EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 12
Issue: 5
Year: 2025

GUT MICROBIOME'S ROLE IN OBESITY AND INSIGHTS INTO PROBIOTIC POTENTIAL - A REVIEW

***Dr. Y. Shanti Prabha**

Sr. Lecturer in Zoology, Dr. V S Krishna Government Degree and PG College (A), Visakhapatnam-530013.

***Corresponding Author: Dr. Y. Shanti Prabha**
Sr. Lecturer in Zoology, Dr. V S Krishna Government Degree and PG College (A), Visakhapatnam-530013.

Article Received on 26/03/2024 **Article Revised on 16/04/2025** **Article Accepted on 06/05/2025**

ABSTRACT
A serious worldwide public health emergency, obesity is a chronic metabolic disease marked by an excessive buildup of adipose tissue. A complicated interaction between lifestyle, environmental, and genetic factors contributes to its multifactorial aetiology, which results in an imbalance between energy expenditure and intake. Type 2 diabetes, heart disease, and several types of cancer are among the many comorbidities that obesity dramatically raises the risk of. A possible supplemental treatment for managing obesity is probiotics, which are live bacteria that provide health advantages when taken in sufficient quantities. By a variety of methods, strains of Lactobacillus, Bifidobacterium, Streptococcus, and Saccharomyces have shown anti-obesity benefits. With an emphasis on their possible incorporation into obesity management regimens, this review article attempts to present a good summary of the state of knowledge about the role of probiotics in obesity.

KEYWORDS: Obesity, metabolic disorder, gut microbiota, inflammation.

INTRODUCTION

Obesity is a multifactorial, chronic, and progressive metabolic disorder that arises from the excessive accumulation of adipose tissue, often due to a persistent imbalance between caloric intake and energy expenditure. One of the primary reasons people become overweight or obese is precisely this imbalancewhen energy intake exceeds expenditure, the surplus is stored as fat. Obesity can generally be classified into two types: primary and secondary. Primary obesity is mostly linked to modifiable lifestyle and environmental factors, such as poor dietary habits and physical inactivity. In contrast, secondary obesity arises from underlying medical conditions, including hormonal disorders like hypothyroidism, polycystic ovary syndrome (PCOS), or certain genetic syndromes.

According to the World Health Organization (WHO, 2023), the global prevalence of obesity has nearly tripled since 1975, with over 650 million adults classified as obese in 2016 and a continuing upward trend across all age groups. This alarming rise has positioned obesity as a major global public health crisis of the 21st century. Carrying excess weight isn't just a cosmetic concernit significantly increases the risk of developing numerous non-communicable diseases, including type 2 diabetes mellitus, cardiovascular diseases (e.g., coronary artery disease, stroke), hypertension, dyslipidemia, non-alcoholic fatty liver disease, osteoarthritis, respiratory conditions like obstructive sleep apnea, and various cancers such as breast, colorectal, and endometrial. Obesity is also closely linked with psychological issues such as depression and anxiety (Bray et al., 2017; Hruby & Hu, 2015; Guh et al., 2009). These comorbidities not only reduce quality of life but also contribute to escalating healthcare costs globally.

Conventional management strategies for obesity have largely focused on lifestyle-based interventions, emphasizing caloric restriction, dietary modifications, increased physical activity, and behavioral therapy. Pharmacological agents such as orlistat, liraglutide, and naltrexone-bupropion have shown efficacy in promoting weight loss when used alongside lifestyle changes. Bariatric surgery, although invasive, remains the most effective treatment for severe or refractory obesity, offering sustained weight reduction and improvements in associated comorbidities (Apovian et al., 2015; Garvey et al., 2016). However, despite these interventions, long-term success remains inconsistent due to the complex and often relapsing nature of obesity.

Recent scientific advances have shifted the paradigm from viewing obesity as merely a consequence of individual behavior to recognizing it as a condition influenced by a multifaceted interplay of genetic, epigenetic, neuroendocrine, environmental, and microbial factors. Twin and family studies estimate the

heritability of obesity to range between 40–70%, reflecting a strong genetic predisposition (Loos & Yeo, 2022). However, genetic susceptibility alone cannot explain the rapid and widespread rise in obesity rates, underscoring the role of environmental and modifiable exposures.

Recent research has highlighted the complex interplay between gut microbiota and obesity, suggesting that an imbalance in the microbial ecosystem may contribute to weight gain and metabolic disorders. Studies have shown that certain bacterial species can influence energy metabolism, fat storage, and appetite regulation, potentially offering new avenues for obesity prevention and treatment. Probiotics, which are live microorganisms that confer health benefits when consumed in adequate amounts, have emerged as a promising approach to modulate the gut microbiome and potentially mitigate obesity-related complications.

Among the emerging contributors, the gut microbiotaa complex and dynamic microbial community inhabiting the human gastrointestinal tracthas gained substantial attention for its role in energy regulation and metabolic health. Increasing evidence suggests that the gut microbiota acts as a key modulator of host metabolism, influencing nutrient absorption, energy harvest, immune responses, and fat storage. Dysbiosis, or an imbalance in gut microbial composition and function, has been implicated in the pathogenesis of obesity. Individuals with obesity frequently display a distinct gut microbial profile compared to lean individuals, including altered ratios of Firmicutes to Bacteroidetes and reduced microbial diversity (Aggarwal et al., 2013; Abenavoli et al., 2019).

Diet appears to be a major determinant of microbial composition. The modern Western dietcharacterized by high fat, high sugar, and low fiber contenthas been shown to disrupt the gut microbiota, promoting the proliferation of potentially pathogenic bacteria and inducing dysbiosis (Turnbaugh et al., 2008; Hildebrandt et al., 2009; Li et al., 2009). Animal and human studies have consistently demonstrated that such dietary-induced dysbiosis is associated with increased energy extraction from food, systemic low-grade inflammation, insulin resistance, and enhanced fat deposition (Turnbaugh et al., 2006; Ridaura et al., 2013; Muscogiuri et al., 2019).

Although the exact mechanisms remain under investigation, several biological pathways have been proposed through which gut dysbiosis contributes to obesity. These include chronic low-grade inflammation, impaired lipid and bile acid metabolism, decreased insulin sensitivity, and altered production of short-chain fatty acids (SCFAs)all of which promote weight gain and metabolic dysfunction (Baothman et al., 2016; Rogers et al., 2016; Bliss & Whiteside, 2018).

In response to these findings, researchers are increasingly exploring microbiota-targeted therapies as adjuncts in obesity management. Among these, probiotics have emerged as a promising strategy to restore gut microbial balance and modulate host metabolism. Defined by the Food and Agriculture Organization (FAO) and the WHO as *"live microorganisms which, when administered in adequate amounts, confer a health benefit on the host"* (FAO/WHO, 2002), probiotics are increasingly being studied for their therapeutic potential in obesity.

Probiotics, particularly strains of *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, and *Saccharomyces*, have demonstrated encouraging anti-obesity effects in both animal models and clinical studies (Ji et al., 2012; Park et al., 2013). These beneficial microbes may exert their effects through various mechanisms, such as enhancing gut barrier integrity, reducing systemic inflammation, modulating appetite-regulating hormones (e.g., leptin and ghrelin), improving SCFA production, and restoring microbial homeostasis. Thereby, probiotics can potentially reduce body weight, improve lipid profiles, and enhance insulin sensitivity.

Importantly, probiotics represent a non-invasive, low-risk, and cost-effective adjunctive tool in the broader management of obesity. However, their effectiveness appears to be strain-specific, dose-dependent, and host-dependent, with outcomes influenced by factors such as diet, age, genetics, and baseline gut microbiota composition. Thus, while the therapeutic promise is considerable, there remains a critical need for well-designed randomized controlled trials and mechanistic studies to determine optimal strains, dosing regimens, and their long-term metabolic impacts.

This review article aims to provide a comprehensive overview of the current understanding of the role of probiotics in obesity, focusing on their potential integration into obesity management strategies. As research continues to unravel the intricate relationship between gut health and systemic metabolism, probiotics may offer a novel, microbiota-targeted approach in addressing the global obesity epidemic.

Review of Literature

Gut Microbiota and Energy Homeostasis

The role of the gut microbiota in regulating energy balance is a rapidly evolving area of research with profound implications for understanding obesity and metabolic disorders. Early studies, notably the work by Turnbaugh et al. (2006), established that the gut microbiota is not a passive bystander in the host's energy balance but actively participates in regulating energy extraction from the diet, thereby influencing fat accumulation and metabolic health. Understanding the gut microbiome's role in obesity is crucial for developing targeted probiotic therapies that could offer new avenues for obesity management.

1. Influence of Gut Microbiota on Energy Harvest

The influence of the gut microbiota on the host's ability to harvest energy from the diet is a key mechanism in the development of obesity. The landmark study by Turnbaugh et al. (2006) demonstrated that the gut microbiota significantly increases the efficiency of dietary energy extraction. In this experiment, germ-free mice (mice raised in a sterile environment with no microbial colonization) were colonized with gut microbiota from conventionally raised mice. Despite consuming less food, these mice exhibited a notable increase in body fat, suggesting enhanced caloric extraction and storage due to microbial activity. This was one of the first definitive pieces of evidence indicating that the gut microbiota can drive adiposity independent of caloric intake.

The production of a wide range of bioactive chemicals by the active gut microbiota is essential to host physiology and can have both beneficial and detrimental effects on health. The fermentation of dietary fibres is the main source of short-chain fatty acids (SCFAs), which include butyrate, propionate, and acetate. These metabolites are among the most researched. According to Koh et al. (2016) and Silva et al. (2020), these SCFAs are known to have a variety of uses, including supplying colonocytes with energy, regulating immunological responses, improving the function of the gut barrier, and having anti-inflammatory properties.

The microbiota's role in energy harvest is also largely mediated through the fermentation of complex polysaccharides, such as dietary fibers, that are otherwise indigestible by the host. Gut bacteria, particularly from the phyla Firmicutes and Bacteroidetes, possess an extensive repertoire of glycoside hydrolases and polysaccharide lyases, enabling them to break down complex carbohydrates into simpler metabolites (Flint et al., 2012). These are subsequently converted into short-chain fatty acids (SCFAs)notably acetate, propionate, and butyrate which are absorbed in the colon and contribute directly to host energy metabolism (den Besten et al., 2013).

SCFAs can account for up to 10% of the daily caloric requirements in humans (Bäckhed et al., 2004). Once absorbed, acetate enters systemic circulation and contributes to lipogenesis in the liver, while propionate serves as a gluconeogenic substrate and butyrate provides energy for colonocytes (Canfora et al., 2015). The presence of these SCFAs not only boosts the caloric yield from food but also modulates lipid and glucose metabolism, potentially promoting hepatic fat accumulation and insulin resistance in susceptible individuals.

Moreover, variations in gut microbial composition can influence the efficiency of energy extraction. Obese individuals often exhibit an increased Firmicutes-to-Bacteroidetes ratio, which has been associated with a greater ability to harvest energy from food (Ley et al., 2006). This microbial shift may potentiate increased SCFA production, enhanced intestinal absorption, and subsequent energy storage in adipose tissue.

Along with SCFAs, gut microorganisms also produce a number of vital vitamins, such as vitamin K and B vitamins (such as B12, biotin, folate, and riboflavin), which support a number of neurological and metabolic functions (LeBlanc et al., 2013). These nutrients from microbes are particularly crucial for people who have impaired absorption or dietary deficits.

Additionally, the microbial breakdown of tryptophan produces indole derivatives, which are among the health-promoting compounds that the gut microbiota helps produce. These substances have anti-inflammatory and antioxidant properties by activating aryl hydrocarbon receptors (AhR) (Zelante et al., 2013). Similar to this, microbial metabolites such equol, which are made from soy isoflavones, have estrogen-like and analgesic properties that may help prevent hormone-related malignancies and lessen menopausal symptoms (Setchell & Clerici, 2010).

Additional research by Ridaura et al. (2013) provided further support for the causal role of gut microbiota in energy harvest and obesity. In their study, germ-free mice were colonized with microbiota from either obese or lean human twin donors. Mice receiving microbiota from obese donors gained significantly more fat mass than those colonized with microbiota from lean donors, even when food intake remained consistent. This underscores the functional transmissibility of an "obese phenotype" through the microbiome.

2. Mechanisms of Energy Extraction: Short-Chain Fatty Acids (SCFAs)

One of the primary metabolites produced by gut bacteria during the fermentation of dietary fibers is **short-chain fatty acids (SCFAs)**, including acetate, propionate, and butyrate. These SCFAs are pivotal in mediating the microbiota-host interaction and have profound effects on energy metabolism. **Acetate**, the most abundant SCFA in the colon, is absorbed into the bloodstream and transported to the liver, where it can be used for fatty acid synthesis or converted to ATP for energy production (den Besten et al., 2013). This can lead to increased lipid storage and fat accumulation, contributing to weight gain. **Propionate** and **butyrate**, on the other hand, have distinct metabolic effects. Propionate is primarily absorbed by the liver, where it is used for gluconeogenesis, potentially influencing glucose homeostasis and energy regulation. Butyrate, produced by certain gut microbes, is the preferred energy source for colonic epithelial cells and plays an essential role in maintaining gut barrier integrity (Canfora et al., 2015). Importantly, butyrate has been shown to have anti-inflammatory properties, and its production by the gut microbiota is associated with improved metabolic health.

These SCFAs also act as signaling molecules, activating G-protein-coupled receptors (GPCRs), such as **GPR41** and **GPR43**, which are present on the gut epithelium and adipocytes. Activation of these receptors has been shown to increase the secretion of gut hormones like **glucagon-like peptide 1 (GLP-1)** and **peptide YY (PYY)**. These hormones are involved in regulating appetite, satiety, and insulin sensitivity, thereby influencing overall energy balance.**GLP-1**, for example, promotes insulin secretion, reduces glucagon levels, and increases satiety, all of which play critical roles in glucose metabolism and weight regulation. Additionally, GLP-1 has been shown to improve gut motility and barrier function, thereby promoting overall metabolic health.**PYY**, which is released in response to feeding, inhibits appetite and regulates energy expenditure, potentially counteracting the effects of excess caloric intake.

3. Gut Microbiota Modulation of Hepatic Lipogenesis and Glucose Homeostasis

Gut microbiota has been implicated in modulating hepatic lipogenesis (the process by which the liver converts excess carbohydrates and proteins into fat) and glucose homeostasis, both of which are critical in the context of obesity and metabolic disease. The liver plays a central role in energy metabolism, and recent studies suggest that microbial metabolites, particularly SCFAs, influence liver function. For example, SCFAs can activate peroxisome proliferator-activated receptor α (PPAR-α), a transcription factor that regulates lipid metabolism and the expression of genes involved in fatty acid oxidation (Canfora et al., 2015). In this manner, gut microbiota can help balance lipid storage and utilization.

Furthermore, the gut microbiota has been shown to affect insulin sensitivity by modulating inflammation and the secretion of hormones that influence glucose metabolism. Inflammation is a key feature of obesity and metabolic syndrome, and SCFAs like butyrate have anti-inflammatory properties that may help mitigate the systemic inflammation associated with obesity. Studies have demonstrated that the microbiota can modulate the release of cytokines and adipokines, which are important regulators of insulin sensitivity and glucose homeostasis (den Besten et al., 2013).

4. Gut Microbiota and Metabolic Disorders

Several studies have highlighted that dysbiosis, or an imbalance in the gut microbiota, is often observed in obese individuals and those with metabolic disorders. Changes in the composition of the microbiota, such as reduced diversity and a higher Firmicutes-to-Bacteroidetes ratio, are linked to impaired energy homeostasis and weight gain. Dysbiosis is associated with low-grade systemic inflammation, insulin resistance, and altered SCFA production, all of which contribute to the development of obesity and related metabolic conditions (Cani et al., 2007).

The role of gut microbiota in the pathogenesis of obesity is also evident in animal models. For instance, studies involving germ-free mice or antibiotic-treated mice have shown that the absence of gut microbiota results in reduced fat deposition and improved metabolic profiles (Ridaura et al., 2013). Conversely, colonizing germ-free mice with microbiota from obese individuals leads to obesity and insulin resistance, emphasizing the role of gut microbiota in promoting energy storage and metabolic dysregulation.

5. Diet and Microbial Influence on Energy Balance

The dietary intake of fiber, fat, and sugar has a profound impact on gut microbial composition and function. A high-fat, low-fiber Western diet has been shown to promote the growth of Firmicutes and reduce the diversity of the microbiota, leading to increased energy harvest and fat deposition. In contrast, fiber-rich diets, which promote the growth of beneficial bacteria like Bifidobacteria and *Akkermansia muciniphila*, can help restore microbial balance and improve metabolic health (David et al., 2014; Everard et al., 2013).

Dietary fibers, particularly prebiotics, which serve as food for beneficial gut microbes, have been shown to increase the production of SCFAs, thereby influencing energy balance and metabolic health. For example, a study by David et al. (2014) demonstrated that increasing fiber intake improved gut microbial diversity, which in turn led to enhanced SCFA production and better glucose metabolism.

6. Therapeutic Potential

The growing evidence linking gut microbiota to energy homeostasis has sparked interest in therapeutic approaches targeting the microbiota, including probiotics, prebiotics, and fecal microbiota transplantation (FMT). Probiotic interventions, particularly those involving strains of *Lactobacillus* and *Bifidobacterium*, have been shown to reduce body weight, improve insulin sensitivity, and modulate SCFA production (Aron-Wisnewsky et al., 2019). However, the effects of probiotics are highly strain-dependent, and more research is needed to identify the most effective strains for weight management. Prebiotics, such as inulin and fructooligosaccharides (FOS), can promote the growth of beneficial gut bacteria and increase SCFA production, thereby improving energy balance and reducing obesity-related symptoms. Similarly, FMT has been explored as a potential therapeutic option for obesity, with studies showing that transplantation of gut microbiota from lean donors to obese recipients can lead to weight loss and improved metabolic function (Ridaura et al., 2013).

Microbial Composition in Obesity

Recent research continues to affirm that gut dysbiosisa disrupted microbial equilibrium in the gastrointestinal tractis closely associated with the pathophysiology of obesity. Gut dysbiosis encompasses not only

compositional shifts in microbial taxa but also functional changes that influence host metabolism, immune function, and energy balance.

A recurrent observation in both animal and human studies is the alteration in the Firmicutes-to-Bacteroidetes (F/B) ratio, which has been widely implicated in obesity. While earlier studies, such as Ley et al. (2006) and Turnbaugh et al. (2009), established a higher F/B ratio in obese individuals, more recent analyses have nuanced this finding. Liu et al. (2021) conducted a systematic review and meta-analysis involving over 1,000 individuals and found that although some studies reported a higher F/B ratio in obesity, the results varied significantly across geographic regions, suggesting that the association may not be universal but context-dependent, influenced by diet, lifestyle, genetics, and ethnicity.

Beyond the F/B ratio, taxonomic profiling using 16S rRNA sequencing and metagenomics has revealed more specific microbial signatures. Obese individuals often show increased abundances of genera such as *Lactobacillus*, *Clostridium*, and *Prevotella*, while beneficial microbes like *Bifidobacterium* and *Akkermansia muciniphila* tend to be depleted (Zhang et al., 2020; Dao et al., 2021). For example, *A. muciniphila* has been associated with improved gut barrier integrity, reduced inflammation, and better glucose tolerance, and its reduced abundance is a notable marker of metabolic dysfunction.

A critical hallmark of obesity-related dysbiosis is the loss of microbial diversity, which is often linked to impaired metabolic flexibility and resilience. Liu et al. (2022) reported that individuals with lower microbial alpha diversity particularly those with reduced levels of butyrate-producing bacteria such as *Faecalibacterium prausnitzii* displayed significantly greater adiposity, insulin resistance, and systemic inflammation. This reduced diversity limits the functional repertoire of the microbiota, including its ability to ferment dietary fibers and produce health-promoting short-chain fatty acids (SCFAs).

Recent research also highlights changes in the functional potential of the microbiota in obesity. For instance, obese individuals exhibit enrichment in microbial genes related to lipopolysaccharide (LPS) biosynthesis, branched-chain amino acid metabolism, and fermentation of carbohydrates to SCFAs, all of which can promote chronic low-grade inflammation and increased fat storage (Kim et al., 2020; Schertzer et al., 2023).

Additionally, microbial co-occurrence networks are altered in obesity, with diminished network connectivity and stability. This weakened ecological structure may further exacerbate dysbiosis and hinder the gut ecosystem's ability to recover from environmental insults such as high-fat diets or antibiotic exposure (Wang et al., 2020).

Probiotics and Modulation of Gut Microbiota in Obesity

Given the pivotal role of gut microbiota in the regulation of host metabolism and the pathogenesis of obesity, modulation of the microbiota through probiotics has emerged as a promising strategy for obesity management. Probiotics defined as *live microorganisms which, when administered in adequate amounts, confer a health benefit on the host* (FAO/WHO, 2002) have shown the potential to reshape gut microbial composition, reduce inflammation, regulate energy homeostasis, and improve metabolic profiles.

Recent studies emphasize the strain-specific nature of probiotic effects in obesity. For instance, supplementation with *Lactobacillus gasseri* BNR17 was shown in a 2021 randomized controlled trial to significantly reduce body weight, BMI, and waist circumference in obese adults, while improving lipid profiles and glucose tolerance (Lim et al., 2021). This supports earlier findings with *Lactobacillus gasseri* SBT2055, which demonstrated reductions in visceral and subcutaneous adipose tissue (Kadooka et al., 2010).

Other strains such as Bifidobacterium breve B-3 and *Lactobacillus rhamnosus* GG have also demonstrated anti-obesity effects, including fat mass reduction, improved insulin sensitivity, and attenuation of pro-inflammatory cytokine expression (Kondo et al., 2020; Sanchez et al., 2021). These effects are believed to occur through the production of beneficial metabolites (e.g., SCFAs), modulation of gut hormones (e.g., GLP-1, PYY), enhancement of intestinal barrier integrity, and suppression of systemic endotoxemia.

Additionally, next-generation probiotics such as *Akkermansia muciniphila* have gained increasing attention. In a notable double-blind, placebo-controlled study by Depommier et al. (2019), pasteurized *A. muciniphila* supplementation in overweight and obese individuals led to significant improvements in insulin sensitivity, plasma cholesterol, and markers of inflammation, even in the absence of significant weight loss suggesting metabolically beneficial effects independent of body weight.

The mechanistic benefits of probiotics in obesity extend beyond mere compositional changes. Probiotics can promote the growth of beneficial commensals and restore microbial diversity, enhance the production of short-chain fatty acids (SCFAs), which regulate energy extraction and fat storage, suppress lipopolysaccharide (LPS)-induced endotoxemia, reducing chronic low-grade inflammation a known driver of insulin resistance and adiposity (Zhao et al., 2022) and influence appetite regulation through interactions with the gut–brain axis and modulation of satiety-related hormones.

Probiotic strains like *Lactobacillus plantarum* and *Lactobacillus casei* have also been reported to improve gut barrier function and reduce intestinal permeability, thus preventing the translocation of pro-inflammatory bacterial components that contribute to metabolic derangement (Han et al., 2020).

Despite promising findings, interindividual variability in probiotic response remains a significant challenge. Factors such as host genetics, baseline gut microbiota, diet, age, and comorbidities influence how a probiotic functions in a given individual (Zmora et al., 2018). A "one-size-fits-all" approach is thus unlikely to be effective, and personalized microbiome-based interventions are increasingly being explored. Moreover, many studies differ in terms of study design, probiotic dosage, treatment duration, and outcome measures, which complicates direct comparisons. While several strains have shown benefit in preclinical and small-scale human trials, large, well-designed randomized controlled trials (RCTs) are still needed to confirm long-term efficacy, safety, and optimal delivery strategies.

All microbial product may not be advantageous. Potentially dangerous substances, such as neurotoxins (such as D-lactic acid, ammonia, and p-cresol), which have been connected to hepatic encephalopathy and neuro-developmental abnormalities, can be produced by the same metabolic processes (Tremlett et al., 2017). By causing inflammation and DNA damage, carcinogenic chemicals including N-nitroso compounds and secondary bile acids (such deoxycholic acid) can encourage colorectal cancer (Louis et al., 2014; O'Keefe, 2016). Furthermore, bacterial cell wall-derived immunotoxins and pro-inflammatory molecules like peptidoglycans and lipopolysaccharides (LPS) can cause systemic inflammation and immune dysregulation, which aids in the aetiology of illnesses like metabolic syndrome and autoimmune disorders (Cani et al., 2008).

CONCLUSION

Understanding the intricate relationship between the gut microbiota and energy homeostasis marks a pivotal shift in how we conceptualize obesitynot merely as a result of caloric imbalance, but as a complex interplay between host metabolism and microbial ecology. It is now evident that our gut bacteria do far more than aid in digestion; they shape how we extract, store, and expend energy. Through the fermentation of dietary fibers into SCFAs, modulation of gut hormones, and influence on hepatic and systemic metabolism, the microbiota serves as a metabolic gatekeeper. The realization that microbial communities can promote or protect against obesity offers exciting opportunities for targeted interventions aimed at restoring balance and metabolic health.

The evolving science of probiotics holds great promise in this context. Carefully selected probiotic strains have shown potential in reshaping the gut ecosystem, enhancing SCFA production, improving insulin sensitivity, reducing fat accumulation, and even modulating appetite. Yet, this is not a one-size-fits-all solution. Individual responses to probiotics vary significantly, shaped by unique microbial landscapes, genetic factors, and lifestyle habits. As such, future therapies must embrace a more personalized approach, possibly integrating precision nutrition, microbiome profiling, and tailored probiotic regimens to maximize benefits for metabolic health.

Looking ahead, the gut microbiota represents a powerful therapeutic target in the global fight against obesity and related metabolic disorders. However, translating these findings into clinical practice demands more robust, long-term studies that address the nuances of microbial strain selection, dosage, delivery mechanisms, and safety. It also requires interdisciplinary collaboration between microbiologists, clinicians, nutritionists, and bioinformaticians. With continued investment in microbiome research and innovation, we stand at the cusp of redefining obesity management from treating symptoms to modifying root causes at the microbial level.

REFERENCES

1. Apovian, C. M., Aronne, L. J., Bessesen, D. H., et al. (2015). Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *Journal of Clinical Endocrinology & Metabolism*, 100(2): 342–362.
2. Bray, G. A., Kim, K. K., & Wilding, J. P. H. (2017). Obesity: a chronic relapsing progressive disease process. *A position statement of the World Obesity Federation.Obesity Reviews*, 18(7): 715–723.
3. FAO/WHO. (2002). Guidelines for the evaluation of probiotics in food. Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food.
4. Garvey, W. T., Mechanick, J. I., Brett, E. M., et al. (2016). American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocrine Practice*, 22(Suppl 3): 1–203.
5. Guh, D. P., Zhang, W., Bansback, N., et al. (2009). The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health*, 9: 88.
6. Hruby, A., & Hu, F. B. (2015). The epidemiology of obesity: a big picture. *Pharmacoeconomics*, 33(7): 673–689.
7. Loos, R. J. F., & Yeo, G. S. H. (2022). The genetics of obesity: from discovery to biology. *Nature Reviews Genetics*, 23: 120–133.
8. Muscogiuri, G., Cantone, E., Cassarano, S., et al. (2019). Gut microbiota: a new path to treat obesity. *International Journal of Obesity Supplements*, 9(1): 10–19.
9. Ridaura, V. K., Faith, J. J., Rey, F. E., et al. (2013). Gut microbiota from twins discordant for obesity

modulate metabolism in mice. *Science*, 341(6150): 1241214.
10. Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., et al. (2006). An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature*, 444: 1027–1031.
11. WHO. (2023). Obesity and overweight. Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
12. Hall, K. D., Heymsfield, S. B., Kemnitz, J. W., et al. (2012). Energy balance and its components: implications for body weight regulation. *The American Journal of Clinical Nutrition*, 95(4): 989–994. https://doi.org/10.3945/ajcn.112.036350
13. Sun, K., Tordjman, J., Clément, K., & Scherer, P. E. (2013). Fibrosis and adipose tissue dysfunction. *Cell Metabolism*, 18(4): 470–477. https://doi.org/10.1016/j.cmet.2013.06.016
14. Kershaw, E. E., & Flier, J. S. (2004). Adipose tissue as an endocrine organ. *The Journal of Clinical Endocrinology & Metabolism*, 89(6): 2548–2556. https://doi.org/10.1210/jc.2004-0395
15. Abenavoli, L., Scarpellini, E., Colica, C., et al. (2019). Gut microbiota and obesity: A role for probiotics. *Nutrients*, 11(11): 2690. https://doi.org/10.3390/nu11112690
16. Aggarwal, S., Yadav, A., & Sharma, V. (2013). Role of gut microbiota in pathogenesis of obesity. *Indian Journal of Medical Specialities*, 4(2): 134–138.
17. Baothman, O. A., Zamzami, M. A., Taher, I., et al. (2016). The role of gut microbiota in the development of obesity and diabetes. *Lipids in Health and Disease*, 15: 108. https://doi.org/10.1186/s12944-016-0278-4
18. Bliss, D. Z., & Whiteside, C. A. (2018). Microbiota, obesity, and gut inflammation. *Nutrition Today*, 53(2): 65–70. https://doi.org/10.1097/NT.0000000000000261
19. Hildebrandt, M. A., Hoffmann, C., Sherrill–Mix, S. A., et al. (2009). High-fat diet determines the composition of the murine gut microbiome independently of obesity. *Gastroenterology*, 137(5): 1716–1724.e2. https://doi.org/10.1053/j.gastro.2009.08.042
20. Ji, Y., Park, S., Chung, Y., et al. (2012). Amelioration of diet-induced obesity by *Lactobacillus rhamnosus* PL60 in murine model. *British Journal of Nutrition*, 107(11): 1706–1714. https://doi.org/10.1017/S0007114511005072
21. Li, J. V., Ashrafian, H., Bueter, M., et al. (2009). Metabolic surgery profoundly influences gut microbial–host metabolic cross-talk. *Gut*, 58(9): 1210–1218. https://doi.org/10.1136/gut.2008.167908
22. Park, D. Y., Ahn, Y. T., Park, S. H., et al. (2013). Supplementation of *Lactobacillus curvatus* HY7601 and *Lactobacillus plantarum* KY1032 in diet-induced obese mice is associated with gut microbial changes and reduction in obesity. *PLoS ONE*, 8(3): e59470. https://doi.org/10.1371/journal.pone.0059470
23. Rogers, C. J., Keating, A. F., Yong, M., et al. (2016). Obesity alters gut microbiota and modulates epigenetic regulation of the host genome. *Obesity*, 24(4): 894–902. https://doi.org/10.1002/oby.21470
24. Turnbaugh, P. J., Bäckhed, F., Fulton, L., & Gordon, J. I. (2008). Diet-induced obesity is linked to marked but reversible alterations in the mouse distal gut microbiome. *Cell Host & Microbe*, 3(4): 213–223. https://doi.org/10.1016/j.chom.2008.02.015
25. Canfora, E. E., Jocken, J. W., & Blaak, E. E. (2015). Short-chain fatty acids in control of body weight and insulin sensitivity. *Nature Reviews Endocrinology*, 11(10): 577–591.
26. Cani, P. D., Amar, J., Iglesias, M. A., et al. (2007). Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes*, 56(7): 1761–1772.
27. den Besten, G., van Eunen, K., Groen, A. K., et al. (2013). The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *Journal of Lipid Research*, 54(9): 2325–2340.
28. David, L. A., Maurice, C. F., Carmody, R. N., et al. (2014). Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, 505(7484): 559–563.
29. Everard, A., Belzer, C., Geurts, L., et al. (2013). Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity. *Proceedings of the National Academy of Sciences*, 110(22): 9066–9071.
30. Ridaura, V. K., Faith, J. J., Rey, F. E., et al. (2013). Gut microbiota from twins discordant for obesity modulate metabolism in mice.
31. Bäckhed, F., Ding, H., Wang, T., et al. (2004). The gut microbiota as an environmental factor that regulates fat storage. *Proceedings of the National Academy of Sciences*, 101(44): 15718–15723.
32. Canfora, E. E., Jocken, J. W., & Blaak, E. E. (2015). Short-chain fatty acids in control of body weight and insulin sensitivity. *Nature Reviews Endocrinology*, 11(10): 577–591.
33. den Besten, G., van Eunen, K., Groen, A. K., et al. (2013). The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *Journal of Lipid Research*, 54(9): 2325–2340.
34. Flint, H. J., Scott, K. P., Duncan, S. H., et al. (2012). Microbial degradation of complex carbohydrates in the gut. *Gut Microbes*, 3(4): 289–306.
35. Ley, R. E., Turnbaugh, P. J., Klein, S., & Gordon, J. I. (2006). Microbial ecology: Human gut microbes associated with obesity. *Nature*, 444(7122): 1022–1023.
36. Ridaura, V. K., Faith, J. J., Rey, F. E., et al. (2013). Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science*, 341(6150): 1241214.
37. Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., et al. (2006). An obesity-associated gut microbiome

with increased capacity for energy harvest. *Nature*, 444(7122): 1027–1131.
38. Dao, M. C., Everard, A., Aron-Wisnewsky, J., Sokolovska, N., Prifti, E., Verger, E. O., ... & Clément, K. (2021). Akkermansia muciniphila and improved metabolic health during a dietary intervention in obesity: relationship with gut microbiome richness and ecology. *Gut*, 70(4): 700–711.
39. Kim, Y., Kim, H. S., & Park, S. (2020). Gut microbiota composition and metabolic syndrome in obese individuals: A systematic review and meta-analysis. *Journal of Clinical Medicine*, 9(11): 3703.
40. Liu, R., Hong, J., Xu, X., Feng, Q., Zhang, D., Gu, Y., ... & Ning, G. (2021). Gut microbiome and serum metabolome alterations in obesity and after weight-loss intervention. *Nature Medicine*, 27(5): 915–922.
41. Liu, X., Zhang, Z., Song, J., & Chen, F. (2022). Gut microbiota diversity and composition in relation to metabolic syndrome: A systematic review and meta-analysis. *Frontiers in Nutrition*, 9: 853121.
42. Schertzer, J. D., Jin, Y., Dube, P., & Wang, Y. (2023). Microbial metabolic pathways in obesity: Implications for targeted therapies. *Trends in Endocrinology & Metabolism*, 34(1): 42–55.
43. Wang, J., Kurilshikov, A., Radjabzadeh, D., et al. (2020). Meta-analysis of human microbiome and obesity reveals consistent alterations in microbial signatures and pathways. *Nature Communications*, 11(1): 5165.
44. Zhang, X., Zhao, Y., Zhang, M., Pang, X., Xu, J., Kang, C., ... & Zhao, L. (2020). Structural modulation of gut microbiota in life-long calorie-restricted mice. *Nature Communications*, 11(1): 4563.
45. Depommier, C., Everard, A., Druart, C., et al. (2019). Supplementation with Akkermansia muciniphila in overweight and obese human volunteers: a proof-of-concept exploratory study. *Nature Medicine*, 25(7): 1096–1103.
46. Han, K., Bose, S., Wang, J. H., et al. (2020). Lactobacillus plantarum HAC01 regulates gut microbiota and adipose tissue accumulation in diet-induced obese mice. *Nutrition & Metabolism*, 17: 62.
47. Kadooka, Y., Sato, M., Ogawa, A., et al. (2010). Effect of Lactobacillus gasseri SBT2055 in fermented milk on abdominal adiposity in adults in a randomized controlled trial. *British Journal of Nutrition*, 104(5): 702–709.
48. Kondo, S., Xiao, J. Z., Satoh, T., et al. (2020). Antiobesity effects of Bifidobacterium breve B-3 supplementation in a randomized controlled trial. *Obesity Research & Clinical Practice*, 14(6): 560–565.
49. Lim, S. M., Kim, D. H., Jung, Y., et al. (2021). Probiotic supplement containing Lactobacillus gasseri BNR17 for weight loss: a randomized, double-blind, placebo-controlled clinical trial. *Nutrients*, 13(1): 219.
50. Sanchez, M., Darimont, C., Drapeau, V., et al. (2021). Effect of Lactobacillus rhamnosus CGMCC1.3724 supplementation on weight loss and maintenance in obese individuals: a randomized controlled trial. *International Journal of Obesity*, 45(3): 590–600.
51. Zmora, N., Zilberman-Schapira, G., Suez, J., et al. (2018). Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features. *Cell*, 174(6): 1388–1405.e21.
52. Zhao, Y., Yu, Y., Zhang, X., et al. (2022). Probiotic modulation of gut microbiota alleviates metabolic syndrome in high-fat diet-fed mice. *Frontiers in Nutrition*, 9: 866400.
53. Miyamoto J, Igarashi M, Watanabe K, Karaki SI, Mukouyama H, Kishino S, Li X, Ichimura A, Irie J, Sugimoto Y, Mizutani T, Sugawara T, Miki T, Ogawa J, Drucker DJ, Arita M, Itoh H, Kimura I. Gut microbiota confers host resistance to obesity by metabolizing dietary polyunsaturated fatty acids. Nat Commun, 2019; 10: 4007. doi: 10.1038/s41467-019-11978-0.
54. Canfora EE, Meex RCR, Venema K, Blaak EE. Gut microbial metabolites in obesity, NAFLD and T2DM. Nat Rev Endocrinol, 2019; 15: 261–273. doi: 10.1038/s41574-019-0156-z.
55. Cani, P. D., et al. (2008). Changes in gut microbiota control metabolic endotoxemia-induced inflammation in high-fat diet–induced obesity and diabetes in mice. *Diabetes*, 57(6): 1470–1481.
56. Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Bäckhed, F. (2016). From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites. *Cell*, 165(6): 1332–1345.
57. LeBlanc, J. G., et al. (2013). B-group vitamin production by lactic acid bacteria–current knowledge and potential applications. *Journal of Applied Microbiology*, 115(6): 1407–1415.
58. Louis, P., Hold, G. L., & Flint, H. J. (2014). The gut microbiota, bacterial metabolites and colorectal cancer. *Nature Reviews Microbiology*, 12(10): 661–672.
59. O'Keefe, S. J. D. (2016). Diet, microorganisms and their metabolites, and colon cancer. *Nature Reviews Gastroenterology & Hepatology*, 13(12): 691–706.
60. Setchell, K. D., & Clerici, C. (2010). Equol: history, chemistry, and formation. *The Journal of Nutrition*, 140(7): 1355S–1362S.
61. Silva, Y. P., Bernardi, A., & Frozza, R. L. (2020). The role of short-chain fatty acids from gut microbiota in gut-brain communication. *Frontiers in Endocrinology*, 11: 25.
62. Tremlett, H., et al. (2017). The gut microbiome in human neurological disease: a review. *Annals of Neurology*, 81(3): 369–382.

63. Zelante, T., et al. (2013). Tryptophan catabolites from microbiota engage AhR as ligand to control immune responses. *Nature*, 494(7438): 361–365.