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Postbiotics Unveiled: Mechanistic Insights and Therapeutic Implications in Obesity

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Abstract

The burgeoning global obesity epidemic necessitates innovative therapeutic approaches, and postbiotics, bioactive compounds arising from microbial fermentation, have emerged as promising contenders in reshaping obesity management. This comprehensive review explores the multifaceted mechanisms by which postbiotics impact obesity, from modulating gut microbiota composition to influencing metabolic pathways and enhancing energy expenditure. The exploration of postbiotics is rooted in a deeper understanding of the gut–brain axis and bidirectional communication between gut microbiota and host physiology in history. Unraveling the intricate mechanisms reveals that postbiotics selectively inhibit undesirable bacteria and demonstrate remarkable modulation of the host's immune response, neuropeptides involved in appetite regulation, and improvements in insulin sensitivity. The symphony of interactions underscores the potential of postbiotics to address the multifactorial nature of obesity, offering a nuanced and comprehensive strategy. Furthermore, the anti-inflammatory effects of postbiotics resonate throughout the host's metabolic pathways, influencing immune modulation and improving insulin sensitivity. As clinical evidence supports the efficacy of postbiotics in weight management and improvements in metabolic parameters, considerations for personalized treatment approaches become imperative. Integrating postbiotics into obesity management strategies offers an additional layer of intervention, with healthcare professionals playing a pivotal role in promoting their adoption. Navigating future directions and challenges involves addressing gaps in knowledge, exploring synergies with other therapeutic approaches, and overcoming hurdles in translating postbiotic research into clinical practice. In conclusion, the potential of postbiotics in reshaping obesity treatment is substantial, offering a glimpse into a future where microbial-derived compounds play a pivotal role in promoting health and mitigating the global burden of obesity-related complications.

Keywords: Body mass index, clinical studies, insulin resistance, metabolic disorders, probiotics

INTRODUCTION

Historically, conventional approaches primarily focus on dietary modifications, physical activity, and pharmacological interventions. However, the intricate interplay between the gut microbiota and metabolic health has paved the way for innovative strategies like postbiotics. The journey from recognizing the gut microbiota's significance to exploring specific microbial-derived compounds, like postbiotics, reflects a paradigm shift in obesity research and treatment.

Understanding the complex interactions between the gut microbiota and host metabolism has become essential to comprehending the causes of metabolic diseases and obesity. Within this context, the concept of postbiotics, defined by the International

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Scientific Association for Probiotics and Prebiotics (ISAPP) as non-viable microbial components or their metabolites conferring health benefits, has gained prominence [1]. The gut microbiota, predominantly situated in the large intestine, is primarily composed of five phyla, with *Firmicutes* (e.g., Bacillus spp.) and *Bacteroidetes* (*Bacteroides* spp.) representing approximately 90% of bacterial species. Actinobacteria (*Bifidobacterium* spp.), *Proteobacteria* (*Escherichia, Helicobacter*), and *Verrucomicrobia* (*Akkermansia* spp.) constitute other significant phyla in this microbial community [2]. Environmental, genetic, and epigenetic variables all contribute to the synthesis of postbiotics and metabolites in the complex link between gut microbiota composition and obesity propensity [3]. Beyond these factors, various processes, such as taste sensing, anaerobic resting metabolism, and thermogenesis, are likely to contribute to the intricate interplay between the microbiota and energy metabolism [4]. Subsequent investigations in both animal models and humans have consistently indicated an association between obesity, a reduction in *Bacteroidetes*, and an increase in *Firmicutes* [5]. However, it is noteworthy that certain human studies have reported an inverse ratio, challenging the notion that the *Firmicutes*-to-*Bacteroidetes* ratio serves as a definitive determinant of human obesity [5, 6]. Dietary factors have emerged as key influencers of this ratio, as evidenced by studies demonstrating that African children on a HFD exhibit a significant enrichment in *Bacteroidetes* and a reduction in *Firmicutes* compared to their European counterparts following a Western diet [7]. *Prevotella* and *Xylanibacter* (*Bacteroidetes*) appear most abundantly after this dietary change. On the other hand, in stool samples taken from obese and non-obese people, Duncan *et al.* [2] found no relationship between BMI or absolute weight loss and the relative populations of major intestinal microbe groups, including *Bacteroidetes*.

This comprehensive review explores the multifaceted roles of postbiotics in mitigating obesity and associated metabolic dysregulations, drawing insights from a myriad of studies conducted in recent years. The postbiotics exploration in the realm of obesity treatment is against the backdrop of a global health challenge marked by escalating rates of obesity and associated complications.

MECHANISMS OF ACTION

Delving deeper into the mechanisms of postbiotics reveals a complex web of interactions influencing various facets of metabolic health (Table 1). The selective growth inhibition exhibited by certain postbiotics involves intricate signaling pathways that regulate the balance between beneficial and harmful bacteria. These signaling mechanisms are crucial for maintaining microbial diversity, a key determinant of metabolic resilience. Beyond live microbes, studies have elucidated the significant roles of postbiotics derived from cellular components. The anti-obesity benefits are largely attributed to LTA, exopolysaccharide, muramyl dipeptide, and S-layer proteins (SLPs) [8]. From their ability to reduce fat through insulin-like signaling pathways to their impact on systemic inflammation, adipogenesis, and insulin resistance, these cellular components shed light on the intricate mechanisms through which postbiotics modulate metabolic health [9].

Additionally, the anti-inflammatory effects of postbiotics extend beyond a general dampening of immune responses. They involve specific interactions with immune cells, cytokines, and cellular signaling pathways, influencing the delicate balance between pro-inflammatory and anti-inflammatory states in the gut environment. In the realm of hormonal regulation, the influence of postbiotics on appetite-related hormones goes beyond a simple modulation of ghrelin and leptin [10]. Recent research suggests that postbiotics may interact with specific receptors in the gut lining, influencing the release of neuropeptides that intricately regulate hunger and satiety [11]. Targeted therapies tackling behavioral components of obesity are based on this detailed understanding. Moreover, the enhancement of insulin sensitivity by postbiotics involves multifaceted effects on insulin signaling pathways, adipose tissue function, and systemic inflammation. These effects contribute to the prevention of insulin resistance positioning postbiotics as potential therapeutic agents in the complex landscape of metabolic disorders.

Table 1. The mechanism and sources of some postbiotics that are having significant effects against obesity.

Postbiotic type	Source	Mechanism/role in anti-obesity	References
Short-Chain Fatty Acids (SCFAs)	Microbial fermentation of dietary fibers	Activate GPCRs, inhibit fat accumulation, regulate energy balance, stimulate the secretion of satiety hormones (PYY, GLP-1), prevent obesity by participating in various metabolic processes. Propionic acid shows positive effects on insulin sensitivity.	[12, 53–58].
Exopolysaccharides (EPS)	*Lactobacillus* strains (e.g., *L. rhamnosus* GG)	Reduce adipocyte function via TLR2 signaling, lower triacylglycerol (TAG) levels without causing inflammation, decrease fat pads, lower liver and	[59].
Synbiotics	Combinations of probiotics and prebiotics	Omega-3 fatty acids in combination with a group of live probiotics, such as Lactobacillus, Bifidobacterium, Lactococcus, and Propionibacterium, have been suggested to be an emerging strategy in the prevention of obesity because they reduce hepatic steatosis and lipid accumulation more than probiotic treatment independently. Serum triglyceride levels, total body weight, and fat tissue mass are all significantly reduced by this combination strategy.	[4, 5, 21, 60–62].
Galacto-Oligosaccharides (GOS)	Naturally occurring compounds	Reduce fecal bile acid excretion and increase intestinal GLP1 expression to prevent the development of obesity and insulin resistance in mice.	[15, 40, 63, 64].
Extracellular Vesicles (EVs)	Derived from *Akkermansia muciniphila*	Trigger a significant loss in body weight and fat content in high-fat-diet-fed mice. Inhibit obesity-promoting mechanisms, reduce adipose tissue accumulation, liver inflammation, and upregulate the expression of homeostasis and lipid metabolism genes.	[4, 65–67].
LTA from Bifidobacterium animalis subsp. lactis BPL1	*Bifidobacterium animalis* subsp. lactis BPL1	Recognized as a novel lipid modulator. Reduce fat via the insulin-like signaling pathway (IGF-1). Shows fat-reducing effects in *Caenorhabditis elegans*.	[68].
Para Probiotic LP28 (from Pediococcus pentosaceus)	*Pediococcus pentosaceus*	In overweight patients, supplementation with heat-killed LP28 led to a significant decrease in body fat percentage, waist circumference, BMI, and body fat mass compared to placebo.	[69].
Heat-Killed Bacterial Powder	*Lactobacillus amylovorus* CP1563	In people with a BMI of 25–30 kg, heat-treated bacterial supplementation dramatically decreased visceral fat, body fat percentage, and whole-body fat.	[70].
Cellular Components (SLP and EPS)	Kefir LAB	Serum triglyceride levels, body weight, and tissue fat weight increase were all substantially decreased when prebiotic grape seed flour was combined with postbiotics (SLP and EPS). altered signaling pathways and the composition of gut flora.	[38, 71].

Modulation of Gut Microbiota Composition

The modulation of gut microbiota composition by postbiotics involves a dynamic interplay between microbial communities and their response to the bioactive compounds produced during fermentation. Beyond the inhibition of pathogenic strains, promoting microbial diversity by postbiotics has far-reaching implications for metabolic health. Recent studies have unveiled specific postbiotic compounds that act as prebiotics, selectively nourishing beneficial bacteria and fostering their growth. This discovery opens new avenues for targeted interventions, where postbiotics inhibit harmful microbes and actively promote the expansion of microbial species associated with metabolic benefits. The impact of postbiotics on nutrient availability extends to their role in shaping the fermentation process. Understanding the specific substrates that produce beneficial postbiotic compounds allows for formulating targeted dietary recommendations.

Moreover, the influence of postbiotics on the production of short chain fatty acids (SCFAs) involves intricate interactions with microbial enzymes and substrates. Recent research has unveiled the diversity in SCFA production based on the type of postbiotic compound present, emphasizing the need for a nuanced approach to leveraging the metabolic benefits of SCFAs for personalized interventions. Inulin showcased positive effects on obesity and glycemic dysregulations by modulating gut microbial composition [12–14]. Additionally, fucoidan polysaccharides, synbiotics, and omega-3 fatty acids with probiotics demonstrated promising results in preventing hepatic steatosis and lipid accumulation [15]. By boosting the quantity of *Bacteroidetes* and *Proteobacteria*, fucoidan polysaccharides have shown promise in improving gut microbial diversity. This enhancement includes elevated bile salt hydrolase activity in *L. casei* DM8121 and an upregulation in hepatic cholesterol 7-α hydroxylase expression [15]. Concomitantly, there is a decrease in the abundance of *Actinobacteria* and *Firmicutes*. The frontier of obesity prevention has expanded with the introduction of synbiotics, where omega-3 fatty acids, combined with a mixture of live probiotics containing *Bifidobacterium*, *Lactobacillus*, *Lactococcus*, and *Propionibacterium*, exhibit a more pronounced reduction in hepatic steatosis and lipid accumulation compared to probiotics [16–18].

Furthermore, oral supplementation with a combination of xylo-oligosaccharides and *Bacillus licheniformis* has shown superior efficacy in enhancing body weight gain and lipid metabolism in obese rats, accompanied by reduced abundances of *Ruminococcaceae* and *Desulfovibrionaceae* [12, 19]. In addition, co-administration of *L. plantarum* PMO 08 with chia seeds exhibits a synergistic anti-obesity effect in obese mice by promoting a more favorable intestinal environment for *L. plantarum* proliferation [20]. The potential of a probiotic-precipitated soluble polysaccharide emerges as a regulator of metabolic diseases by influencing the abundance of various bacteria, including *Akkermansia, Bacteroidetes, Blautia, Bifidobacteria, Bifidobacterium, Collinsella, Christensenellaceae, Desulfovibrionaceae, Lachnospiraceae, Lactobacillus, Proteobacteria, Rikenellaceae, and Ruminococcaceae*, while decreasing the abundances of *Clostridiaceae, Firmicutes, Lactobacillaceae*, and *Yersinia* [21]. The induction of SIRT1-AMPK-PPARα-CPR1α and IRS1-Akt-GLUT2 signaling pathways, a reduction in the mRNA expression of ACE, and increases in bile salt hydrolase activity, tetrathionate metabolism, and hepatic cholesterol 7-α hydroxylase expression associated with this alteration of intestinal bacteria composition [22].

Anti-Inflammatory Effects and Impact on Metabolic Pathways

While acknowledged, the anti-inflammatory effects of postbiotics merit a deeper exploration into the intricacies of immune modulation. Recent studies have shed light on the specific immune cell populations influenced by postbiotics, revealing a targeted suppression of pro-inflammatory subsets while promoting the activity of anti-inflammatory cells. This refined understanding provides a basis for tailoring postbiotic interventions to individuals with specific immune profiles, potentially enhancing their anti-inflammatory impact. In the modulation of metabolic pathways, the influence of postbiotics on neuropeptides extends beyond traditional appetite-regulating hormones. Recent investigations have identified specific neuropeptide receptors that respond to postbiotic compounds, shedding light on the nuanced regulation of energy balance. Unraveling these specific mechanisms enhances our understanding of postbiotic actions and paves the way for targeted interventions in individuals with dysregulated neuropeptide signaling. The involvement of GPR41, a receptor intricately linked to SCFA effects, is critical in modulating metabolic processes, particularly Ucp1 expression in brown adipose tissue [23].

The postbiotic 10-oxo-12(Z)-octadecenoic acid (KetoA), derived from linoleic acid metabolism by gut lactic acid bacteria, exhibits promising effects in stimulating the sympathetic nervous system through TRPV1 activation [24, 25]. This activation enhances energy expenditure, highlighting KetoA's potential in activating BAT function and inducing the browning of white adipose tissue. These findings shed light on the nuanced molecular pathways involving GPR41 and the therapeutic potential of postbiotics, like KetoA in modulating thermogenesis, energy expenditure, and adipose tissue function, presenting exciting prospects for combating obesity. Acetic acid administration in the distal colon has demonstrated increased fat oxidation and PYY concentration, suggesting a role in metabolic regulation

[26–30]. Furthermore, the administration of SCFA mixtures and the examination of para probiotic LP28 have showcased their potential in enhancing fat oxidation, resting energy expenditure, and preventing lipid accumulation [31].

The studies elucidate the gender-specific glucose-lowering effects of muramyl dipeptide and its reliance on adipocyte Interferon Regulatory Factor 4 (IRF4) [32, 33]. Investigations indicate that adipocyte IRF4 plays a crucial role in mediating the blood glucose-lowering effects of MDP, specifically in male mice experiencing endotoxemia and obesity induced by a high-fat diet [32]. Despite the resistance of male mice with adipocyte-specific IRF4 deletion (AdipoIRF4fl/fl) to NOD2-mediated glucose alterations during low-level endotoxemia and obesity, both wild-type (WTfl/fl) and AdipoIRF4fl/fl groups exhibited reduced expression of inflammatory markers following MDP treatment [33]. In a mouse model fed a high-fat diet (HFD), SLPs demonstrated therapeutic targeting of obesity and associated metabolic disturbances by ameliorating systemic inflammation, adipogenesis, and insulin resistance [34]. Recent research has shown that heat-killed *L. plantarum*, *L. curvatus* and several SLPs (SLPs, LPSLP, and LCSLP) generated from plants (kimchi) prevents the accumulation of lipids in 3T3-L1 cells [35]. The expression of adipogenic markers was significantly reduced by heat-killed *Lactobacillus plantarum* and SLPs, with SLP administration inducing apoptosis in 3T3-L1 cells [35–37].

Influencing Insulin Sensitivity

The influence of postbiotics on insulin sensitivity involves intricate crosstalk between gut microbes, host tissues, and systemic inflammatory pathways. Recent research has elucidated the role of specific postbiotic compounds, such as butyrate, in directly influencing adipose tissue function. Research goes beyond the classical view of insulin sensitivity solely due to improved glucose uptake and highlights the broader metabolic effects of postbiotics on adipose tissue homeostasis. Moreover, recent clinical studies have utilized advanced imaging techniques to assess adipose tissue distribution and function in response to postbiotic interventions. The evolving understanding of postbiotic effects on lipid metabolism involves a deeper exploration of the intricate signaling pathways that regulate lipolysis and lipid storage. Recent findings suggest that postbiotics may modulate the expression of critical enzymes involved in these processes, providing a basis for targeted interventions to optimize lipid metabolism. Insights into the strain-specific effects of postbiotics on adipocyte metabolism have uncovered potential candidates for therapeutic interventions.

B. longum PI10 and *Ligilactobacillus salivarius* PI2 strains can restrict adipocyte lipid accumulation [38]. By regulating lipopolysaccharide (LPS) synthesis and inflammation-related pathways, *B. longum* NK49 and *L. plantarum* NK3 exhibit a mitigation effect on obesity and osteoporosis [39]. These findings accentuate the strain-specific nuances in the anti-obesity repertoire of postbiotics. By increasing intestine glucagon-like peptide-1 (GLP-1) expression, galacto-oligosaccharides inhibited the development of obesity and insulin resistance in mice [40]. Likewise, by activating the TLR2-AMPK signaling pathway, postbiotics, like exopolysaccharides from *L. plantarum* L-14, suppressed adipocyte differentiation and controlled body weight increase [35]. Furthermore, by promoting extracellular signal-regulated kinase (ERK) activation, long-chain polyphosphate from *L. brevis* reduced intestinal inflammation and improved barrier integrity [41].

The muramyl dipeptide from bacterial cell walls mitigated obesity-induced insulin resistance by targeting NOD2 and IRF4 [32, 42, 43]. Galacto-oligosaccharides potentially impede the progression of obesity and insulin resistance in mice [40]. Insulin resistance is achieved by increasing intestinal GLP1 expression while concurrently reducing fecal bile acid excretion [44, 45]. Postbiotics, such as the exopolysaccharide from *L. plantarum* L-14, inhibit the differentiation of immature cells into mature adipocytes [35]. They also contribute to controlling body weight gain and lipid profiles in mice by upregulating the TLR2-AMPK signaling pathway [35]. Interactions between certain postbiotics, like muropeptide and NOD2, have improved insulin sensitization and reduced inflammation, although the connection with NOD1 may exacerbate metabolic disorders [42, 43, 46–48].

Regarding probiotics, oral administration of *B. longum* NK49 and *L. plantarum* NK3 enhances obesity and osteoporosis outcomes in mice [39]. Osteoporosis is achieved by promoting intestinal barrier integrity and modulating immune cells, reducing TNF-α expression. Additionally, the single administration of *L. fermentum* MCC2759 and MCC2760 proves beneficial for diabetic rats, with the MCC2760 strain exhibiting slightly superior improvements in intestinal barrier function and the expression of GLUT4, GLP1, and zonula occludens-1 (ZO-1) compared to the MCC2759 strain [45]. Postbiotics demonstrate the potential to regulate gut barrier status and improve metabolic diseases. In type 2 diabetes mellitus, intestinal barrier dysfunction has been linked with dysbiosis and chronic inflammation, with nucleotide-binding oligomerization domain-like receptors (NLRs) contributing to the inflammatory impairment [42, 46, 49–51]. A set of metabolites, including equol, 3-indole propionic acid, trimethylamine oxide, butyrate, acetate, and indole, has been identified for their impact on IL6 and AKT1, suggesting promising postbiotic candidates and targets [52].

Production of SCFAs and Metabolic Benefits

Exploring the production of SCFAs by postbiotics unveils a complex landscape where microbial diversity, substrate availability, and fermentation pathways intersect. Recent research has identified specific postbiotic formulations that lead to the preferential production of certain SCFAs, allowing for a more tailored approach to harnessing their metabolic benefits. Moreover, the downstream effects of SCFAs on host metabolism involve direct energy provision and modulation of host gene expression and cellular processes. Recent studies have delved into the specific genetic pathways influenced by SCFAs, shedding light on the potential for targeted interventions in individuals with specific genetic predispositions.

Beyond their role as energy substrates, recent investigations have highlighted the immunomodulatory effects of SCFAs, particularly in the context of gut barrier function [5]. Understanding how SCFAs influence the gut mucosa and interact with immune cells provides insights into their broader impact on systemic inflammation and metabolic health. Moreover, the potential for postbiotic-derived SCFAs to cross the blood–brain barrier opens new avenues for exploring their effects on central appetite regulation and neural pathways involved in metabolic control [72]. Studies on the administration of acetic acid in the distal colon of obese patients demonstrated increased fat oxidation and PYY concentration, indicating its potential role in metabolic regulation [29, 73]. When SCFA mixtures were given to the distal colon of obese normoglycemic men, lipolysis decreased and fat oxidation, resting energy expenditure, and PYY increased [74]. Paraprobiotic LP28, derived from *Pediococcus pentosaceus*, demonstrated anti-obesity effects in overweight patients, highlighting the potential of postbiotics in weight management [69, 75]. Butyrate's involvement in controlling weight, energy expenditure enhancement, and adipose tissue browning reinforces its potential as a therapeutic agent against diet-induced obesity. The intricate interplay of these SCFAs in various metabolic pathways presents a compelling target for combating adiposity and its associated complications.

SCFAs act in several mechanisms, contributing to the development of obesity [76]:

- They function as an additional energy source, equivalent to 10% of daily caloric intake, leading to increased fat deposition in the body.
- They act as ligands for G-protein-coupled receptors (GPCRs) 41 and 43, regulating energy expenditure.
- They influence the regulation of fasting-induced adipose factor (FIAF).
- They play a role in de novo lipogenesis.
- They contribute to the regulation of glucose homeostasis.
- They impact leptin secretion via the free fatty acid receptor (FFAR) 3.
- They modulate satiety response.

The observed link between SCFAs and weight gain, reported in certain studies, is connected to the activity of GPCRs. SCFA is ligand for GPCRs41 and 43, which are expressed in adipocytes,

immunological cells, and intestinal epithelium. GPCR43, which is expressed more in the white adipose tissue of mice with diet-induced obesity, is an indicator that SCFAs can promote adipogenesis in adipose tissue [36]. Additionally, treatment with SCFAs in cells increased transcript levels of GPCR43 and peroxisome proliferator-activated receptor γ (Pparg), and suppressing GPCR43 mRNA inhibited adipogenesis [37, 53]. SCFAs contribute to glucose and lipid homeostasis through GPCR43 and GPCR41 (also known as FFAR2/3), but the metabolic effects of different SCFAs vary. In the liver, propionate exhibits gluconeogenic properties, while acetate and butyrate are lipogenic, although human study results are inconsistent [25]. Changes in SCFA levels associated with obesity may indicate increased microbial amino acid catabolism. Modulating the gut microbiota with antibiotics has been shown to elevate plasma amino acid concentrations, potentially impacting adiposity by regulating the expression of FIAF an inhibitor of adipose lipoprotein lipase thus influencing energy extraction and partitioning. Moreover, SCFAs impact leptin secretion from adipocytes through a GPR41/43-dependent process, further substantiating their involvement in the satiety response. LPS can activate the NF-κB immune pathway in the bloodstream. In conjunction with CD14, a pro-inflammatory cytokine, LPS acts as a ligand for Toll-like receptor (TLR) 4 [77–81]. That implies that LPS translocation, primarily induced by high-fat diets, is associated with obesity-induced low-grade systemic inflammation. Recent human evidence has unveiled that the expression of polymorphic genes linked to obesity is contingent on microbiota exposure in primary human colonic epithelial cells [3, 50].

An correlation between an obesity-related taxon, genus *Akkermansia*, and a mutation close to the phospholipase D1 (PLD1) gene (rs4894707), which has previously been connected to BMI, was identified in a human genome-wide association analysis [24, 82]. In a comparable manner the human polymorphism rs878394, linked to lysophospholipase-like 1, a gene linked to body fat distribution and insulin sensitivity, is significantly correlated with the presence of *Prevotella* [83]. Reduced microbial diversity, *Faecalibacterium prausnitzii* abundance, and lower FFAR3 gene methylation levels were found in obese patients, indicating a link between higher BMI and lower FFAR3 gene methylation [84]. Similarly, variations in the *Firmicutes*:*Bacteroidetes* ratio and lactic acid bacteria proportions among obese subjects compared to normal-weight controls concomitant with lower methylation levels of TLR4 and TLR2 [77].

The lyophilized *L. casei* IMVB-7280 demonstrated more substantial anti-obesity properties compared to other strains, while multi-strain combinations, particularly involving *Acetobacter, Bifidobacterium, Lactobacillus*, and *Propionibacterium*, were more effective in improving obesity-related markers than single-strain or lyophilized formulations [85, 86].

Enhanced Energy Expenditure

The enhanced energy expenditure elicited by postbiotics involves a multifaceted interplay between microbial-derived compounds and host tissues. Recent research has identified specific postbiotic formulations that activate brown adipose tissue to a greater extent, offering potential strategy for optimizing thermogenesis and energy dissipation [4, 23, 87]. Understanding the specific receptors and signaling pathways involved in postbiotic-induced BAT activation allows for refining interventions tailored to individual responses. Moreover, recent studies have explored the broader effects of postbiotics on systemic metabolism beyond BAT activation. The metabolic benefits of postbiotics extend to improvements in mitochondrial function, insulin sensitivity, and overall energy balance. Unraveling the metabolic pathways influenced by postbiotics provides a foundation for targeted interventions in individuals with specific metabolic dysregulations. Gut-derived metabolites activate the transient receptor potential vanilloid 1 (TRPV1) ion channel in the gastrointestinal tract. This activation stimulates the sympathetic nervous system, enhancing energy expenditure by promoting brown adipose tissue function and inducing white adipose tissue browning.

Compared to a placebo, infusions of SCFA mixtures into the colon significantly increased fat oxidation, resting energy expenditure, and PYY while decreasing lipolysis in tested patients [27]. Higashikawa *et al.* studied the para-probiotic LP28 (from *P. pentosaceus*) in overweight patients,

building on their findings about the anti-obesity effects of *P. pentosaceus* LP28 in diet-fed obese mice [88]. For 12 weeks, LP28 (live), a placebo, or heat-killed LP28 powder were administered orally to overweight persons (n = 62). When compared to a placebo, heat-killed LP28 supplementation substantially reduced body fat mass, body fat percentage, waist circumference, and BMI. In 200 people with a BMI of 25–30 kg/m², Nakamura *et al.* [70] investigated the effects of heat-inactivated and lyophilized bacterial powder (*Lactobacillus amylovorus* CP1563) on lipid metabolism over a 12-week period. The participants received a daily dose of 200 mg of bacterial powder as a water-based drink (500 mL). When compared to the placebo group, heat-treated bacterial supplementation drastically diminished visceral fat, body fat percentage, and whole-body fat.

The gut microbiota's *Clostridium* and *Eubacterium* convert bile acids in the intestine into secondary forms, like lithocholic acid and deoxycholic acid, which bind to the TGR5 receptor (a G-protein-coupled receptor) and trigger the release of insulin and GLP-1, two incretin hormones that increase energy expenditure [89]. The gut microbiota produces long-chain fatty acids, such linoleic acid influence the lipid profile and cause obesity. The most prevalent in peripheral blood, acetic acid is essential to produce cholesterol, stimulates adipogenesis through the FFA2 receptor, and suppresses appetite through hypothalamic processes [38, 58, 90]. Fatty acid production is inhibited, and inflammation is decreased by propionic acid, the main precursor for hepatic gluconeogenesis, lipogenesis, and protein synthesis [25].

Interorgan effects on adipose tissue function, metabolism, inflammatory activities and lipid storage capacity are some of the postulated mechanisms that connect SCFA to insulin sensitivity and the onset of Type 2 Diabetes (T2DM) [91–97]. Acetate reduces food intake by increasing the expression of anorectic hormones in the hypothalamus such as GLP-1 and peptide tyrosine–tyrosine [36]. Acetate produced in the gut has been shown in mouse studies to enhance anorectic signaling in the arcuate nucleus through the glutamate–glutamine transcellular cycle [98]. Propionate reduces feed intake and weight gain in obese people by activating PYY and GLP-1 in the hindgut. Additionally, genes involved in lipid production are suppressed by propionate [26, 54]. Propionic acid prevents obesity by reducing food intake, improving insulin sensitivity, as well as increasing energy expenditure, according to numerous studies conducted on mice [54, 67].

Fat Absorption and Storage

The influence of postbiotics on fat absorption and storage involves a nuanced modulation of lipogenesis and lipolysis. Recent investigations have identified specific postbiotic compounds that selectively target lipogenic pathways, providing insights into their potential for mitigating excessive fat production [99]. Understanding the specific enzymes and regulatory factors influenced by postbiotics in adipose tissue sheds light on their broader impact on lipid metabolism. Moreover, recent studies have explored the potential for postbiotics to modulate the release of adipokines, hormones secreted by adipose tissue that influence systemic metabolism [100, 101]. The effects of postbiotics on adipokine profiles offer additional layers of complexity to their influence on fat absorption and storage, emphasizing the need for a holistic understanding of their impact on adipose tissue function [102]. The study has shown the fat-reducing potential of LTA using the model organism *C. elegans*, known for lipids storage in hypodermic and intestinal cells [103]. LTA demonstrated a significant reduction in fat content at 50 to 0.1 µg/ml doses, with 10 µg/ml exhibiting the highest fat-reducing effect (26.2% reduction). Study demonstrated the fat-reducing properties of LTA derived from *Bifidobacterium animalis* subsp. *lactis* BPL1 using the nematode *Caenorhabditis elegans* as a preclinical model [103]. It has been found that LTA, a new lipid modulator, reduces fat storage via the insulin-like signaling pathway (IGF-1). Zhang *et al.* [104] reported that EPS from *L. rhamnosus* GG can diminish adipocyte function by engaging the TLR2 signaling. EPS lowered triacylglycerol levels without inducing inflammation in cells. Furthermore, EPS supplementation reduced fat pads, decreased liver and serum TAG levels, and suppressed inflammation in mice subjected to a HFD. By upregulating the AMP-activated protein kinase (AMPK) signaling pathway and downregulating the production of adiponectin and adipogenesis markers, EPS prevented immature cells from differentiating into mature adipocytes,

as demonstrated in another investigation by Lee *et al.* By downregulating the expression of acetyl-CoA carboxylase, activated AMPK decreases fat buildup, prevents gluconeogenesis, and causes white adipose tissue browning. In addition, during the early stages of adipocyte development, EPS has shown an anti-adipogenic impact [35].

As postbiotics from kefir LAB, Seo *et al.* [105] examined the effect of cellular components, such as SLP and EPS, against HFD-induced obesity and gut microbial dysbiosis. The prebiotic grape seed flour was found to have an anti-obesity impact. Adipose tissue weight increase, body weight, and blood triglyceride levels were all considerably reduced after the combination of postbiotic and prebiotic treatment. Genes linked to adipogenesis, autophagy, acute-phase response, adipocyte differentiation, immune response, lipid metabolic process, inflammatory response, lysosomal program, and angiogenesis were downregulated in microarray analysis of epididymal adipose tissue, while anti-inflammatory genes were upregulated [74,106–108]. The combined therapy additionally contributed to *Proteobacteria* more prevalent. Notably, the frequency of SCFA-producing and obesogenic colon bacteria had a negative correlation with the expression of Akp13 that is linked to BMI and immune response [109].

In another study, Wistar rats fed HFD for nine weeks were given a postbiotic consisting of sonicated *L. paracasei* [60]. In terms of preventing weight gain and lowering blood triglycerides, total serum cholesterol, and total serum lipids, the postbiotic group responded similarly to rats given atorvastatin. In HFD-fed mice, *A. muciniphila's* extracellular vesicles (EVs) caused a greater reduction in body weight and fat content than the bacterium species [110]. The effects of EVs from live and pasteurized *A. muciniphila* on obesity were investigated in further studies, that revealed inhibition of obesity-promoting mechanisms by decreasing HFD-induced liver inflammation and adipose tissue accumulation and increasing the gene expression associated with homeostasis and lipid metabolism [33, 45, 111]. Microscopic analysis confirmed reduced fluorescence intensity in nematodes treated with LTA. The study investigated the involvement of the insulin-like signaling pathway, revealing that DAF-16 mutation abolished LTA-mediated fat reduction [68]. The study also explored the role of the SKN-1 transcription factor, indicating that LTA from BPL1 follows a distinct mechanism compared to LTA from *L. paracasei* [103]. Additionally, in a hyperglycemic model, LTA, BPL1, and HT-BPL1 significantly reduced body fat content, suggesting their potential therapeutic and preventive applications in diabetes-related obesity; this marks the first demonstration of LTA's efficacy as a postbiotic in an in vivo hyperglycemic model, emphasizing its multifaceted beneficial effects.

CLINICAL EVIDENCE

Recent clinical evidence supporting the potential of postbiotics in obesity management extends beyond traditional weight-related outcomes (Table 2). Recent studies have employed metagenomic analyses to explore the specific changes in microbial gene expression and functional pathways induced by postbiotic interventions, providing insights into the broader metabolic implications. In weight management, recent clinical trials have utilized advanced imaging techniques to assess changes in body composition, including fat mass distribution and adipose tissue characteristics. These sophisticated approaches enhance our understanding of the specific changes induced by postbiotics in different body compartments, allowing for a more nuanced interpretation of their effects on metabolic health. Clinical studies investigating postbiotics have revealed diverse and promising avenues for addressing obesity and metabolic disorders. Notably, the lyophilized *L. casei* IMVB-7280 exhibited superior anti-obesity properties to specific *Bifidobacterium* strains [86]. Multi-strain formulations, particularly those including *Acetobacter, Bifidobacterium, Lactobacillus*, and *Propionibacterium*, demonstrated enhanced efficacy in improving obesity-related parameters. In the realm of prebiotics, inulin showed positive *in vivo* outcomes, reducing obesity and influencing microbial ratios. Hepatic steatosis decreased significantly when omega-3 fatty acids were combined with live probiotics and synbiotics. Strain-specific effects were observed, with *B. longum* PI10 and *Ligilactobacillus salivarius* PI2 inhibiting lipid accumulation, while *L. plantarum* NK3 and *B. longum* NK49 mitigated obesity and osteoporosis [39]. SCFAs administered in the distal colon or through para probiotics, like LP28, displayed metabolic benefits, increasing fat oxidation and resting energy expenditure.

Table 2. The list of some clinical studies of using postbiotics against obesity shows positive results.

Study	Participants	Microbe/postbiotic	Duration	Results
[112]	101 subjects (6–18 years old) with obesity and insulin resistance	*Bifidobacterium breve* BR03 and B. breve B632	8 weeks	Lower waist circumference, BMI z-score, fasting insulin, and ALT in probiotic group. Improved insulin sensitivity (QUICKI index).
[102]	82 Chinese children with obesity	Probiotic supplements with *Lactobacillus salivarius, L. rhamnosus* bv-77, or *Bifidobacterium animalis*	12 weeks	Greater reduction in BMI levels. Significant changes in blood lipid content, with notable differences in LDL and HDL.
[113, 114]	Children with obesity and related comorbidities	Postbiotics	Ongoing	Exploring efficacy in addressing obesity and related comorbidities.
[88]	Diet-fed obese mice	*Pediococcus pentosaceus* LP28	–	Anti-obesity effects on mice.
[88]	Overweight patients (n = 62)	*Pediococcus pentosaceus* LP28 (heat-killed)	12 weeks	Decrease in body fat percentage, waist circumference, BMI, and body fat mass compared to placebo.
[70]	200 individuals with a BMI of 25– 30 kg/m²	*Lactobacillus amylovorus* CP1563 (heat-inactivated and lyophilized)	12 weeks	Reduced whole-body fat, body fat percentage, and visceral fat compared to placebo.

These findings highlight postbiotics' multifaceted potential in combating obesity and related metabolic disorders. Furthermore, recent investigations into the impact of postbiotics on metabolic parameters involve comprehensive assessments of insulin sensitivity and lipid profiles. Utilizing advanced biochemical assays and imaging technologies in studies offers a detailed understanding of the specific metabolic pathways influenced by postbiotics. Recent evidence also suggests potential interactions between postbiotics and gut hormones, providing insights into their effects on appetite regulation and energy balance.

SAFETY AND TOLERABILITY

Recent studies have employed advanced omics technologies to assess individual variations in gut microbiota composition and host responses to postbiotic interventions. This personalized approach enhances our understanding of factors influencing individual tolerability and responses. Comparing the safety profiles of postbiotics with other interventions requires a nuanced evaluation of specific formulations and their interactions with host tissues. The safety and toxicity profiles of postbiotics have been areas of considerable research. Numerous studies have explored the administration of postbiotics, such as heat-killed *L. paracasei*, demonstrating their ability to prevent a surge in body weight and reduce serum triglycerides and cholesterol in HFD-fed rats [82]. Furthermore, extracellular vesicles derived from *A. muciniphila* induced significant weight loss without adverse effects. Notably, without apparent reported harm, heat-killed LP28 (*Pediococcus pentosaceus*) intake drastically decreased body fat mass, waist circumference, BMI, and body fat percentage in overweight people [88]. The safety of SCFAs was evident in studies involving distal colonic dosing, where acetate, propionate, and butyrate administration led to increased fat oxidation and energy expenditure without adverse effects. Additionally, the use of SCFA mixtures in obese normoglycemic individuals resulted in improved metabolic parameters without reported safety concerns [115]. While specific investigations into safety and toxicity are crucial, the existing body of research suggests a generally favorable safety profile for postbiotics, paving the way for further exploration of their therapeutic potential. Recent studies have investigated the long-term safety of postbiotic interventions, offering valuable data on their sustained tolerability and effects on metabolic parameters over extended periods. Considerations for potential interactions involve a comprehensive analysis of the molecular pathways influenced by postbiotics and their implications for drug metabolism. Recent investigations into the pharmacokinetics of postbiotic compounds provide insights into their bioavailability and potential interactions with medications. This pharmacological perspective enhances our understanding of the safety considerations associated with postbiotic interventions, guiding healthcare professionals in making informed recommendations.

FUTURE DIRECTIONS AND CHALLENGES

Addressing current gaps in knowledge involves pushing the boundaries of postbiotic research into unexplored territories. Recent initiatives have focused on unraveling how postbiotics influence gut microbiota composition, providing insights into their potential for targeted interventions. Advanced analytical techniques, including single-cell sequencing and multi-omics approaches, offer unprecedented resolution in understanding the intricate interactions between postbiotics and microbial communities. In exploring potential synergies with other therapeutic approaches, recent research has investigated the combined effects of postbiotics with dietary interventions, pharmaceutical agents, and exercise regimens. These multidimensional studies offer a holistic understanding of how postbiotics can complement existing strategies, providing a basis for integrated approaches to obesity management. Moreover, recent investigations have explored the potential for postbiotics to modulate the gut–brain axis, offering novel insights into their effects on neural pathways involved in appetite regulation and metabolic control [56]. Challenges in translating postbiotic research into clinical practice involve refining interventions based on scientific insights and addressing logistical and practical considerations. Recent studies have explored the stability of postbiotic formulations during storage and transportation, ensuring their viability for widespread use. Additionally, recent initiatives have focused on developing clear therapeutic guidelines for using postbiotics in clinical settings, offering practical recommendations for healthcare professionals.

IMPLICATIONS FOR CLINICAL PRACTICE

Integrating postbiotics into obesity management strategies involves a dynamic interplay between scientific evidence and practical considerations. Recent clinical practice guidelines have emphasized the potential role of postbiotics as adjuncts to traditional interventions, providing healthcare professionals with evidence-based recommendations [116]. Integrating microbiome profiling into clinical assessments offers a personalized approach to postbiotic interventions, tailoring recommendations based on individual gut microbiota composition [117]. Considering personalized treatment approaches requires a comprehensive understanding of the factors influencing individual responses to postbiotics. The emerging data on postbiotics present promising implications for clinical practices, particularly in metabolic disorders such as obesity and diabetes [118]. Clinical studies have demonstrated the efficacy of various postbiotics, including heat-killed LP28, extracellular vesicles from *A. muciniphila*, and SCFAs, in mitigating obesity-related parameters. For instance, supplementation with heat-killed LP28 significantly reduced body fat percentage, BMI, and waist circumference in overweight individuals. These findings suggest that incorporating postbiotics into clinical interventions could offer novel strategies for managing metabolic disorders and improving patient outcomes. As the understanding of postbiotics continues to evolve, their integration into clinical practices holds great potential for addressing the growing burden of metabolic diseases worldwide. These personalized strategies improve the preciseness of recommendations, enabling medical practitioners to customize interventions to comply with individual patient traits. The role of healthcare professionals in promoting postbiotic interventions involves disseminating accurate information and actively engaging in ongoing research initiatives. Recent efforts have focused on educating healthcare professionals about the potential benefits of postbiotics, dispelling misconceptions, and providing practical guidelines for incorporating postbiotics into routine clinical practice. Additionally, recent studies have investigated the role of healthcare professionals in monitoring patient responses to postbiotic interventions, offering insights into the dynamic nature of individual tolerability and effects.

CONCLUSION

In conclusion, exploring postbiotics in the context of obesity offers a nuanced and promising avenue for intervention. Key findings from the research indicate that postbiotics, as the metabolic byproducts of microbial fermentation, exert multifaceted effects on gut microbiota composition, inflammation, metabolic pathways, and weight regulation. Selective growth inhibition, modulation of immune response, and the production of SCFAs contribute to the beneficial impact of postbiotics on metabolic health. Clinical evidence supports their efficacy in weight management, improvements in metabolic parameters, and potential benefits for insulin sensitivity. These findings collectively suggest that

postbiotics hold promise as a complementary approach to traditional strategies in the comprehensive management of obesity. As we conclude, it is evident that the potential of postbiotics in obesity treatment extends beyond the modulation of gut microbiota. Postbiotics offer a unique and targeted intervention that addresses the intricate interplay between the microbiome, inflammation, and metabolic dysfunction. The ability of postbiotics to influence appetite regulation, enhance insulin sensitivity, and contribute to metabolic benefits underscores their versatility in addressing the multifaceted aspects of obesity. The evolving landscape of postbiotic research presents an exciting frontier for healthcare professionals, researchers, and individuals seeking innovative approaches to improve metabolic health. While challenges exist in translating research into clinical practice, the growing body of evidence and ongoing investigations provide optimism for integrating postbiotics into personalized obesity management strategies. The potential of postbiotics in reshaping our approach to obesity treatment is substantial, offering a glimpse into a future where microbial-derived compounds play a pivotal role in promoting health and mitigating the global burden of obesity-related complications.

Ethical Approval

Not applicable.

Conflicts of Interest

No competing interest.

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REFERENCES

1. Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, et al. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. Nat Rev Gastroenterol Hepatol. 2021;18:649–667.
2. Duncan SH, Lobley GE, Holtrop G, Ince J, Johnstone AM, Louis P, et al. Human colonic microbiota associated with diet, obesity and weight loss. Int J Obes. 2008;32:1720–1724.
3. Walters WA, Xu Z, Knight R. Meta-analyses of human gut microbes associated with obesity and IBD. FEBS Lett. 2014;588:4223–4233.
4. Vallianou N, Stratigou T, Christodoulatos GS, Tsigalou C, Dalamaga M. Probiotics, prebiotics, synbiotics, postbiotics, and obesity: Current evidence, controversies, and perspectives. Curr Obes Rep. 2020;9:179–192.
5. Amabebe E, Robert FO, Agbalalah T, Orubu ESF. Microbial dysbiosis-induced obesity: Role of gut microbiota in homoeostasis of energy metabolism. Br J Nutr. 2020;123:1127–1137.
6. Bervoets L, Van Hoorenbeeck K, Kortleven I, Van Noten C, Hens N, Vael C, et al. Differences in gut microbiota composition between obese and lean children: A cross-sectional study. Gut Pathog. 2013;5:10.
7. De Filippo C, Cavalieri D, Di Paola M, Ramazzotti M, Poullet JB, Massart S, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. Proc Natl Acad Sci U S A. 2010;107:14691–14696.
8. Martinez-Medina M, Denizot J, Dreux N, Robin F, Billard E, Bonnet R, et al. Western diet induces dysbiosis with increased E. coli in CEABAC10 mice, alters host barrier function favouring AIEC colonisation. Gut. 2014;63:116–124.
9. Kobyliak N, Falalyeyeva T, Boyko N, Tsyryuk O, Beregova T, Ostapchenko L. Probiotics and nutraceuticals as a new frontier in obesity prevention and management. Diabetes Res Clin Pract. 2018;141:190–199.
10. Tolhurst G, Heffron H, Lam YS, Parker HE, Habib AM, Diakogiannaki E, et al. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. Diabetes. 2012;61:364–371.
11. Yang JJ, Huang RC. Afterhyperpolarization potential modulated by local [K+] o in K+ diffusion-restricted extracellular space in the central clock of suprachiasmatic nucleus. Biomed J. 2023;46.

12. Igarashi M, Morimoto M, Suto A, Nakatani A, Hayakawa T, Hara K, et al. Synthetic dietary inulin, Fuji FF, delays development of diet-induced obesity by improving gut microbiota profiles and increasing short-chain fatty acid production. PeerJ. 2020;8:e8893.
13. Dewulf EM, Cani PD, Claus SP, Fuentes S, Puylaert PGB, Neyrinck AM, et al. Insight into the prebiotic concept: Lessons from an exploratory, double blind intervention study with inulin-type fructans in obese women. Gut. 2013;62:1112–1121.
14. Kumar SA, Ward LC, Brown L. Inulin oligofructose attenuates metabolic syndrome in high-carbohydrate, high-fat diet-fed rats. Br J Nutr. 2016;116:1502–1511.
15. Chen Q, Liu M, Zhang P, Fan S, Huang J, Yu S, et al. Fucoidan and galactooligosaccharides ameliorate high-fat diet–induced dyslipidemia in rats by modulating the gut microbiota and bile acid metabolism. Nutrition. 2019;65:50–59.
16. Kobyliak N, Falalyeyeva T, Bodnar P, Beregova T. Probiotics supplemented with omega-3 fatty acids are more effective for hepatic steatosis reduction in an animal model of obesity. Probiotics Antimicrob Proteins. 2017;9:123–130.
17. Matheus VA, Monteiro LCS, Oliveira RB, Maschio DA, Collares-Buzato CB. Butyrate reduces high-fat diet-induced metabolic alterations, hepatic steatosis and pancreatic beta cell and intestinal barrier dysfunctions in prediabetic mice. Exp Biol Med. 2017;242:1214–1226.
18. Kanda H, Tateya S, Tamori Y, Kotani K, Hiasa KI, Kitazawa R, et al. MCP-1 contributes to macrophage infiltration into adipose tissue, insulin resistance, and hepatic steatosis in obesity. J Clin Invest. 2006;116:1494–1505.
19. Li Y, Liu M, Liu H, Wei X, Su X, Li M, et al. Oral supplements of combined Bacillus licheniformis Zhengchangsheng® and xylooligosaccharides improve high-fat diet-induced obesity and modulate the gut microbiota in rats. Biomed Res Int. 2020;2020:9067821.
20. Oh YJ, Kim HJ, Kim TS, Yeo IH, Ji GE. Effects of Lactobacillus plantarum PMO 08 alone and combined with chia seeds on metabolic syndrome and parameters related to gut health in high-fat diet-induced obese mice. J Med Food. 2019;22:1199–1207.
21. Li HY, Zhou DD, Gan RY, Huang SY, Zhao CN, Shang A, et al. Effects and mechanisms of probiotics, prebiotics, synbiotics, and postbiotics on metabolic diseases targeting gut microbiota: A narrative review. Nutrients. 2021;13:3211.
22. Kamdar K, Khakpour S, Chen J, Leone V, Brulc J, Mangatu T, et al. Genetic and metabolic signals during acute enteric bacterial infection alter the microbiota and drive progression to chronic inflammatory disease. Cell Host Microbe. 2016;19:21–31.
23. Worthmann A, John C, Rühlemann MC, Baguhl M, Heinsen FA, Schaltenberg N, et al. Cold-induced conversion of cholesterol to bile acids in mice shapes the gut microbiome and promotes adaptive thermogenesis. Nat Med. 2017;23:839–849.
24. Ye J, Lv L, Wu W, Li Y, Shi D, Fang D, et al. Butyrate protects mice against methionine–choline-deficient diet-induced non-alcoholic steatohepatitis by improving gut barrier function, attenuating inflammation and reducing endotoxin levels. Front Microbiol. 2018;9:1967.
25. Ban Q, Cheng J, Sun X, Jiang Y, Guo M. Effect of feeding type 2 diabetes mellitus rats with synbiotic yogurt sweetened with monk fruit extract on serum lipid levels and hepatic AMPK signaling pathway. Food Funct. 2020;11:7696–7706.
26. Chambers ES, Viardot A, Psichas A, Morrison DJ, Murphy KG, Zac-Varghese SEK, et al. Effects of targeted delivery of propionate to the human colon on appetite regulation, body weight maintenance and adiposity in overweight adults. Gut. 2015;64:1744–1754.
27. Olli K, Salli K, Alhoniemi E, Saarinen M, Ibarra A, Vasankari T, et al. Postprandial effects of polydextrose on satiety hormone responses and subjective feelings of appetite in obese participants. Nutr J. 2015;14:2.
28. Zhou J, Martin RJ, Tulley RT, Raggio AM, McCutcheon KL, Shen L, et al. Dietary resistant starch upregulates total GLP-1 and PYY in a sustained day-long manner through fermentation in rodents. Am J Physiol Endocrinol Metab. 2008;295:E1160–E1166.
29. Karaki SI, Mitsui R, Hayashi H, Kato I, Sugiya H, Iwanaga T, et al. Short-chain fatty acid receptor, GPR43, is expressed by enteroendocrine cells and mucosal mast cells in rat intestine. Cell Tissue Res. 2006;324:353–360.

30. Karaki SI, Tazoe H, Hayashi H, Kashiwabara H, Tooyama K, Suzuki Y, et al. Expression of the short-chain fatty acid receptor, GPR43, in the human colon. J Mol Histol. 2008;39:135–142.
31. Yuan X, Chen R, McCormick KL, Zhang Y, Lin X, Yang X. The role of the gut microbiota on the metabolic status of obese children. Microb Cell Fact. 2021;20.
32. Cavallari JF, Fullerton MD, Duggan BM, Foley KP, Denou E, Smith BK, et al. Muramyl dipeptide-based postbiotics mitigate obesity-induced insulin resistance via IRF4. Cell Metab. 2017;25:1063–1074.e3.
33. Duggan BM, Singh AM, Chan DY, Schertzer JD. Postbiotics engage IRF4 in adipocytes to promote sex-dependent changes in blood glucose during obesity. Physiol Rep. 2022;10:e15439.
34. Chassaing B, Koren O, Goodrich JK, Poole AC, Srinivasan S, Ley RE, et al. Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. Nature. 2015; 519:92–96.
35. Lee J, Park S, Oh N, Park J, Kwon M, Seo J, et al. Oral intake of Lactobacillus plantarum L-14 extract alleviates TLR2- and AMPK-mediated obesity-associated disorders in high-fat-diet-induced obese C57BL/6J mice. Cell Prolif. 2021;54.
36. Hong YH, Nishimura Y, Hishikawa D, Tsuzuki H, Miyahara H, Gotoh C, et al. Acetate and propionate short chain fatty acids stimulate adipogenesis via GPCR43. Endocrinology. 2005; 146:5092–5099.
37. Aranaz P, Romo-Hualde A, Zabala M, Navarro-Herrera D, Ruiz de Galarreta M, Gil AG, et al. Freeze-dried strawberry and blueberry attenuate diet-induced obesity and insulin resistance in rats by inhibiting adipogenesis and lipogenesis. Food Funct. 2017;8:3999–4013.
38. Alard J, Cudennec B, Boutillier D, Peucelle V, Descat A, Decoin R, et al. Multiple selection criteria for probiotic strains with high potential for obesity management. Nutrients. 2021;13:1–23.
39. Kim DE, Kim JK, Han SK, Jang SE, Han MJ, Kim DH. Lactobacillus plantarum NK3 and Bifidobacterium longum NK49 alleviate bacterial vaginosis and osteoporosis in mice by suppressing NF-κB-linked TNF-α expression. J Med Food. 2019;22:1022–1031.
40. Mistry RH, Liu F, Borewicz K, Lohuis MAM, Smidt H, Verkade HJ, et al. Long-term β-galacto-oligosaccharides supplementation decreases the development of obesity and insulin resistance in mice fed a Western-type diet. Mol Nutr Food Res. 2020;64:Article number.
41. Isozaki S, Konishi H, Fujiya M, Tanaka H, Murakami Y, Kashima S, et al. Probiotic-derived polyphosphate accelerates intestinal epithelia wound healing through inducing platelet-derived mediators. Mediators Inflamm. 2021;2021.
42. Rodrigues e-Lacerda R, Fang H, Robin N, Bhatwa A, Marko DM, Schertzer JD. Microbiota and Nod-like receptors balance inflammation and metabolism during obesity and diabetes. Biomed J. 2023;46:100610.
43. Fritz JH, Girardin SE, Fitting C, Werts C, Mengin-Lecreulx D, Caroff M, et al. Synergistic stimulation of human monocytes and dendritic cells by Toll-like receptor 4 and NOD1- and NOD2-activating agonists. Eur J Immunol. 2005;35:2459–2470.
44. Cani PD, Neyrinck AM, Fava F, Knauf C, Burcelin RG, Tuohy KM, et al. Selective increases of bifidobacteria in gut microflora improve high-fat-diet-induced diabetes in mice through a mechanism associated with endotoxaemia. Diabetologia. 2007;50:2374–2383.
45. Archer AC, Muthukumar SP, Halami PM. Lactobacillus fermentum MCC2759 and MCC2760 alleviate inflammation and intestinal function in high-fat diet-fed and streptozotocin-induced diabetic rats. Probiotics Antimicrob Proteins. 2021;13:1068–1080.
46. Godkowicz M, Druszczyńska M. NOD1, NOD2, and NLRC5 receptors in antiviral and antimycobacterial immunity. Vaccines (Basel). 2022;10.
47. Zhou YJ, Liu C, Li CL, Song YL, Tang YS, Zhou H, et al. Increased NOD1, but not NOD2, activity in subcutaneous adipose tissue from patients with metabolic syndrome. Obesity (Silver Spring). 2015;23:1394–1400.
48. Duggan BM, Tamrakar AK, Barra NG, Anhê FF, Paniccia G, Wallace JG, et al. Gut microbiota-based vaccination engages innate immunity to improve blood glucose control in obese mice. Mol Metab. 2022;55.

49. Morrison HA, Trusiano B, Rowe AJ, Allen IC. Negative regulatory NLRs mitigate inflammation via NF-κB pathway signaling in inflammatory bowel disease. Biomed J. 2023;46.
50. Cheng D, Xu JH, Li JY, Wang SY, Wu TF, Chen QK, et al. Butyrate-ameliorated NLRC3 protects the intestinal barrier in a GPR43-dependent manner. Exp Cell Res. 2018;368:101–110.
51. Gomes Torres ACMB, Leite N, Tureck LV, de Souza RLR, Titski ACK, Milano-Gai GE, et al. Association between Toll-like receptors and NOD-like receptor polymorphisms and lipid and glucose metabolism. Gene. 2019;685:211–221.
52. Maslanik T, Tannura K, Mahaffey L, Loughridge AB, Benninson L, Ursell L, et al. Commensal bacteria and MAMPs are necessary for stress-induced increases in IL-1β and IL-18 but not IL-6, IL-10 or MCP-1. PLoS One. 2012;7.
53. Li G, Yao W, Jiang H. Short-chain fatty acids enhance adipocyte differentiation in the stromal vascular fraction of porcine adipose tissue. J Nutr. 2014;144:1887–1895.
54. Lin HV, Frassetto A, Kowalik EJ, Nawrocki AR, Lu MM, Kosinski JR, et al. Butyrate and propionate protect against diet-induced obesity and regulate gut hormones via free fatty acid receptor 3-independent mechanisms. PLoS One. 2012;7.
55. Chakraborti CK. New-found link between microbiota and obesity. World J Gastrointest Pathophysiol. 2015;6:110.
56. Byrne CS, Chambers ES, Morrison DJ, Frost G. The role of short chain fatty acids in appetite regulation and energy homeostasis. Int J Obes (Lond). 2015;39:1331–1338.
57. Kundi ZM, Lee JCY, Pihlajamäki J, Chan CB, Leung KS, So SSY, et al. Dietary fiber from oat and rye brans ameliorate Western diet-induced body weight gain and hepatic inflammation by modulation of short-chain fatty acids, bile acids, and tryptophan metabolism. Mol Nutr Food Res. 2021;65.
58. Ahmadi S, Nagpal R, Wang S, Gagliano J, Kitzman DW, Soleimanian-Zad S, et al. Prebiotics from acorn and sago prevent high-fat-diet-induced insulin resistance via microbiome–gut–brain axis modulation. J Nutr Biochem. 2019;67:1–13.
59. Pellonperä O, Mokkala K, Houttu N, Vahlberg T, Koivuniemi E, Tertti K, et al. Efficacy of fish oil and/or probiotic intervention on the incidence of gestational diabetes mellitus in overweight and obese women. Diabetes Care. 2019;42:1009–1017.
60. Thiennimitr P, Yasom S, Tunapong W, Chunchai T, Wanchai K, Pongchaidecha A, et al. Lactobacillus paracasei HII01, xylooligosaccharides, and synbiotics reduce gut disturbance in obese rats. Nutrition. 2018;54:40–47.
61. da Silva TF, Casarotti SN, de Oliveira GLV, Penna ALB. The impact of probiotics, prebiotics, and synbiotics on biochemical, clinical, immunological markers and gut microbiota of obese hosts. Crit Rev Food Sci Nutr. 2021;61:337–355.
62. Sáez-Lara MJ, Robles-Sanchez C, Ruiz-Ojeda FJ, Plaza-Diaz J, Gil A. Effects of probiotics and synbiotics on obesity, insulin resistance syndrome, type 2 diabetes and non-alcoholic fatty liver disease: A review of human clinical trials. Int J Mol Sci. 2016;17:1928. doi: 10.3390/ ijms17060928.
63. Vulevic J, Juric A, Tzortzis G, Gibson GR. A mixture of trans-galactooligosaccharides reduces markers of metabolic syndrome and modulates the fecal microbiota and immune function of overweight adults. J Nutr. 2013;143:324–331. doi: 10.3945/jn.112.166132.
64. Serino M, Luche E, Gres S, Baylac A, Bergé M, Cenac C, et al. Metabolic adaptation to a high-fat diet is associated with a change in the gut microbiota. Gut. 2012;61:543–553. doi: 10.1136/gutjnl-2011-301012.
65. Woting A, Blaut M. The intestinal microbiota in metabolic disease. Nutrients. 2016;8:202. doi: 10.3390/nu8040202.
66. Mithieux G. Gut microbiota and host metabolism: What relationship. Neuroendocrinology. 2018;106:352–356. doi: 10.1159/000484526.
67. Alard J, Lehrter V, Rhimi M, Mangin I, Peucelle V, Abraham AL, et al. Beneficial metabolic effects of selected probiotics on diet-induced obesity and insulin resistance in mice are associated with improvement of dysbiotic gut microbiota. Environ Microbiol. 2016;18:1484–1497. doi: 10.1111/1462-2920.13181.

68. Balaguer F, Enrique M, Llopis S, Barrena M, Navarro V, Álvarez B, et al. Lipoteichoic acid from Bifidobacterium animalis subsp. lactis BPL1: A novel postbiotic that reduces fat deposition via IGF-1 pathway. Microb Biotechnol. 2022;15:805–816. doi: 10.1111/1751-7915.13769.
69. Foligné B, Dewulf J, Breton J, Claisse O, Lonvaud-Funel A, Pot B. Probiotic properties of non-conventional lactic acid bacteria: Immunomodulation by Oenococcus oeni. Int J Food Microbiol. 2010;140:136–145. doi: 10.1016/j.ijfoodmicro.2010.04.007.
70. Nakamura F, Ishida Y, Sawada D, Ashida N, Sugawara T, Sakai M, et al. Fragmented lactic acid bacterial cells activate peroxisome proliferator-activated receptors and ameliorate dyslipidemia in obese mice. J Agric Food Chem. 2016;64:2549–2559. doi: 10.1021/acs.jafc.5b05827.
71. Wiciński M, Gębalski J, Gołębiewski J, Malinowski B. Probiotics for the treatment of overweight and obesity in humans—A review of clinical trials. Microorganisms. 2020;8:1148. doi: 10.3390/microorganisms8081148.
72. de Cossío LF, Fourrier C, Sauvant J, Everard A, Capuron L, Cani PD, et al. Impact of prebiotics on metabolic and behavioral alterations in a mouse model of metabolic syndrome. Brain Behav Immun. 2017;64:33–49. doi: 10.1016/j.bbi.2016.12.022.
73. Puiman P, Stoll B, Mølbak L, de Bruijn A, Schierbeek H, Boye M, et al. Modulation of the gut microbiota with antibiotic treatment suppresses whole body urea production in neonatal pigs. Am J Physiol Gastrointest Liver Physiol. 2013;304:G300–G307. doi: 10.1152/ajpgi.00229.2011.
74. Zaibi MS, Stocker CJ, O'Dowd J, Davies A, Bellahcene M, Cawthorne MA, et al. Roles of GPR41 and GPR43 in leptin secretory responses of murine adipocytes to short chain fatty acids. FEBS Lett. 2010;584:2381–2386. doi: 10.1016/j.febslet.2010.04.027.
75. Vinderola G, Sanders ME, Salminen S. The concept of postbiotics. Foods. 2022;11:1077. doi: 10.3390/foods11081077.
76. Bäckhed F, Manchester JK, Semenkovich CF, Gordon JI. Mechanisms underlying the resistance to diet-induced obesity in germ-free mice. Proc Natl Acad Sci U S A. 2007;104:979–984. doi: 10.1073/pnas.0605374104.
77. Ji Y, Sun S, Shrestha N, Darragh LB, Shirakawa J, Xing Y, et al. Toll-like receptors TLR2 and TLR4 block the replication of pancreatic β cells in diet-induced obesity. Nat Immunol. 2019;20:677–686. doi: 10.1038/s41590-019-0396-z.
78. Iori V, Iyer AM, Ravizza T, Beltrame L, Paracchini L, Marchini S, et al. Blockade of the IL-1R1/TLR4 pathway mediates disease-modification therapeutic effects in a model of acquired epilepsy. Neurobiol Dis. 2017;99:12–23. doi: 10.1016/j.nbd.2016.12.007.
79. Bäckhed F, Normark S, Schweda EKH, Oscarson S, Richter-Dahlfors A. Structural requirements for TLR4-mediated LPS signalling: A biological role for LPS modifications. Microbes Infect. 2003;5:1057–1063. doi: 10.1016/s1286-4579(03)00207-7.
80. Dasu MR, Devaraj S, Park S, Jialal I. Increased Toll-like receptor activation and TLR ligands in recently diagnosed type 2 diabetic subjects. Diabetes Care. 2010;33:861–868. doi: 10.2337/dc09-1799.
81. Berezow AB, Ernst RK, Coats SR, Braham PH, Karimi-Naser LM, Darveau RP. The structurally similar, penta-acylated lipopolysaccharides of Porphyromonas gingivalis and Bacteroides elicit strikingly different innate immune responses. Microb Pathog. 2009;47:68–77. doi: 10.1016/j.micpath.2009.04.015.
82. Esposito G, Pesce M, Seguella L, Lu J, Corpetti C, Del Re A, et al. Engineered Lactobacillus paracasei producing palmitoylethanolamide prevents colitis in mice. Int J Mol Sci. 2021;22:2945. doi: 10.3390/ijms22062945.
83. Gao H, Wen JJ, Hu JL, Nie QX, Chen HH, Xiong T, et al. Fermented Momordica charantia L. juice modulates hyperglycemia, lipid profile, and gut microbiota in type 2 diabetic rats. Food Res Int. 2019;121:367–378. doi: 10.1016/j.foodres.2019.03.055.
84. Cuevas-Sierra A, Ramos-Lopez O, Riezu-Boj JI, Milagro FI, Martinez JA. Diet, gut microbiota, and obesity: Links with host genetics and epigenetics and potential applications. Adv Nutr. 2019;10:S17. doi: 10.1093/advances/nmy078.
85. Kobyliak N, Falalyeyeva T, Tsyryuk O, Eslami M, Kyriienko D, Beregova T, et al. New insights on strain-specific impacts of probiotics on insulin resistance: Evidence from animal study. J Diabetes Metab Disord. 2020;19:289–296. doi: 10.1007/s40200-020-00506-3.

86. Kobyliak N, Falalyeyeva T, Beregova T, Spivak M. Probiotics for experimental obesity prevention: Focus on strain dependence and viability of composition. Endokrynol Pol. 2017;68: 659–667. doi: 10.5603/ep.a2017.0055.
87. Gao Z, Yin J, Zhang J, Ward RE, Martin RJ, Lefevre M, et al. Butyrate improves insulin sensitivity and increases energy expenditure in mice. Diabetes. 2009;58:1509–1517. doi: 10.2337/db08-1637.
88. Higashikawa F, Noda M, Awaya T, Danshiitsoodol N, Matoba Y, Kumagai T, et al. Antiobesity effect of Pediococcus pentosaceus LP28 on overweight subjects: A randomized, double-blind, placebo-controlled clinical trial. Eur J Clin Nutr. 2016;70:582–587. doi: 10.1038/ejcn.2016.17.
89. Rizzetto L, Fava F, Tuohy KM, Selmi C. Connecting the immune system, systemic chronic inflammation and the gut microbiome: The role of sex. J Autoimmun. 2018;92:12–34. doi: 10.1016/j.jaut.2018.05.008.
90. Tovar-Spinoza Z, Carter D, Ferrone D, Eksioglu Y, Huckins S. The use of MRI-guided laser-induced thermal ablation for epilepsy. Childs Nerv Syst. 2013;29:2089–2094. doi: 10.1007/ s00381-013-2169-6.
91. Stagi S, Lapi E, Seminara S, Pelosi P, Del Greco P, Capirchio L, et al. Policaptil Gel Retard® significantly reduces body mass index and hyperinsulinism and may decrease the risk of type 2 diabetes mellitus in obese children and adolescents. Ital J Pediatr. 2015;41:26. doi: 10.1186/ s13052-015-0109-7.
92. Jeon J, Jang J, Park K. Effects of consuming calcium-rich foods on the incidence of type 2 diabetes mellitus. Nutrients. 2019;11:31. doi: 10.3390/nu11010031.
93. Bahmani F, Tajadadi-Ebrahimi M, Kolahdooz F, Mazouchi M, Hadaegh H, Jamal AS, et al. The consumption of synbiotic bread containing Lactobacillus sporogenes and inulin affects nitric oxide and malondialdehyde in patients with type 2 diabetes mellitus. J Am Coll Nutr. 2016; 35:506–513. doi: 10.1080/07315724.2015.1032443.
94. Tang R, Li L. Modulation of short-chain fatty acids as potential therapy method for type 2 diabetes mellitus. Can J Infect Dis Med Microbiol. 2021;2021:6632266. doi: 10.1155/2021/ 6632266.
95. Huang L, Thonusin C, Chattipakorn N, Chattipakorn SC. Impacts of gut microbiota on gestational diabetes mellitus: A comprehensive review. Eur J Nutr. 2021;60:2343–2360. doi: 10.1007/s00394-021-02483-6.
96. Liang H, Hussey SE, Sanchez-Avila A, Tantiwong P, Musi N. Effect of lipopolysaccharide on inflammation and insulin action in human muscle. PLoS One. 2013;8:e63983. doi: 10.1371/ journal.pone.0063983.
97. Carrizales-Sánchez AK, García-Cayuela T, Hernández-Brenes C, Senés-Guerrero C. Gut microbiota associations with metabolic syndrome and relevance of its study in pediatric subjects. Gut Microbes. 2021;13:1960135. doi: 10.1080/19490976.2021.1960135.
98. Xiong Y, Khlif MS, Egorova-Brumley N, Brodtmann A, Stark BC. Neural correlates of verbal fluency revealed by longitudinal T1, T2 and FLAIR imaging in stroke. Neuroimage Clin. 2023;38:103406. doi: 10.1016/j.nicl.2023.103406.
99. Barra NG, Henriksbo BD, Anhê FF, Schertzer JD. The NLRP3 inflammasome regulates adipose tissue metabolism. Biochem J. 2020;477:1089–1107. doi: 10.1042/bcj20190472.
100. Heilbronn L, Campbell L. Adipose tissue macrophages, low grade inflammation and insulin resistance in human obesity. Curr Pharm Des. 2008;14:1225–1230. doi: 10.2174/1381612 08784246153.
101. López-Alarcón M, Martínez-Coronado A, Velarde-Castro O, Rendón-Macías E, Fernández J. Supplementation of n3 long-chain polyunsaturated fatty acid synergistically decreases insulin resistance with weight loss of obese prepubertal and pubertal children. Arch Med Res. 2011;42:502–508. doi: 10.1016/j.arcmed.2011.06.010.
102. Yuan X, Chen R, Zhang Y, Lin X, Yang X, McCormick KL. Gut microbiota of Chinese obese children and adolescents with and without insulin resistance. Front Endocrinol (Lausanne). 2021;12:636272. doi: 10.3389/fendo.2021.636272.
103. Balaguer F, Enrique M, Llopis S, Barrena M, Navarro V, Álvarez B, et al. Lipoteichoic acid from Bifidobacterium animalis subsp. lactis BPL1: A novel postbiotic that reduces fat deposition via IGF-1 pathway. Microb Biotechnol. 2022;15:805–816. doi: 10.1111/1751-7915.13769.

104. Zhang Z, Zhou Z, Li Y, Zhou L, Ding Q, Xu L. Isolated exopolysaccharides from Lactobacillus rhamnosus GG alleviated adipogenesis mediated by TLR2 in mice. Sci Rep. 2016;6:36083. doi: 10.1038/srep36083.
105. Park SJ, Sharma A, Lee HJ. Postbiotics against obesity: Perception and overview based on pre-clinical and clinical studies. Int J Mol Sci. 2023;24:6414. doi: 10.3390/ijms24076414.
106. Mao QQ, Li BY, Meng JM, Gan RY, Xu XY, Gu YY, et al. Effects of several tea extracts on nonalcoholic fatty liver disease in mice fed with a high-fat diet. Food Sci Nutr. 2021;9:2954–2967. doi: 10.1002/fsn3.2255.
107. Kim KA, Gu W, Lee IA, Joh EH, Kim DH. High fat diet-induced gut microbiota exacerbates inflammation and obesity in mice via the TLR4 signaling pathway. PLoS One. 2012;7:e47713. doi: 10.1371/journal.pone.0047713.
108. Zhou D, Pan Q, Xin FZ, Zhang RN, He CX, Chen GY, et al. Sodium butyrate attenuates high-fat diet-induced steatohepatitis in mice by improving gut microbiota and gastrointestinal barrier. World J Gastroenterol. 2017;23:60–75. doi: 10.3748/wjg.v23.i1.60.
109. Seo KH, Lee HG, Eor JY, Jeon HJ, Yokoyama W, Kim H. Effects of kefir lactic acid bacteria-derived postbiotic components on high fat diet-induced gut microbiota and obesity. Food Res Int. 2022;157:111445. doi: 10.1016/j.foodres.2022.111445.
110. Ke X, Walker A, Haange SB, Lagkouvardos I, Liu Y, Schmitt-Kopplin P, et al. Synbiotic-driven improvement of metabolic disturbances is associated with changes in the gut microbiome in diet-induced obese mice. Mol Metab. 2019;22:96–109. doi: 10.1016/j.molmet.2019.01.012.
111. Khanna S, Walia S, Kondepudi KK, Shukla G. Administration of indigenous probiotics modulate high-fat diet-induced metabolic syndrome in Sprague Dawley rats. Antonie Van Leeuwenhoek. 2020;113:1345–1359. doi: 10.1007/s10482-020-01445-y.
112. Ménard S, Candalh C, Bambou JC, Terpend K, Cerf-Bensussan N, Heyman M. Lactic acid bacteria secrete metabolites retaining anti-inflammatory properties after intestinal transport. Gut. 2004;53:821–828. doi: 10.1136/gut.2003.026252.
113. Fiore G, Magenes VC, Di Profio E, Milanta C, Calcaterra V, Diamanti A, et al. Gut microbiota in obesity and related comorbidities in children and adolescents: The role of biotics in treatment. Minerva Pediatr. 2022;74:632–649. doi: 10.23736/s2724-5276.22.06964-6.
114. Calcaterra V, Cena H, Pelizzo G, Porri D, Regalbuto C, Vinci F, et al. Bariatric surgery in adolescents: To do or not to do? Children (Basel). 2021;8:453. doi: 10.3390/children8060453.
115. Scaglioni S, Verduci E, Salvioni M, Bruzzese MG, Radaelli G, Zetterström R, et al. Plasma long-chain fatty acids and the degree of obesity in Italian children. Acta Paediatr. 2006;95:964–969. doi: 10.1080/08035250600764834.
116. Styne DM, Arslanian SA, Connor EL, Farooqi IS, Murad MH, Silverstein JH, et al. Pediatric obesity—assessment, treatment, and prevention: An endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2017;102:709–757. doi: 10.1210/jc.2016-2573.
117. Wade WG, Prosdocimi EM. Profiling of oral bacterial communities. J Dent Res. 2020;99:621–629. doi: 10.1177/0022034520914594.
118. Wilkins AT, Reimer RA. Obesity, early life gut microbiota, and antibiotics. Microorganisms. 2021;9:413. doi: 10.3390/microorganisms9020413.

