implications for public health and healthcare systems [1-3]. The rise in these conditions is primarily linked to modern lifestyle factors, including poor dietary habits, physical inactivity, and altered microbiota composition [4, 5]. Central to understanding and addressing these metabolic disorders is the interplay between macronutrients, gut microbiota, and the body's metabolic responses [6-8]. Growing body research has highlighted how the balance and quality of macronutrients proteins, fats, and carbohydrates can influence the development and progression of obesity and diabetes, underscoring the need for dietary strategies that target these metabolic pathways [9-11]. Furthermore, the gut microbiota, an intricate ecosystem of microorganisms residing in the intestines, plays a crucial role in regulating energy balance, glucose metabolism, and inflammation, all of which are implicated in these conditions [12, 13].

Recent studies have illuminated the complex relationship between diet and gut microbiota composition [14-16]. Certain dietary patterns can either promote or inhibit the growth of specific microbial populations, which in turn can modulate host metabolism. For example, high-fat diets (HFD), high-sugar (HS) diets have been shown to disrupt the diversity of gut microbiota, promoting an inflammatory state that exacerbates IR and adiposity [17, 18]. Conversely, diets rich in fiber, plant-based foods, and fermented products can foster healthy microbiota, enhance metabolic functions and reduce the risk of obesity and T2D [19, 20]. This evolving understanding of the gut microbiome's role in metabolism presents an opportunity to develop more personalized and effective dietary interventions that focus on modifying the microbiota as a means of improving metabolic health [21-23].

Dietary strategies aimed at combating obesity and diabetes must, therefore, consider both macronutrient composition and its impact on the gut microbiota [24, 25]. While traditional dietary approaches emphasize calorie restriction and macronutrient balance, emerging evidence suggests that microbiota-targeted interventions, such as prebiotics, probiotics, and postbiotics, could offer significant benefits in managing metabolic diseases [26, 27]. This integrated approach, combining macronutrient optimization with microbiota modulation, holds promise for developing comprehensive dietary guidelines and

treatments that not only address the symptoms of obesity and diabetes but also tackle their root causes at the metabolic and microbial level [28, 29]. As research in this field continues to evolve, the hope is to establish practical, evidence-based dietary strategies that can be implemented at both individual and population levels to reduce the global burden of these chronic conditions.

Obesity and T2D are escalating global health crises, significantly impacting socioeconomic burdens worldwide [30, 31]. These metabolic disorders are characterized by a cluster of complications, including IR, chronic low-grade inflammation, and dyslipidemia [32, 33]. The intricate interplay between dietary macronutrients, the gut microbiota, and host metabolism has emerged as a critical area of research, offering potential therapeutic avenues for managing and preventing these diseases [34, 35]. This article explores the current understanding of this relationship, highlighting how dietary strategies can be tailored to modulate the gut microbiota, improve metabolic health, and combat obesity and diabetes [36, 37].

The Gut Microbiota and Its Metabolic Influence

The human gut harbors a vast and diverse community of microorganisms, including bacteria, fungi, and viruses, collectively known as the gut microbiota [37, 38]. This complex ecosystem plays a pivotal role in various physiological processes, including nutrient metabolism, immune system regulation, and maintenance of gut barrier integrity [34, 39]. Dysbiosis, an imbalance in the gut microbiota composition, has been strongly associated with the development of obesity, IR, and T2D [30, 32, 33]. The gut microbiota exerts its metabolic influence through the production of metabolites like SCFAs, modulation of immune responses, and interaction with the gut-brain axis [40, 41]. Understanding these interactions provides insights into potential therapeutic strategies for metabolic diseases.

While the gut microbiota's influence on metabolic health is well-documented, the specific mechanisms and causal relationships require further exploration. The potential for gut microbiota-targeted therapies in managing metabolic diseases is promising, yet variability in individual responses and the need for personalized approaches remain challenges. Future research should focus on elucidating the precise mechanisms by which the gut microbiota affects metabolic processes and developing targeted therapies to harness its therapeutic potential [42, 43].

Gut microbiota dysbiosis in obesity and diabetes

Studies have revealed distinct gut microbiota profiles in individuals with obesity and T2D compared to healthy individuals [30, 32, 44]. For instance, women with gestational diabetes mellitus (GDM) exhibit gut microbiota dysbiosis similar to that observed in T2D, with an enrichment of certain bacterial populations like *Ruminococcaceae* [30]. In T2D, dysbiosis is characterized by reduced levels of beneficial bacteria like *Bifidobacterium* and *Roseburia*, which are crucial for maintaining gut barrier integrity and regulating immune responses [45, 46]. Specific bacterial strains, including *Lactobacillus* and *Clostridium*, are involved in bile acid metabolism and cholesterol homeostasis, influencing lipid levels and contributing to hypercholesterolemia [45, 47].

Specific microbial taxa, such as those derived from *Proteobacteria* and *Bacteroidetes*, including *Escherichia* and NK3B31 group, are significantly more abundant in post-GDM women with glucose intolerance, indicating a potential "gut microbiota signature" in these metabolic conditions [48]. Furthermore, a low bacterial gene richness and *Bacteroides* enterotype have been associated with increased levels of imidazole propionate, a microbially produced metabolite that impairs glucose metabolism [44].

Dysbiosis can lead to increased intestinal permeability, allowing harmful substances to enter the bloodstream and trigger inflammation. This inflammation is a key factor in the development of IR and obesity-related complications [49, 50]. Alterations in the gut microbiota can enhance energy extraction from diet, contributing to obesity. The *firmicutes/bacteroidetes* ratio is often altered in obesity, leading to increased energy harvest [45]. The production of SCFAs by gut bacteria plays a crucial role in glucose metabolism and insulin sensitivity. Dysbiosis can disrupt SCFA production, affecting metabolic health [45, 51].

SCFAs: Key microbial metabolites

SCFAs serve as an essential energy source for intestinal epithelial cells and influence host energy metabolism by activating G protein-coupled receptors such as FFAR2 and FFAR3, which are involved in energy homeostasis and adipose-insulin signaling [52]. SCFAs impact adipose tissue metabolism by modulating processes like adipogenesis, lipolysis, and inflammation. They can also affect adipose tissue indirectly through gut hormones and signaling pathways to the brain and liver [53, 54]. SCFAs act as epigenetic regulators by inhibiting histone deacetylases, thereby influencing gene expression related to metabolic pathways [52].

The gut microbiota produces SCFAs, amino acids, and bile acids, which are absorbed into the bloodstream and influence human signaling pathways, thereby affecting physiological processes [55]. SCFAs, derived from microbial fermentation, modulate anti-inflammatory and immune system pathways, playing a role in maintaining metabolic health [56]. Dysbiosis can lead to the production of pro-inflammatory compounds, contributing to low-grade inflammation and metabolic disorders [55, 57].

The gut microbiota ferments dietary fibers and resistant starch, producing SCFAs such as acetate, propionate, and butyrate (Table 1) [38, 58]. These SCFAs are crucial modulators of various metabolic

Table 1: SCFAs and their association with diabetes and obesity.

SCFA	Produced by	Primary functions	Effect on diabetes	Effect on obesity
Acetate	Many gut microbes (e.g., *Bifidobacteria*, *Akkermansia*)	- Energy source - Lipid synthesis precursor - Appetite regulation (via central pathways)	May raise insulin secretion and lipogenesis	Promotes fat storage and mixed effect on weight gain
Propionate	*Bacteroides*, *Veillonella* spp.	- Gluconeogenesis substrate in liver - Appetite suppressant (via peptide YY, GLP-1)	Improves insulin sensitivity and lowers blood glucose	Reduces weight gain and modulates satiety hormones
Butyrate	*Faecalibacterium prausnitzii*, *Roseburia* spp.	- Colonocyte fuel - Anti-inflammatory - Enhances gut barrier integrity	Enhances insulin sensitivity and reduces inflammation	Protects against diet-induced obesity and increase energy expenditure
Valerate and isobutyrate	Protein fermentation by certain *Clostridia*	- Less abundant - May act as signaling molecules	Unknown or variable	Unclear role; possible obesogenic effects in excess

pathways, influencing glucose homeostasis, lipid metabolism, and inflammation [38, 58, 59]. Butyrate, for example, serves as a primary energy source for colonocytes and plays a vital role in maintaining gut barrier function [38]. SCFAs also modulate systemic inflammation and insulin sensitivity, highlighting the importance of dietary fiber in promoting a beneficial gut microbiota composition and SCFA production [58-60].

Alterations in gut microbiota composition, often seen in obesity, affect SCFA production. SCFAs have been shown to modulate energy balance and adipose tissue function, which are crucial in obesity management [53, 61]. SCFAs help maintain adipose tissue homeostasis, and their dysregulation can lead to adipose tissue dysfunction, contributing to obesity and its complications [54]. SCFAs improve insulin sensitivity and glucose metabolism by modulating insulin signaling pathways and incretin production, which are vital in diabetes management [38, 62]. By influencing inflammatory responses, SCFAs can mitigate low-grade inflammation associated with IR and T2D [63, 64].

While SCFAs have shown promise in influencing metabolic health, the complexity of their interactions with host metabolism and the gut microbiota necessitates further research. Conflicting data on SCFA concentrations at different disease stages highlights the need for more studies to fully understand their role in the pathogenesis of obesity and diabetes. Additionally, the potential for SCFAs to serve as therapeutic agents or diagnostic markers remains an exciting area for future exploration, with the possibility of developing targeted interventions to modulate SCFA production and activity for improved metabolic health outcomes.

Macronutrient Intake and Gut Microbiota Modulation

Diet is a major determinant of gut microbiota composition and function [35, 37, 65]. Different macronutrients-carbohydrates, proteins, and fats can differentially influence the gut microbiota, leading to distinct metabolic outcomes (Table 2) [35]. Diet significantly impacts gut microbiota composition. A high-fiber diet can decrease inflammation and improve insulin sensitivity, while a diet high in fat and sugar can lead to dysbiosis and metabolic syndrome [57]. Therapeutic interventions targeting the gut microbiota, such as probiotics, prebiotics, and fecal microbiota transplantation, have shown potential in improving metabolic outcomes. Probiotics, particularly *Lactobacillus* and *Bifidobacterium* strains, may enhance glycemic control in diabetes [47, 56]. Long-term interventions targeting the gut microbiota have demonstrated more substantial metabolic benefits compared to short-term interventions [47].

Dietary fiber: a prebiotic for gut health

Dietary fiber, a type of carbohydrate that the human body cannot digest, serves as a primary food source for gut bacteria [37, 58, 59]. Increased dietary fiber intake promotes the growth of beneficial bacteria, leading to increased SCFA production and improved glucose and lipid metabolism [58-60]. Moreover, low fiber intake has been associated with specific gut microbial changes and metabolic abnormalities in post-GDM women [48].

Dietary fibers can aid in weight management by modulating gut microbiota, which influences energy balance and fat storage. The presence of SCFAs in the gut can reduce inflammation and improve gut barrier function, contributing to weight loss and reduced obesity risk (Figure 1) [35, 66, 67]. High dietary fiber intake is associated with improved glycemic control. Studies have shown that dietary fiber can significantly improve glycated hemoglobin (HbA1c) levels, a marker of long-term glucose control, in individuals with T2D [68]. The modulation of gut microbiota by dietary fiber also supports the production of SCFAs, which enhance insulin sensitivity and glucose uptake [58, 68].

A systematic review and meta-analysis [68] presented yielded several important findings regarding the role of dietary fiber in modulating gut microbiota dysbiosis in patients with T2D. A total of nine studies met the inclusion criteria for this review, focusing on various aspects of dietary fiber's impact on gut health and diabetes management. The review identified significant changes in gut microbiota composition due to dietary fiber intake, which may help restore balance in dysbiosis conditions often seen in T2D patients. There were significant differences in the levels of SCFAs, specifically acetic acid, propionic acid, and butyric acid, between the dietary fiber group and the placebo group ($p < 0.05$). These SCFAs are important for gut health and metabolic processes. The analysis showed a significant improvement in HbA1c levels in the dietary fiber group, with a mean difference of −0.18 (95% CI, −0.29, −0.06) compared to the placebo group ($p = 0.002$). This indicates that dietary fiber may help in better glycemic control. No significant differences were observed in fasting blood glucose levels or the homeostatic model assessment of IR (HOMA-IR) between the two groups ($p > 0.05$). This suggests that while dietary fiber may improve certain metabolic markers, it does not significantly affect all aspects of glucose metabolism. The study found

Table 2: Macronutrient intake and gut microbiota modulation in diabetes and obesity.

Macronutrient	Effect on gut microbiota	Key microbial shifts	Impact on diabetes	Impact on obesity
Carbohydrates (esp. complex carbs and fibers)	↑ SCFA production ↑ Microbial diversity ↑ Beneficial bacteria (e.g., *Bifidobacteria*, *Faecalibacterium*)	↑ Butyrate producers ↑ *Bacteroidetes*, ↓ *Firmicutes* ratio	↓ Improved insulin sensitivity ↓ Inflammation	↓ Body weight ↑ Satiety via SCFAs (GLP-1, peptide YY)
Simple sugars	↓ Microbial diversity ↑ Opportunistic pathogens	↑ *Firmicutes*, ↓ *Bacteroidetes* ↑ *Clostridium*, *Escherichia coli*	↑ IR ↑ Gut permeability ("leaky gut")	↑ Fat accumulation ↑ Low-grade inflammation
Fats – saturated	↑ Endotoxin-producing bacteria ↓ Barrier integrity	↑ *Bilophila wadsworthia*, *Ruminococcus*	↑ IR ↑ Inflammatory cytokines	↑ Obesity risk ↑ Adiposity through endotoxemia
Fats – unsaturated	Modest ↑ in beneficial bacteria ↓ Inflammation	↑ *Akkermansia*, *Lactobacillus*	↓ IR ↓ Inflammatory markers	↓ Adiposity, Better metabolic profile
Proteins (excess, esp. animal)	↑ Putrefactive fermentation ↑ Harmful metabolites (ammonia, phenols)	↑ *Bacteroides*, ↓ SCFA producers	↑ IR (in context of low fiber)	↑ Obesity (when combined with HFD)
Proteins (plant-based, moderate)	↑ SCFA production ↑ Microbial diversity	↑ *Prevotella*, ↑ *Bifidobacteria*	↓ Glucose intolerance ↑ Insulin sensitivity	↓ Body fat ↑ Lean mass preservation

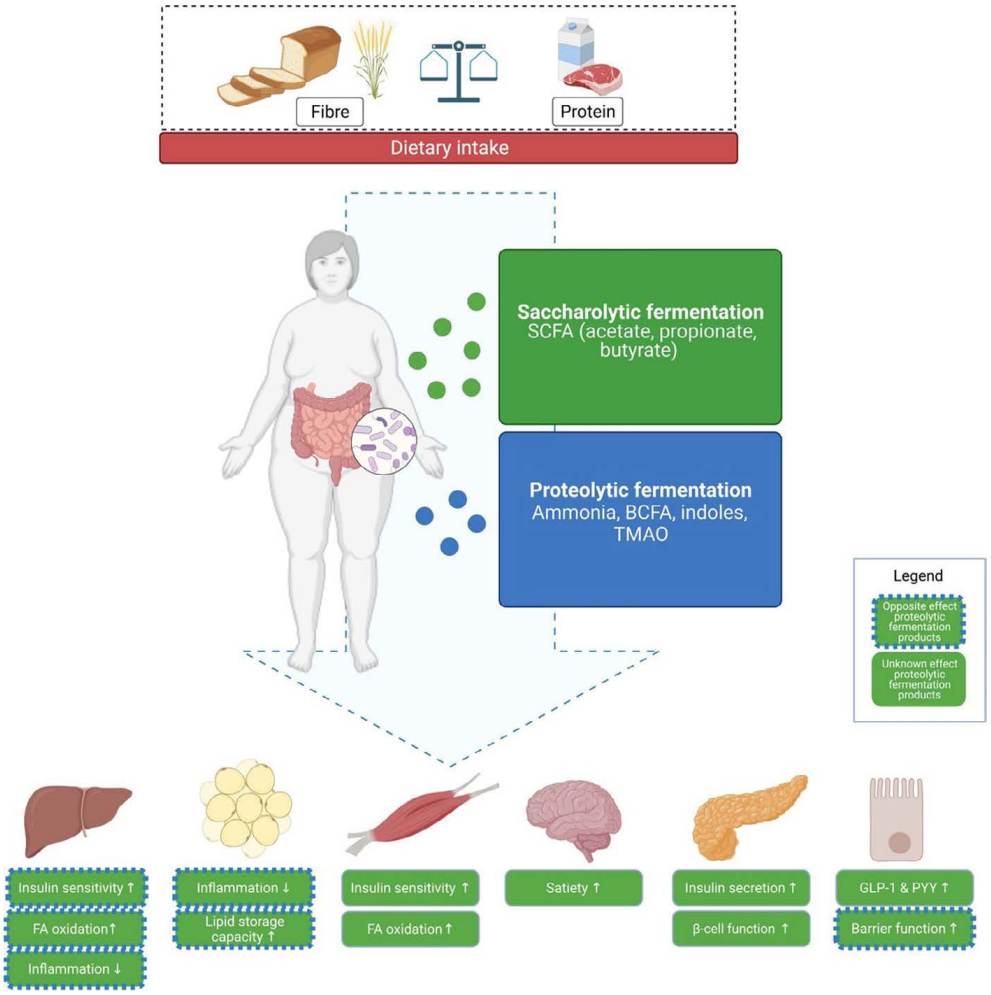

Figure 1: The interplay between dietary components, carbohydrate- and protein-fermenting gut microbes, and host metabolic processes is a key factor in metabolic regulation [35].

no significant differences in the occurrence of adverse events between the dietary fiber and placebo groups, indicating that increasing dietary fiber intake is generally safe for patients. The improvement in HbA1c may be partly due to increased production of glucagon-like peptide-1 and enhanced glucose uptake facilitated by specific gut bacteria like *Bifidobacterium lactis*. In conclusion, the findings suggest that dietary fiber plays a beneficial role in managing T2D by improving certain metabolic parameters and promoting a healthier gut microbiota [68].

Proteins and gut microbiota

The gut microbiota also metabolizes proteins, producing various metabolites that can impact host health [35, 65]. Branched-chain amino acid (BCAA), abundant in animal-based dietary sources, are both produced and degraded by gut microbiota, and circulating BCAA levels are associated with IR and T2D [65]. Altered microbial metabolism of histidine, an amino acid, can lead to elevated levels of imidazole propionate, contributing to the development of T2D [44]. Specific microbial phyla, such as *Proteobacteria* and *Bacteroidetes*, have been associated with obesity-related T2D. These phyla show significant correlations with body mass index (BMI), although not directly with HbA1c levels [69]. Metaproteomic, the study of protein compositions in microbial communities, has identified unique protein signatures associated with obesity and diabetes. These include alterations in proteins involved in carbohydrate metabolism and inflammation [70].

Fats and gut microbiota

Dietary fats, particularly saturated fatty acids, can negatively impact the gut microbiota and promote metabolic inflammation [33, 35]. HFD has been shown to induce gut microbiota dysbiosis, leading to increased gut permeability and systemic inflammation [32, 33]. In contrast, monounsaturated fatty acids, such as those found in olive oil, may have beneficial effects on gut microbiota composition and metabolic health [48, 71].

A study by Girdhar et al. [72] investigates the relationship between gut microbiota, pancreatic growth, exocrine function, and gut hormones, particularly in the context of obesity and metabolic syndrome. Mice fed a HFD exhibited a significant 40% increase in pancreas weight. This suggests that dietary fat can lead to pancreatic hypertrophy, which may be linked to metabolic changes associated with obesity. The study found that HFD led to decreased levels of glucagon-like peptide-1 and peptide YY in the plasma, while glucose-dependent insulinotropic peptide levels increased. These changes indicate that a HFD can disrupt normal gut hormone signaling, which is crucial for metabolic regulation. Quantitative proteomics revealed that out of 138 host proteins identified in fecal samples, 32 were significantly altered by the HFD. Notably, pancreatic enzymes such as amylase and elastase were among the most significantly changed proteins, highlighting the impact of diet on pancreatic enzyme production. The

study demonstrated that the changes in pancreatic enzyme levels due to HFD could be reversed by antibiotic treatment (vancomycin or metronidazole). This suggests that gut microbiota plays a crucial role in mediating the effects of diet on pancreatic function. The alterations observed in pancreatic growth and function could be reproduced by transferring gut microbiota from donor C57BL/6J mice to germ-free mice. This indicates that gut microbiomes are a key factor influencing pancreatic health. In a clinical observation, one week of vancomycin administration significantly increased amylase and elastase levels in obese prediabetic men, further supporting the findings that gut microbiota alterations can affect pancreatic function in humans as well. Overall, the study concludes that changes in gut microbiota associated with obesity can significantly alter pancreatic growth, exocrine function, and gut hormone levels, potentially contributing to the metabolic disturbances seen in obesity and diabetes [72].

Another study by Suriano et al. [73] investigated the effects of different diets on obesity, metabolic disorders, and gut microbiota in mice. Mice feed a HFD exhibited the most significant increases in body weight and fat mass compared to those on other diets. This indicates that fat intake plays a crucial role in promoting obesity. The HFD also led to the most impaired glucose and insulin profiles among the different dietary groups. This suggests that HFD may contribute more significantly to IR than HS diets. The study found that the HS, HF/HS, and HFD affected hepatic cholesterol levels and the expression of mRNA markers related to immune cells, inflammation, and oxidative stress in various organs. This highlights the complex relationship between diet composition and metabolic health. Mice on the HFD showed a decrease in microbial load by the end of the experiment. This suggests that HFD may negatively impact gut microbiota density. The study revealed that different diets (HS, HF/HS, and HFD) led to specific changes in the abundance of certain bacterial taxa within the gut microbiota. This indicates that the type of macronutrients consumed can distinctly influence gut microbiota composition. The findings suggest that changes in gut microbiota composition may not only be a consequence of obesity but could also play a significant role in the development of metabolic disorders. This emphasizes the importance of considering gut health in dietary interventions for obesity and related conditions. Overall, the study concludes that dietary fat, rather than sugar, is a more critical factor in driving changes in gut microbiota and the development of obesity and metabolic disorders in mice [73].

Role of polyphenols

Polyphenols, bioactive compounds found in plants, have antioxidant and anti-inflammatory properties [36, 37, 74]. They can prevent or reverse disease progression through various mechanisms, including modulation of the gut microbiota [36]. Polyphenols can act as prebiotics, promoting the growth of beneficial bacteria and leading to the production of beneficial metabolites [36, 74]. The crosstalk between polyphenols and gut microbiota plays a central regulatory role in host energy metabolism and related illnesses [36].

Polyphenols have been shown to stimulate the browning of white adipose tissue and activate brown adipose tissue, processes that enhance energy expenditure and reduce body fat accumulation. This is partly mediated by the gut microbiota, which metabolizes polyphenols into bioactive compounds that influence adipose tissue function [75, 76]. Higher intakes of polyphenols, particularly flavonoids, have been inversely associated with BMI and waist circumference, suggesting a potential role in weight management [77]. Polyphenols can improve insulin sensitivity and reduce IR, as evidenced by their inverse association with the HOMA-IR in some studies [77, 78]. While some studies report no significant changes in blood glucose levels, others have found that polyphenols can lower HbA1c, a marker of long-term glucose control, indicating potential benefits for glycemic management [78].

Polyphenols can modulate inflammatory pathways, reducing the chronic low-grade inflammation associated with obesity and diabetes. This is achieved through the regulation of inflammatory cytokines and immune cell activity [79, 80]. The antioxidant properties of polyphenols help in reducing oxidative stress, a key factor in the pathogenesis of diabetes and its complications [81, 82]. Polyphenols influence the composition of the gut microbiota, promoting the growth of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*. These changes can enhance the production of SCFAs, which are beneficial for metabolic health [76, 80]. The interaction between polyphenols and gut microbiota leads to the production of metabolites that can modulate energy metabolism and inflammation, contributing to the management of obesity and diabetes [75, 76].

A study by Turan-Demirci et al. [77] investigated the relationship between dietary polyphenol, flavonoid, and lignan intakes and obesity and diabetes-related traits. The study included 331 participants, with 156 classified as overweight/obese and 175 as normal weight, all aged between 18 and 50 years. Dietary intake was assessed using a 24 h dietary recall method, and the phytochemical index (PI) score was calculated based on the percentage of energy intake from phytochemical-rich foods. Participants with higher PI scores had significantly higher total polyphenol intakes and some subclasses of polyphenols compared to those with lower scores ($p < 0.05$ for each). Total polyphenol intake was inversely associated with BMI ($\beta = -0.269$, $p = 0.049$) and waist circumference ($\beta = -0.127$, $p = 0.021$). Flavonoid intake also showed similar inverse associations with BMI ($\beta = -0.262$, $p = 0.048$) and waist circumference ($\beta = -0.130$, $p = 0.016$). Waist-to-hip ratio was inversely associated with both total polyphenol ($\beta = -20.724$, $p = 0.032$) and flavonoid intakes ($\beta = -22.199$, $p = 0.018$) after adjusting for potential confounders. The study found that neither the dietary PI score nor total and subclass polyphenol intakes were associated with a better metabolic profile, except for lignan intake, which was inversely associated with the HOMA-IR ($\beta = -0.048$, $p = 0.011$). The findings suggest that higher dietary polyphenol intake may play a role in preventing obesity and diabetes. The study emphasizes the need for validated tools to assess polyphenol intake in clinical practice. These results highlight the potential benefits of dietary polyphenols in managing obesity and diabetes-related traits [77].

While the potential benefits of polyphenols in managing obesity and diabetes are promising, the evidence is not yet conclusive. Many studies highlight the need for further research to fully understand the mechanisms and to establish effective dietary recommendations. Additionally, the variability in individual responses to polyphenol intake, influenced by factors such as genetics and gut microbiota composition, suggests that personalized approaches may be necessary to optimize their benefits.

Dietary Strategies for Obesity and Diabetes Management

Given the profound impact of diet on gut microbiota and host metabolism, dietary interventions hold great promise for preventing and managing obesity and T2D [23, 25, 35, 37]. Various dietary approaches (Table 3) have been studied for their effectiveness in weight

Table 3: Dietary strategies for obesity and diabetes management.

Dietary strategy	Core features	Effects on gut microbiota	Impact on obesity	Impact on diabetes
MD	High in fruits, vegetables, legumes, olive oil, whole grains, and fish	↑ *Bifidobacteria*, *Akkermansia*, ↑ SCFA producers	↓ Body weight ↓ Visceral fat	↓ HbA1c ↑ Insulin sensitivity ↓ Inflammation
Low-carbohydrate diet	< 130 g/day carbs; higher protein and fat intake	↓ SCFA producers if fiber is low ↑ *Bacteroides*	Rapid weight loss ↑ Fat oxidation	↓ Fasting glucose May ↑ IR if long-term
High-fiber diet	> 25 to 30 g/day dietary fiber (soluble + insoluble)	↑ SCFA (esp. butyrate) ↑ *Faecalibacterium prausnitzii*	↑ Satiety ↓ Energy intake	↓ Postprandial glucose ↓ HbA1c
IF	Time-restricted eating (e.g., 16:8 or 5:2 methods)	↑ Microbial richness ↑ Diurnal microbiota cycling	↓ Body weight ↓ Fat mass	↓ Fasting insulin ↓ HOMA-IR
Ketogenic diet	Very low carb (< 50 g/day), HFD, moderate protein	↓ *Bifidobacteria* ↑ *Alistipes*, ↑ Proteobacteria	Significant short-term weight loss	↓ HbA1c Mixed long-term glycemic control outcomes
Plant-based diet (Vegetarian/Vegan)	High in fiber, phytonutrients, no animal products	↑ *Prevotella*, *Roseburia*, ↑ microbial diversity	↓ BMI ↑ Lean mass to fat ratio	↓ Glucose levels ↑ Insulin sensitivity
DASH diet	Rich in fruits, vegetables, low-fat dairy; low sodium and saturated fat	↑ Beneficial bacteria (limited data)	↓ Body weight ↓ Blood pressure (beneficial in metabolic syndrome)	↓ Blood glucose ↓ IR
Caloric restriction	Reduction of total daily caloric intake (e.g., 500 to 750 kcal deficit)	↑ SCFA producers ↓ Pro-inflammatory microbes	Effective weight loss	↓ Insulin levels ↓ Systemic inflammation

management and glycemic control, with the Mediterranean diet (MD) frequently highlighted for its benefits. However, no single diet fits all, and personalization is key to successful management.

MD

The MD, characterized by high consumption of vegetables, fruits, fruits, nuts, cereals, whole grains, and olive oil, as well as moderate consumption of fish and poultry, and limited intake of sweets and red meat, has been extensively studied for its health benefits [71, 83]. The MD has been shown to improve weight loss, reduce dyslipidemia, modulate the gut microbiota, and decrease inflammatory mediators [71]. It is considered a valuable nutritional intervention for managing obesity and preventing several non-communicable diseases, including cardiovascular disease and T2D [71].

The MD has been associated with substantial weight loss, particularly when combined with calorie restriction and physical activity. This weight loss is crucial for reversing the negative effects of obesity, such as dyslipidemia and inflammation [71]. Additionally, MD has been associated with a reduced risk of developing T2D and its complications. Studies show that higher MD intake can decrease the incidence of diabetes by 19 - 30% [71]. The MD has been linked to improved glucoregulation, with studies showing a 30% lower relative risk of developing T2D compared to low-fat diets [84]. In patients with T2D, adherence to the MD has resulted in significant reductions in fasting plasma glucose and hemoglobin A1c levels, indicating better glycemic control [85]. The diet's high content of polyphenols and unsaturated fatty acids from olive oil and nuts enhances insulin sensitivity and reduces IR, which are critical factors in diabetes management [86].

A modified version of the MD, which includes higher monounsaturated fats and proteins, has shown significant improvements in body composition, including reductions in body fat and waist circumference [87]. The study involved eleven adults (8 men and 3 women) with overweight or obesity, who followed a modified MD aimed at achieving a 10% weight loss. The average age of participants was 37 years, and they had a mean BMI of 34.5 kg/m^2. Participants successfully lost an average of 10.4 kg (approximately 10% of their initial body weight) after following the diet for about 13 weeks. This weight loss was statistically significant ($p < 0.001$). Significant improvements were observed in body composition, including reductions in waist circumference and body fat percentage. These changes were statistically significant ($p < 0.05$). The modified MD led to notable improvements in metabolic health. Fasting insulin levels and IR (measured by the HOMA-IR index) decreased significantly ($p = 0.001$), and fasting glucose levels also improved ($p = 0.007$). After the dietary intervention, participants showed lower postprandial plasma glucose concentrations during both the oral glucose tolerance test (OGTT) and mixed-meal tolerance test (MMTT). Specifically, postprandial glucose responses were approximately 14% and 30% lower for the OGTT, and 12% lower for the MMTT, respectively ($p < 0.05$). Insulin levels during the postprandial tests also decreased significantly, with reductions of about 44% for the OGTT and 45% for the MMTT ($p < 0.05$). The study found improvements in the adiponectin-leptin ratio, indicating better metabolic health. Leptin levels decreased significantly ($p = 0.005$), while there was a trend towards increased adiponectin levels, which is beneficial for insulin sensitivity. Overall, the modified MD was effective in improving body composition, insulin sensitivity, and metabolic profiles in overweight and obese adults, demonstrating that dietary modifications can have significant health benefits [87].

IF

IF is an eating pattern that cycles between periods of eating and voluntary fasting on a regular schedule. IF has shown increasing positive effects, including anti-aging, neuroprotection, and obesity control. The gut microbiota is sensitive to dietary structure and habits, suggesting a potential association between IF and gut microbiota. IF can optimize host energy metabolism at various physical positions, including adipose tissue, liver, and intestines, and further improve milieu internal homeostasis [88].

A study by Sukkriang and Buranapin [89] aimed to evaluate the effects of two types of IF on weight reduction and metabolic outcomes in patients with obesity and T2D. A total of 99 participants completed the study, which was divided into three groups: (i) IF 16:8, (ii) IF 14:10, and (iii) control group (normal diet). The IF 16:8 group experienced a significant weight change of −4.02% from baseline (95% CI, −4.40 to −3.64). The IF 14:10 group had a weight change of −3.15% (95% CI, −3.41 to −2.89). The control group showed a minimal weight change of −0.55% (95% CI, −1.05 to −0.05). Both IF groups had significantly

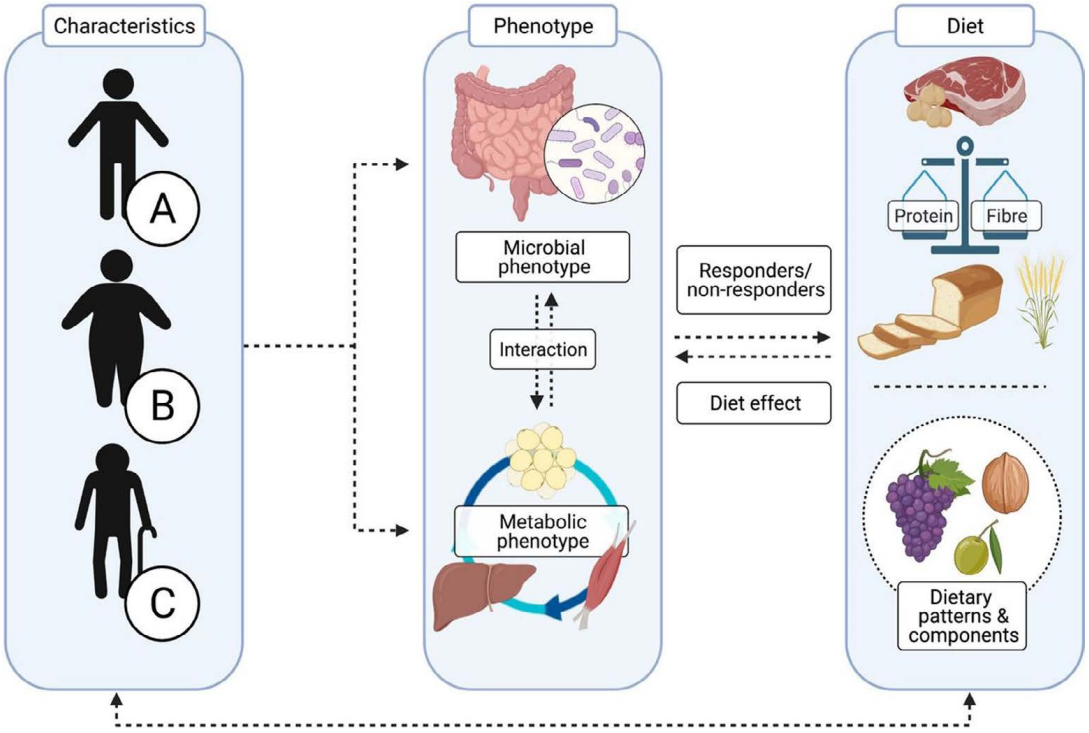

Figure 2: Effective implementation of precision nutrition depends on thorough profiling of each individual's physiological and metabolic characteristics [35].

greater weight loss compared to the control group ($p < 0.001$ for both comparisons). The weight loss in the IF 16:8 group was significantly greater than that in the IF 14:10 group ($p < 0.001$). Both IF groups showed significant improvements in metabolic outcomes compared to the control group. This included: (i) a decrease in fasting blood sugar, (ii) a reduction in HbA1C levels, and (iii) Improvements in lipid profiles (cholesterol and triglycerides). These metabolic improvements were statistically significant, indicating that IF had beneficial effects on glucose and lipid metabolism in obese diabetic patients. The study concluded that both IF 16:8 and IF 14:10 diets were effective in promoting weight loss and improving metabolic health in patients with obesity and T2D when followed for three days a week over three months. Overall, the results suggest that IF can be a valuable dietary approach for managing obesity and metabolic health in individuals with T2D [89].

Personalized nutrition

Interindividual responsiveness to specific dietary interventions may be partially determined by differences in baseline gut microbiota composition and functionality between individuals with distinct metabolic phenotypes [35]. Precision-based nutritional strategies, tailored to an individual's gut microbial and metabolic profile, may offer a more effective approach to improving body weight control and metabolic health (Figure 2) [35]. This approach requires detailed metabolic and microbial phenotyping to better understand the link between diet, the gut microbiome, and host metabolism [35].

A study by Yavarna and Parida [90] presented significant findings regarding the effectiveness of a personalized intervention aimed at improving health outcomes for individuals with diabetes and obesity. The study involved 41 participants, with 68% having diabetes or prediabetes and 32% classified as obese. The average age was 47 years, and 76% of the participants were male. Participants received personalized coaching remotely for a period ranging from 3 to 6 months, depending on their initial health status and motivation. There was a significant decrease in HbA1c levels by an average of 1.64% points among participants in the diabetic/prediabetic program. Fasting glucose levels dropped by 24%. Postprandial (after meal) glucose levels decreased by 27%. Participants in the diabetic/prediabetic program lost an average of 3.4% of their body weight, while those in the Weight loss program experienced a more substantial weight reduction of 7.5%. Waist circumference decreased by 3.2% in the diabetic/prediabetic group and by 6.8% in the weight loss group. Participants who were on insulin injections reduced their insulin doses by an impressive 67% by the end of the intervention. Those non-insulin oral hypoglycemic agents reduced their medication use by 27%. The findings indicate that a personalized program combining plant-based whole foods, time restricted eating, and fractionized exercise can lead to significant improvements in metabolic health markers and a reduction in medication needs for individuals with diabetes and obesity [90].

Conclusion

The intricate relationship between macronutrients, the gut microbiota, and host metabolism offers a promising avenue for developing effective dietary strategies against obesity and diabetes. Modulating the gut microbiota through dietary interventions, such as increasing dietary fiber intake, adopting an MD, or practicing IF, can improve metabolic health and prevent or manage these chronic diseases. Future research should focus on developing personalized nutrition strategies based on individual gut microbial and metabolic profiles to optimize dietary recommendations and improve health outcomes. This detailed metabolic and microbial phenotyping is necessary to better understand the link between diet, the gut microbiome, and host metabolism.

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Conflict of Interest

None.

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