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REVIEW ARTICLE

Synbiotic Formulations with Lactic Acid Bacteria to Modulate GLP-1/PYY Pathways in Obesity

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Abstract

Obesity is an escalating global public health challenge, closely linked to gut microbiota dysbiosis and disruption of the gut-brain axis. Intestinal L cells secrete the incretins GLP-1 and PYY, which suppress appetite, slow gastric emptying, and improve glucose–insulin balance. Their activity is strongly modulated by short chain fatty acids (SCFAs-acetate, propionate, butyrate) generated by fiber fermentation. Via FFAR2/FFAR3 receptors, SCFAs increase GLP-1/PYY secretion, strengthen the intestinal barrier, and dampen low grade inflammation, enhancing insulin sensitivity and weight control. Growing evidence shows that SCFA-producing probiotics (e.g., *Bifidobacterium animalis*, *Clostridium butyricum, Butyricimonas virosa*), fermentable prebiotics (inulin/FOS), and polyphenols can synergistically potentiate this pathway. Polyphenols act through two routes: direct activation of L cells (taste/GPCR signaling) and the indirect promotion of SCFA production by reshaping the microbiota. This review examines the potential for developing a functional symbiotic, combining SCFAs producing strains with an appropriate prebiotic and bioactive polyphenols as a natural strategy to enhance appetite regulation, glycemic control, and energy homeostasis through the modulation of the GLP-1/PYY pathway.

KEYWORDS
GLP-1, short-chain fatty acids, obesity, probiotics, satiety hormone regulation

Introduction

Obesity represents one of the most serious public health challenges of the 21st century, with its prevalence continuing to rise in both developed and developing countries. It is a metabolic disorder with a complex pathogenesis involving genetic, environmental, and behavioral factors; however, an increasing body of evidence suggests that the gut microbiota plays a pivotal role in its development. Disruption of the intestinal microbial balance, known as dysbiosis, leads to alterations in the host metabolism, chronic low grade inflammation, and impaired communication between the gut and the central nervous system.

One of the key components of this communication is the gut–brain axis, in which enteroendocrine L-cells play a central role. These cells secrete satiety hormones such as glucagon-like peptide-1 (GLP-1) and peptide YY (PYY), which regulate appetite, gastric emptying, and glucose–insulin homeostasis. The secretion of these hormones is strongly modulated by microbiota derived metabolites, particularly short-chain fatty acids (SCFAs).

In recent years, there has been growing interest in natural strategies to stimulate the enteroendocrine cells lining the intestinal epithelium to enhance satiety hormone production, mimicking the mechanism of action of pharmacological agents currently used in diabetes management. Such strategies may rely on the use of probiotics, prebiotics, and plant derived bioactive compounds such as polyphenols. These components, individually or in combination as synbiotics, can support microbial balance, increase SCFA production, and strengthen incretin signaling. Consequently, the development of nutritional and microbiota-targeted strategies aimed at activating enteroendocrine cells emerges

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as a promising approach in the prevention and treatment of obesity and metabolic disorders.

The aim of this review was to evaluate the role of gut microbiota-derived SCFAs, probiotics, prebiotics, and polyphenols in the regulation of GLP-1 and PYY secretion and to assess their potential for the development of a functional synbiotic strategy supporting appetite control, glucose homeostasis, and obesity management. A literature search was conducted using combinations of relevant keywords, including *GLP-1, PYY, obesity, probiotics, prebiotics, polyphenols,* and *dietary*, in the NCBI, PubMed, Elsevier, Google Scholar, and Web of Science databases. The initial search identified 978 records. After the verification of publication type and the exclusion of review articles, 467 original research articles remained. The screening of titles and abstracts reduced the number of potentially relevant publications to 189. These articles were subsequently assessed based on the full text, resulting in 46 studies that were considered relevant to the scope and objectives of the review. Of these, 26 of the most relevant and representative studies were selected for inclusion in the summary table, while the remaining eligible publications were used to support the narrative discussion.

The growing challenge of obesity

In highly urbanized societies, populations increasingly face chronic non communicable diseases (NCDs), commonly referred to as "diseases of civilization." These include obesity, cardiovascular diseases, diabetes, cancer, and autoimmune disorders (Kopp 2019). Many of these conditions share a common denominator-overweight or obesity which frequently precedes the onset of other diet-related diseases such as diabetes and atherosclerosis. According to data from the World Health Organization (WHO 2022), the number of obese individuals (BMI ≥ 30 kg/m²) worldwide has exceeded one billion, and projections suggest that by 2035 it may reach approximately 1.53 billion adults. Since 1990, the prevalence of being overweight and obesity has more than doubled among adults and increased more than fourfold among children (WHO 2025). This phenomenon has been described as a global epidemic that initially affected mainly affluent societies but now extends to middle- and low-income countries. With the exception of certain regions in sub Saharan Africa and Southeast Asia, obesity has already become more prevalent than being underweight (Ahmed and Mohamed 2025).

These data are alarming, as the rising prevalence of obesity contributes to a higher incidence of non-communicable diseases, including cancer, ultimately increasing mortality rates in the coming decades. This underscores the urgent need for effective preventive measures (Mendis et al. 2025).

The causes of obesity are multifactorial. From a socio epidemiological perspective, the so-called social determinants of health including sociodemographic structure, lifestyle patterns, and dietary practices-play an important role by modulating exposure to risk factors and shaping population health behaviors. Changes in the availability of highly processed foods, patterns of urbanization, and the organization of work and leisure time promote a positive energy balance and long-term weight gain (Poulain 2024).

Public health strategies aimed at mitigating the current situation operate on two levels. First, population level actions focus on encouraging healthier eating habits and increasing physical activity. Second, systemic measures include the reformulation of food products (reducing sugar, salt, and fat content), limiting the advertising of unhealthy foods, improving access to healthy options, and addressing societal pressures surrounding "ideal body image" and the stigmatization of individuals with obesity (Poulain 2024).

Against this background, the implementation of effective treatment for individuals with obesity particularly those at high risk of complications is crucial. The cornerstone of therapy remains an energy restricted diet combined with regular physical activity, supplemented in selected cases with pharmacotherapy. The importance of pharmacological treatment has increased with the introduction of GLP 1 receptor agonists such as semaglutide (Ozempic) (Salvador et al. 2025). In patients with type 2 diabetes, semaglutide lowers blood glucose by enhancing glucose dependent insulin secretion, inhibiting glucagon release, and slowing gastric emptying, thereby additionally reducing appetite (Kalra and Sahay 2020).

Semaglutide is a synthetic analog of human GLP-1, a peptide obtained through chemical synthesis. As a GLP-1 receptor agonist, it is widely used in the treatment of type 2 diabetes and obesity. However, challenges remain, including limited oral bioavailability, gastrointestinal adverse effects, and the high cost of therapy (Xu and Kuipers 2025).

Given these limitations of pharmacotherapy, the development of natural, biologically targeted interventions aimed at modulating the gut–brain axis appears to be a promising complementary strategy. The first step in designing an effective therapy or formulation is to understand the etiology of obesity and the functioning of the gut–brain axis, which regulates hunger and satiety hormones.

Obesity is a chronic metabolic disease characterized by the pathological accumulation of adipose tissue relative to lean body mass, negatively affecting overall health. Coexisting disturbances include appetite dysregulation and impaired energy homeostasis, both of which worsen as the disease progresses (Milano and Capasso 2018). Obesity develops, among other mechanisms, as a consequence of the neurohormonal dysregulation of adipose tissue metabolism. Under such conditions, the predominance of insulin signaling over catecholaminergic activity promotes lipogenesis, inhibits lipolysis, and enhances triacylglycerol accumulation within adipocytes.

The central nervous system, via the sympathetic nervous system, modulates lipolysis, adipocyte browning, and thermogenesis. Conversely, insulin acts both centrally, by suppressing sympathetic activity, and peripherally, by increasing glucose uptake, promoting lipogenesis, and inhibiting lipolysis. Other hormones, including leptin, glucagon, cortisol, ACTH, thyroid and parathyroid hormones, and growth hormone, as well as ghrelin and glucose dependent insulinotropic polypeptide (GIP), also influence fat redistribution and turnover. Notably, elevated ghrelin and GIP levels promote visceral fat deposition (Muller et al. 2019; Radziszewska et al. 2024).

The gut as an endocrine organ and the role of SCFAs in satiety hormone regulation

The gastrointestinal tract is the largest endocrine organ in the body. Embedded within it, intestinal L-cells secrete GLP-1 and PYY which delay gastric emptying, suppress appetite, and reduce energy intake. In addition, GLP-1 enhances glucose dependent insulin secretion, inhibits glucagon release, and supports the survival and proliferation of β-cells (Tolhurst et al. 2012; Wang et al. 2023). The density of L-cells increases distally, with the ileum and colon containing the highest numbers. Direct contact of luminal nutrients with their apical surface markedly enhances GLP-1 secretion. Gut hormones therefore represent a crucial component of the gut–brain–adipose axis, integrating signals about nutrient composition with the regulation of appetite and adipocyte metabolism.

The pharmacological mimicking of these signals through GLP-1 analogs or dual GIP/GLP-1 receptor agonists reduces fat mass by limiting food intake and directly modulating adipose-tissue metabolism. Meanwhile, PYY and cholecystokinin (CCK) further promote lipid oxidation, reduce inflammation, and improve insulin sensitivity (Wang et al. 2023; Radziszewska et al. 2024).

SCFA (acetate, propionate, and butyrate) are endogenous metabolites produced in the distal intestine via the microbial fermentation of non-digestible carbohydrates (such as soluble fiber, resistant starch, and inulin). Under physiological conditions, they reach high concentrations in the colon, where they serve as key chemical signals for L-cells located at their highest density. SCFAs directly stimulate L-cells through G-protein coupled receptors FFAR2/GPR43 and FFAR3/GPR41 (Wang et al. 2017).

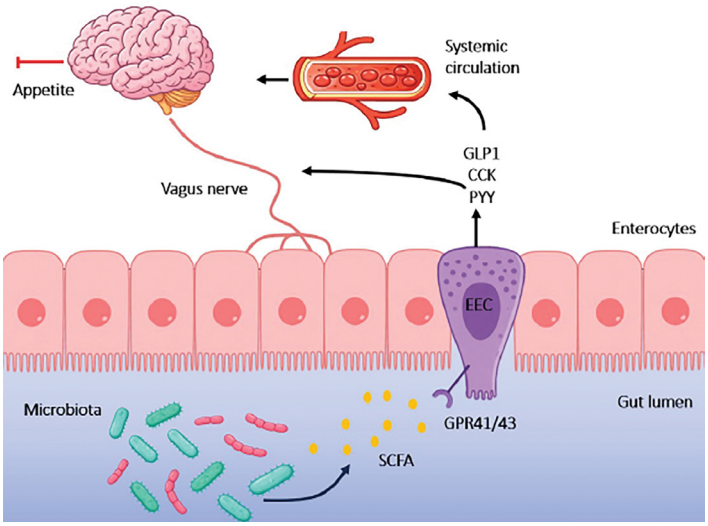


Figure 1. Schematic overview of the microbiota–SCFA–GLP-1/PYY axis in appetite regulation

At the same time, butyrate serves as the primary energy substrate for colonocytes and a differentiation factor for the intestinal epithelium. It enhances mucin production and tight junction protein expression, thereby supporting intestinal barrier integrity and reducing the translocation of pro-inflammatory stimuli (Dieck et al. 2022; Oudat and Okour 2025). From a metabolic perspective, SCFAs also modulate immune responses and low grade inflammation, and in experimental models, butyrate supplementation prevents and reverses diet induced insulin resistance (Yu et al. 2025).

At the microbiome level, SCFA production results from the cooperative activity of bacterial taxa primarily Bacteroidetes (acetate and propionate producers) and Firmicutes/Clostridiales (butyrate producers) (Wang et al. 2017). Therefore, prebiotic and probiotic interventions designed to enhance SCFA production in the colon constitute a rational physiological strategy to reinforce the L-cell → GLP-1/PYY → satiety and glycemic control axis, forming a cornerstone of biologically based strategies for obesity treatment (Figure 1).

SCFA-producing microbes and synbiotics

Recent scientific evidence consistently indicates that SCFA-producing bacteria and their metabolites play a pivotal role as enhancers of the L-cell → GLP-1/PYY → satiety axis and in improving metabolic parameters. *Butyricimonas virosa*, a butyrate producing bacterium, was shown to attenuate body weight gain, reduce glycemia and insulin resistance, and diminish hepatic steatosis in mice fed with a high fat diet. Notably, these effects persisted even after administration of heat inactivated cells, suggesting a postbiotic mechanism mediated by metabolites or structural components that sensitize tissues to incretin signaling and indirectly potentiate GLP-1 action (Lee et al. 2022).

Similarly, *Clostridium butyricum* (a butyrogenic species) lowered fasting glucose and improved lipid profiles while increasing GLP-1 and insulin concentrations in two type 2 diabetes models. It also reshaped the gut microbiota, decreasing Allobaculum abundance and improving the Firmicutes/Bacteroidetes ratio. Butyrate, as the end product of fermentation, serves as a critical link between: (i) the "nutritional and trophic" effects that sustain, mature, and maintain colonic epithelial integrity, and (ii) FFAR-dependent stimulation of L-cells (Jia et al. 2017).

The literature consistently highlights the role of *Bifidobacterium* in promoting satiety pathways through microbiota modulation toward enhanced SCFA production and the secondary stimulation of GLP-1/PYY secretion. In the study by Aoki et al. (2017), *Bifidobacterium animalis* subsp. *lactis* GCL2505 increased the relative abundance of *Bifidobacterium* in the microbiota, elevated acetate and GLP-1 concentrations in the intestine and plasma, and reduced visceral fat accumulation while improving glucose tolerance. A similar mechanism was demonstrated for *Bifidobacterium animalis* subsp. *lactis* A12: both live cells and cell-free supernatant (CFS) attenuated weight gain and dyslipidemia in high-fat diet–fed mice, increased SCFA levels (acetate, propionate, butyrate), and elevated serum GLP-1 (Li et al. 2022).

Lactobacillus casei Q14 administered in fermented yogurt to rats with type 2 diabetes elevated GLP-1 and PYY, reduced fasting glucose, and shifted the microbiota toward butyrate- and acetate-producing taxa (notably Bacteroides). This illustrates a key principle: the food matrix itself, such as fermented dairy, can serve as a functional carrier of both metabolites and live cultures, amplifying the effects along the gut–brain–pancreas axis (Qu et al. 2018).

Furthermore, numerous studies suggest that combinations of multiple SCFA-producing strains may be more effective in combating obesity than single strains. In a murine model of type 2 diabetes, the combination of *Bifidobacterium animalis* subsp. *lactis* BLa80 and *Lactobacillus acidophilus* LA85 produced the greatest

Table 1. Effects of bacteria, short-chain fatty acids, and bioactive compounds on GLP-1 and the metabolism of carbohydrates and lipids

Factor (bacteria, prebiotic, extract, SCFA, etc.)	Model (in vitro / in vivo / clinical)	Effect (GLP-1, PYY, etc.)	Dose and intervention duration	References
A. Synbiotic and synbiotic-like approaches (live micro-organisms combined with a prebiotic / fermentable substrate, or delivered in a fermented food matrix)				
Lactobacillus fermentum (supplemented in infant formula)	in vivo: Minipigs (piglets) on one of three diets: MAT (maternal milk), PL (formula with vegetable fats), FLF (formula with milk fat and *L. fermentum*)	↑ GLP-1, ↑ GLP-2, ↑ PYY, ↑ insulin	Supplementation for the first 28 days of life (infant feeding period). *Lactobacillus fermentum:* 10^8 CFU/mL in FLF formula	Lemaire et al. 2018
Lactobacillus casei Q14 (Lac-Q14) – probiotic strain, used as a starter for yogurt fermentation	in vivo – type 2 diabetic rats (STZ + high-fat diet)	↑ GLP-1, ↑ PYY, ↑ insulin	Yogurt containing 2.3×10^9 CFU/mL Lac-Q14; administered daily for 6 weeks	Qu et al. 2018
14 strains from fermented camel milk including *Lactobacillus plantarum, Lactobacillus helveticus, Lactobacillus pentosus, Lactobacillus rhamnosus* and 4 yeast strains (including *Issatchenkia orientalis*, *Candida ethanolica, Kluyveromyces marxianus).*	in vivo (db/db mice) type 2 diabetes	↑ GLP-1, ↑ SCFA, ↓ glucose, ↑ lipids, ↑ gut barrier function	Low doses: $1x10^8$ CFU/mL for 10 *Lactobacillus* strains and $1x10^6$ CFU/mL for 4 yeast strains. High doses: $1x10^{10}$ CFU/mL for 10 *Lactobacillus* strains and $1x10^8$ CFU/mL for 4 yeast strains.	Wang et al. 2020
Sodium butyrate (NaBut); Inulin (HP-inulin) – prebiotic	clinical: RCT, double-blind, T2D, n=60; 4 arms: butyrate alone, inulin alone, butyrate + inulin, placebo	↑ GLP-1; ↓ diastolic blood pressure;	600 mg/d (6 caps./day), 45 days; 10 g/d, 45 days	Roshanravan at al. 2017
Complex probiotic (14 strains): *Lactobacillus plantarum, Lactobacillus helveticus, Lactococcus lactis, Lactobacillus pentosus, Lactobacillus paracasei, Lactobacillus paracasei subsp. tolerans, Lactobacillus mucosae, Lactobacillus rhamnosus, Lactobacillus harbinensis, Lactobacillus hilgardii, Issatchenkia orientalis, Candida ethanolica, Kluyveromyces marxianus* and *Pichia membranifaciens*	in vivo: db/db mice (T2D)	GLP-1, ↑ PYY; ↓ glycemia; ↑ insulin	no data	Wang et al. 2020
WBF-011 synbiotic formulation (5 strains, incl. *Akkermansia muciniphila, Clostridium butyricum*) + chicory-root inulin	clinical: T2D adults, double-blind RCT, placebo-controlled	↑ butyrate in plasma; improved postprandial glycemia	12 weeks.	McMurdie et al. 2022
Lactococcus lactis-GLP-1-DA@GN - engineered probiotic continuously secreting GLP-1 with dopamine (DA) "hook" and β-glucan (GN) coating	in vitro/ex vivo/in vivo: simulated digestion (SSF/SGF/SIF)	↑ GLP-1 (ELISA);	1×10^9 CFU/mL p.o., 1×/d for 9 weeks.; GN 40 mg/kg b.w	Ji et al. 2025
B. Probiotic approaches (live micro-organisms and paraprobiotics administered without a prebiotic component)				
Butyricimonas virosa (live and heat-inactivated)	in vivo (diet-induced obese mice on high-fat diet - HFD)	Improvement: body weight, serum glucose, insulin resistance, liver steatosis. GLP-1R↑ and PPARα↑	*Butyricimonas virosa* strain administered intragastrically at a dose of 1×10^8 CFU in 200 µl suspension daily for 6 weeks of high-fat diet (HFD)	Lee et al. 2022
Bifidobacterium animalis subsp. *lactis* GCL2505 (BlaG) *Bifidobacterium longum* subsp. *longum* JCM1217T (BloJ)	in vivo (all mice on high-fat diet (HFD)) and in vivo (5-week-old male mice)	↑ Acetate and GLP-1 levels in intestine and plasma	*Bifidobacterium longum* subsp. *animalis* (BlaG) administered orally at a dose of 1×10^9 CFU/day, daily for 7 weeks. *Bifidobacterium longum* (BlaG or BloJ) administered orally at a dose of 1×10^9 CFU/day for 7 weeks.	Aoki et al. 2017

Factor (bacteria, prebiotic, extract, SCFA, etc.)	Model (in vitro / in vivo / clinical)	Effect (GLP-1, PYY, etc.)	Dose and intervention duration	References
B. Probiotic approaches (live micro-organisms and paraprobiotics administered without a prebiotic component)				
Bifidobacterium animalis subsp. *lactis* BLa80 *Lactobacillus acidophilus* LA85 Used individually and in combination (Mix)	in vivo (type 2 diabetes (T2DM) mice – induced by high-fat diet (HFD) + streptozotocin (STZ))	↑ GLP-1 – significantly higher blood levels in the group receiving BLa80 + LA85 combination, ↑ SCFA Microbiota changes (↑ *Akkermansia, Bifidobacterium*)	Dose: 1 × 10^9 CFU daily (orally) – for each bacterium (or mixture), 8 weeks intervention after diabetes induction.	Zhu et al. 2025
(*Bifidobacterium*, *Lactobacillus*, *Enterococcus*, *Bacillus cereus*; Si Lian Kang, S20060010)	clinical (T2DM patients)	↑ propionate, ↑ isovalerate	15 T2DM patients, therapy duration: not specified exactly, but clinical observation included measurements before and after therapy	Min et al. 2025
Clostridium butyricum CGMCC0313.1 (CB0313.1) – butyrate-producing bacterium (SCFA)	in vivo: 2 mouse models: 1) db/db (genetic obesity), 2) high-fat diet (HFD) + streptozotocin (STZ)	↑ GLP-1, ↑ insulin, ↓ fasting glucose, improved glucose and insulin tolerance, ↓ lipids, ↓ inflammation	- db/db mice: 5 weeks from 3 weeks of age; HFD+STZ mice: 13 weeks from 4 weeks of age (both interventions: daily oral dose)	Jia et al. 2017
mixture of 8 probiotic strains (*Lactobacillus* spp., *Bifidobacterium* spp., *Streptococcus thermophilus*)	in vivo: mice, C57BL/6J (HFD and LFD diet) in vitro: L (intestinal) cells	↑ GLP-1, ↓ body weight, ↓ food intake	5 mg/kg body weight (orally); 8 weeks (both preventive and therapeutic models)	Yadav et al. 2013
Bifidobacterium animalis subsp. *lactis* A12 (live cells) *B. lactis* A12 *Bifidobacterium animalis* subsp. *lactis* BB12 (live cells, reference strain)	in vivo (C57BL/6J mice that were fed a high-fat diet (HFD))	↑ (SCFA) ↑ GLP-1 ↑ leptin resistance. Reduced fat accumulation in the liver.	Dose: 1x10^9 CFU of each strain daily. Intervention duration: 10 weeks.	Li et al. 2022
Lactobacillus casei CCFM419 (probiotic)	in vivo: C57BL/6J mice; HFD 4 weeks. + STZ (100 mg/kg i.p.),	↑ GLP-1; ↑ ↑ SCFA (butyrate, acetate)	10^8, 10^9, 10^10 CFU·mL^{-1}, oral administration 1×/day for 12 weeks.; strongest metabolic and inflammatory effects usually at 10^9 CFU	Wang et al. 2019
Lactobacillus paracasei subsp. *paracasei* G15 (probiotic); *Lactobacillus casei* Q14 (probiotic)	in vivo: male Wistar rats; T2D induction: HFD 6 weeks.	↑ GLP-1, ↑ PYY; ↑ acetate and butyrate in feces;	Oral administration of lyophilized powder in saline; suspension prepared to 4×10^9 CFU/mL; 6 weeks of treatment	Li et al. 2017
Bifidobacterium animalis subsp. *lactis* MN-Gup (probiotic) – low dose *Bifidobacterium animalis* subsp. *lactis* MN-Gup (probiotic) – high dose	in vivo: C57BL/6J T2D mice	↑ GLP-1 (serum); ↑ total SCFA and acetate; microbiota: ↑ *Bifidobacterium,* ↓*Escherichia-Shigella/Staphylococcus; Bifidobacterium*	2 × 10^9 CFU/kg/d, 6 weeks (orally).; 1 × 10^{10} CFU/kg/d, 6 weeks (orally).	Zhang et al. 2024
C. Prebiotics, dietary fibers, SCFAs, postbiotics and other bioactive compounds (no live micro-organisms administered)				
Purified anthraquinone glycoside preparation from rhubarb (RAGP)	in vivo (type 2 diabetic rats)	↑ GLP-1. Histological improvement of pancreas and ileum. ↑ *Lactobacillus* ↑ SCFA-producing bacteria, ↓ *Lachnospiraceae* NK4A136, ↓ *Desulfovibrio*	100 or 400 mg/kg b.w. (RAGP) and 100 mg/kg b.w. (metformin). Oral administration once daily for 6 weeks	Cui et al. 2019
Slimpro (fish protein hydrolysate); Blue whiting hydrolysates; Fructooligosaccharides (FOS, ITFs); Propionate and butyrate (SCFA)	in vitro (STC-1), in vivo (mice)	↑ GLP-1, ↑ CCK, ↑PYY, ↓ghrelin	no data	Pizarroso et al. 2021

Factor (bacteria, prebiotic, extract, SCFA, etc.)	Model (in vitro / in vivo / clinical)	Effect (GLP-1, PYY, etc.)	Dose and intervention duration	References
C. Prebiotics, dietary fibers, SCFAs, postbiotics and other bioactive compounds (no live micro-organisms administered)				
Soluble corn fiber. Bacteria: *Parabacteroides, Ruminococcus, Oscillospira, Clostridium leptum* group, *Bifidobacterium* ssp.	Randomized, double-blind, placebo-controlled cross-over design; 20 healthy adults (mean age: 29 years, normal BMI).	↑ GLP-1 secretion, ↑ SCFA production	21 g/d soluble corn fiber, 21 days (3 weeks) supplementation with 21-day washout period in cross-over design	Dieck et al. 2022
Stearic acid; plant extracts such as quinine, aloin	in vitro study: Primary crypt cell cultures (mainly jejunum) isolated from obese patients.	↑ GDF15; ↑ GLP-1	Stearic acid 0.15 mM, stimulation time 4 hours.	Wang et al. 2024
SCFA (acetate, propionate, butyrate – of microbial origin)	clinical – cross-sectional study (160 participants BMI 19.2–41.0 kg/m², including 93 with insulin resistance measured by hyperinsulinemic-euglycemic clamp)	↑ GLP-1 (associated with circulating SCFA), ↓ lipolysis (glycerol), ↓ triglycerides	Single-point measurement of SCFA levels (feces and plasma); cross-sectional analysis	Muller et al. 2019
SCFA (acetate, propionate, butyrate); Lactate / acylamides (microbiota metabolites)	ex vivo/in vitro: EC colon cells	↑ 5-HT (potentially)	no data	Lund et al. 2018
Lactobacillus rhamnosus GG supernatant (LGGs)	in vitro: human L cells NCI-H716 with palmitic acid (PA)-induced lipotoxicity	↑ GLP-1 secretion ↓ proglucagon (GCG) accumulation	PA 400 µM, 6–24 h; LGGs 24 h	Wang et al. 2025
SCFA: acetate, propionate, butyrate;	in vitro: mixed primary mouse colon cultures	↑ GLP-1 after 2 h: acetate 1 mM, propionate 1 mM; butyrate 1 mM (marked with concomitant IBMX 100 µM	1 mM (single SCFA), 2 h; cocktail 140 mM	Tolhurst et al. 2012

increase in GLP-1 (compared to monotherapy), enhanced acetate and propionate production, promoted the expansion of health associated taxa (*Akkermansia*, *Bifidobacterium*), and improved glycemic control (Zhu et al. 2025).

Multistrain probiotic cocktails (containing 10–14 *Lactobacillus* strains ± yeasts such as *Lactobacillus plantarum*, *L. pentosus, L. rhamnosus, Candida ethanolica*, and *Kluyveromyces marxianus)* in db/db mice (a model of type 2 diabetes and obesity) increased GLP-1 (and often PYY) secretion, elevated fecal SCFA levels, improved glycemia and the lipid profile, and upregulated anti-inflammatory and barrier strengthening proteins (Claudin-1, ZO-1, mucin-2). These findings indicate that SCFA-dependent GLP-1 elevation co-occurs with reduced low grade inflammation and enhanced barrier integrity, leading to improved insulin sensitivity and reduced lipotoxicity (Wang et al. 2020).

In clinical conditions, the co-administration of a probiotic cocktail *(Bifidobacterium, Lactobacillus, Enterococcus, Bacillus cereus)* with a GLP-1 receptor agonist increased intestinal propionate and isovalerate levels; notably, SCFA concentrations were inversely correlated with glycemia and BMI. This points to an additive effect whereby the pharmacological activation of GLP-1 may be potentiated by microbiota driven increases in SCFA production, improving glycemic control independently of drug dosage (Min et al. 2022).

In early-life models, *Lactobacillus fermentum* supplementation in infant formula (combined with milk lipids) increased GLP-1, GLP-2, PYY, and insulin levels during the neonatal period, with hormonal effects persisting into adulthood (Lemaire et al. 2018). This suggests that the intestinal pancreatic programming window is particularly sensitive to probiotic–nutritional stimuli (SCFAs, FFAR/TGR5 signaling, and the trophic action of GLP-2) that durably "set" incretin secretion thresholds and metabolic responsiveness.

Among other strains shown to enhance the GLP-1/PYY axis through SCFA synthesis and related mechanisms contributing to reduced body weight and inflammation are *Lactobacillus casei* CCFM419 (Wang et al. 2017), *Lactobacillus paracasei* subsp. *paracasei* G15, *Lactobacillus casei* Q14 (Li et al. 2017), and *Lactobacillus rhamnosus* GG (Wang et al. 2025).

In summary, the common denominator of these experiments is an increase in local SCFA availability, activation of FFAR2/FFAR3 receptors, and elevated GLP-1/PYY secretion. This cascade enhances satiety, delays gastric emptying, and improves glycemia while concurrently strengthening intestinal barrier function and reducing inflammation. These findings support a synbiotic approach: combining acetate- and butyrate producing strains with appropriate prebiotics and a food matrix-and, in selected clinical settings, co-administering GLP-1 receptor agonists may yield additive metabolic benefits. However, heterogeneity in dosing, treatment duration, and interspecies differences remains a limitation. Future studies should standardize the measurement of active GLP-1, SCFA profiles (fecal and plasma), and barrier biomarkers to precisely calibrate dosing and therapeutic protocols in humans.

Importantly, plant extracts rich in polyphenols naturally complement this framework as a third pillar. They can directly activate

enteroendocrine (L/EEC) cells through taste or GPCR receptors, stimulating GLP-1/PYY secretion, and indirectly modulate the microbiota toward greater SCFA production. Both mechanisms converge on enhanced GLP-1/PYY release, which suppresses appetite, delays gastric emptying, and improves glycemic control thus supporting the therapeutic goals in obesity management.

Polyphenols and natural extracts

Accumulating evidence indicates that plant extracts (polyphenols, herbal mixtures) and prebiotics can enhance incretin signaling-particularly GLP-1-through two complementary pathways:

(1) direct activation of enteroendocrine (EEC/L) cells by bitter compounds or polyphenols, and

(2) indirect modulation of the gut microbiota toward an increased production of SCFAs, which act on FFAR2/FFAR3 receptors. Both mechanisms converge in the elevation of GLP-1 and PYY levels, resulting in appetite suppression, delayed gastric emptying, and improved glycemic control.

An anthraquinone rich rhubarb extract (RAGP) in type 2 diabetic rodents lowered blood glucose and insulin resistance, accompanied by a marked increase in plasma GLP-1 and histological improvement of the pancreas and intestine. RAGP also corrected dysbiosis, increasing *Lactobacillus* and butyrogenic taxa while decreasing *Desulfovibrio* (Cui et al. 2019).

A herbal combination of yerba mate–guarana–damiana increased postprandial GLP-1 and reduced energy intake in humans. Grape seed extract and Gallic acid (GA) in rodents reduced body weight, prolonged the action of endogenous GLP-1, and decreased active ghrelin. Ferulic acid (FA) increased circulating GLP-1, leptin, and adiponectin while inhibiting hepatic gluconeogenesis, thereby improving glycemia independently of other pathways. Importantly, proanthocyanidins (as a mixture) directly stimulated GLP-1, PYY, and CCK secretion in ex vivo intestinal preparations (Zuñiga-Martínez et al. 2024).

Curcumin strongly stimulated GLP-1 and CCK secretion in STC-1 cells only in its undigested form; after simulated digestion its activity markedly declined. In contrast, green tea extracts retained or even enhanced GLP-1-stimulating potential following digestion, suggesting that their metabolites remain bioactive toward enteroendocrine cells. Although the specific metabolites responsible for this effect were not identified, green tea catechins and their transformation products are likely contributors. In particular, epicatechin (EC) and epigallocatechin gallate (EGCG) are plausible candidates, as both compounds have been reported to stimulate GLP-1 secretion, while the gastrointestinal and microbial metabolism of gallated catechins may additionally generate bioactive derivatives such as degalloylated catechins and gallic acid (Ceremoni et al. 2021). Clinically, this implies that extract bioactivity depends on gastrointestinal transformation: preparations whose digestion products still activate EECs (e.g., catechins) have greater translational potential. Consequently, results obtained with "raw" extracts in vitro should not be directly extrapolated to in vivo intestinal conditions without assessing stability and metabolism (Planes-Muñoz et al. 2018).

An additional factor that should be considered when evaluating the effects of polyphenols is the substantial interindividual variability in their microbial biotransformation. The composition of the host gut microbiota determines both the rate of polyphenol degradation and the profile and concentrations of the resulting metabolites, which may differ considerably in their bioavailability and biological activity. Distinct microbial metabotypes have been described, for example, for ellagitannins and flavan-3-ols, resulting in the differential production of urolithins and phenyl-γ-valerolactones, respectively. Importantly, these metabolic phenotypes have been associated with differences in physiological responses to polyphenol-rich interventions. Therefore, variability in gut microbiota composition may contribute to the heterogeneous effects of polyphenols observed between individuals and should be considered when interpreting their influence on gut microbiota and host metabolic outcomes (Tomás-Barberán et al. 2016; Kerimi et al. 2020; Lessard-Lord et al. 2023).

The prebiotic inulin provides strong evidence for the indirect microbiota mediated stimulation of GLP-1 secretion. In a type 2 diabetes model, the effect was clearly dose dependent: a 25% inulin diet markedly increased plasma GLP-1 and PYY, up regulated intestinal PYY and CCK expression, improved glucose tolerance, reduced leptin levels, and produced a greater reduction of adipose tissue. These findings indicate that SCFAs derived from inulin fermentation not only activate FFAR2/FFAR3 on L-cells but may also enhance energy expenditure through increased lipid oxidation and thermogenesis (Singh et al. 2018).

Collectively, the data demonstrate that modulating the gut microbiota toward greater SCFA production triggers the cascade: SCFA → FFAR2/FFAR3 activation on L-cells → ↑ GLP-1/PYY → enhanced satiety, delayed gastric emptying, improved glycemic control, strengthened intestinal barrier, and reduced low grade inflammation. In conclusion, polyphenols constitute a significant component of this multifactorial system; some directly stimulate enteroendocrine cells via taste or GPCR receptors, while others indirectly favor SCFA production. Crucially, their efficacy depends on post digestive stability green tea catechins which retain activity, whereas certain curcuminoids lose it. These combined pathways converge on elevated GLP-1/PYY secretion, leading to reduced appetite, slower gastric emptying, and improved glucose control-aligning naturally with the therapeutic goals in obesity management.

Conclusion

The rising prevalence of obesity represents one of the most serious global public health challenges. Obesity, a metabolic disease of multifactorial etiology, is closely associated with disturbances in energy balance, dysregulation of the gut–brain axis, and gut microbiota dysbiosis. A key component of this axis is the enteroendocrine L-cell, which, in response to dietary and microbial stimuli, secretes the satiety hormones GLP-1 and PYY that influence appetite, glucose metabolism, and insulin sensitivity.

In recent years, increasing attention has been given to SCFAs produced by the microbial fermentation of carbohydrates in the gut. Through the activation of FFAR2 and FFAR3 receptors on L-cells, SCFAs enhance GLP-1/PYY secretion, support intestinal barrier integrity, reduce low grade inflammation, and improve insulin sensitivity. Numerous studies have demonstrated that SCFA-producing probiotics (e.g., *Bifidobacterium animalis* subsp. *lactis*, *Clostridium butyricum, Butyricimonas virosa)* and fermentable prebiotics (such as inulin and FOS) effectively strengthen incretin signaling and improve metabolic parameters.

Additionally, plant extracts rich in polyphenols may act via dual mechanisms directly activating L-cells through taste and G-protein–coupled receptors (GPCRs), and indirectly modulating the gut microbiota toward increased SCFA production. Compounds that remain bioactive after digestion, such as green tea catechins and proanthocyanidins, are of particular importance.

Collectively, the available data suggest that a synergistic approach combining probiotics, prebiotics, and polyphenols representing the concept of a functional synbiotic may constitute a promising strategy to support the treatment of obesity and metabolic disorders. Such formulations, targeting the SCFA–FFAR2/3–GLP-1/PYY axis, may exert additive effects to GLP-1 receptor agonist–based pharmacotherapy, offering a natural, biologically guided intervention that promotes body weight regulation, glycemic control, and energy homeostasis.

References

Ahmed, S.K. and Mohammed, R.A. 2025. Obesity: Prevalence, causes, consequences, management, preventive strategies and future research directions. *Metab. Open*, 27, 100375. https://doi.org/10.1016/j.metop.2025.100375

Aoki, R., Kamikado, K., Suda, W., Takii, H., Mikami, Y., Suganuma, N., Hattori, M. and Koga, Y. 2017. A proliferative probiotic *Bifidobacterium* strain in the gut ameliorates progression of metabolic disorders via microbiota modulation and acetate elevation. *Sci. Rep.*, 7, 43522. https://doi.org/10.1038/srep43522

Chao, J., Coleman, R.A., Keating, D.J. and Martin, A.M. 2025. Gut microbiome regulation of gut hormone secretion. *Endocrinology*, 166(4), bqaf004. https://doi.org/10.1210/endocr/bqaf004

Cremonini, E., Daveri, E., Mastaloudis, A. and Oteiza, P.I. 2021. (-)-Epicatechin and anthocyanins modulate GLP-1 metabolism: evidence from C57BL/6J Mice and GLUTag cells. *J. Nutr.*, 151(6), 1497–1506. https://doi.org/10.1093/jn/nxab029

Cui, H.-X., Zhang, L.-S., Luo, Y., Yuan, K., Huang, Z.-Y. and Guo, Y. 2019. A purified anthraquinone-glycoside preparation from rhubarb ameliorates type 2 diabetes mellitus by modulating the gut microbiota and reducing inflammation. *Front Microbiol.*, 10, 1423. https://doi.org/10.3389/fmicb.2019.01423

Hamamah, S., Amin, A., Al-Kassir, A.L., Chuang, J. and Covasa, M. 2023. Dietary fat modulation of gut microbiota and impact on regulatory pathways controlling food intake. *Nutrients*, 15(15), 3365. https://doi.org/10.3390/nu15153365

Ji, H., Wan, Y., Li, S., Zhou, D., Gu, F., Sun, J., Yan, X., Le, Y., Chen, T., Nie, S. and Wan, H. 2025. Remolding probiotics for effective treatment of type 2 diabetes via oral administration. *Biomaterials,* 315, 122970. https://doi.org/10.1016/j.biomaterials.2024.122970

Jia, L., Li, D., Feng, N., Shamoon, M., Sun, Z., Ding, L., Zhang, H., Chen, W., Sun, J. and Chen, Y.Q. 2017. Anti-diabetic effects of Clostridium butyricum CGMCC0313.1 through promoting the growth of gut butyrate-producing bacteria in type 2 diabetic mice. *Sci. Rep.*, 7, 7046. https://doi.org/10.1038/s41598-017-07335-0

Kalra, S. and Sahay, R. 2020. A review on semaglutide: An oral glucagon-like peptide-1 receptor agonist in management of type 2 diabetes mellitus. *Diabetes Ther.*, 11(9), 1965–1982. https://doi.org/10.1007/s13300-020-00894-y

Kerimi, A., Kraut, N.U., Encarnacao, J.A. and Williamson, G. 2020. The gut microbiome drives inter- and intra-individual differences in metabolism of bioactive small molecules. *Sci. Rep.*, 10(1), 19590. https://doi.org/10.1038/s41598-020-76558-5

Kopp, W. 2019. How western diet and lifestyle drive the pandemic of obesity and civilization diseases. *Diabetes Metab. Syndr. Obes.*, 12, 2221–2236. https://doi.org/10.2147/DMSO.S216791

Lee, H., An, J., Kim, J., Choi, D., Song, Y., Lee, C.-K., Kong, H., Kim, S.B. and Kim, K. 2022. A novel bacterium, Butyricimonas virosa, preventing HFD-induced diabetes and metabolic disorders in mice via GLP-1 receptor. *Front. Microbiol.*, 13, 858192. https://doi.org/10.3389/fmicb.2022.858192

Lemaire, M., Dou, S., Cahu, A., Formal, M., Le Normand, M., Rome, V., Nogret, I., Ferred-Bernard, S., Rhimi, M., Cuinet, I., Canlet, C., Tremblay-Franco, M., Le Ruyet, P., Baudry, C., Gérard, P., Le Huërou-Luron, I. and Blat, S. 2018. Addition of dairy lipids and probiotic Lactobacillus fermentum in infant formula programs gut microbiota and entero-insular axis in adult minipigs. *Sci. Rep.*, 8, 11656. https://doi.org/10.1038/s41598-018-29971-w

Lessard-Lord, J., Roussel, C., Guay, V. and Desjardins, Y. 2023. Characterization of the interindividual variability associated with the microbial metabolism of (−)-epicatechin. *J. Agric. Food Chem.*, 71(37), 13814–13827. https://doi.org/10.1021/acs.jafc.3c05491

Li, K.-K., Tian, P.-J., Wang, S.-D., Lei, P., Qu, L., Huang, J.-P., Shan, Y.-J. and Li, B. 2017. Targeting gut microbiota: *Lactobacillus* alleviated type 2 diabetes via inhibiting LPS secretion and activating GPR43 pathway. *J. Funct. Foods,* 38(Part A), 561–570. https://doi.org/10.1016/j.jff.2017.09.049

Li, T., Yang, J., Zhang, H., Xie, Y., Liu, H., Ren, J., Ren, F. and Jin, J. 2022. *Bifidobacterium animalis* subsp. *lactis* A12 prevents obesity-associated dyslipidemia by modulating gut-microbiota-derived short-chain fatty acid production and energy metabolism in high-fat-diet-fed mice. *Food Nutr. Res*., 66, 8670. https://doi.org/10.29219/fnr.v66.8670

Lund, M.L., Egerod, K.L., Engelstoft, M.S., Dmytriyeva, O., Theodorsson, E., Patel, B.A. and Schwartz, T.W. 2018. Enterochromaffin 5-HT cells-A major target for GLP-1 and gut microbial metabolites. *Mol. Metab.*, 11, 70–83. https://doi.org/10.1016/j.molmet.2018.03.004

Lyu, M., Wang, Y.-F., Fan, G.-W., Wang, X.-Y., Xu, S.-Y. and Zhu, Y. 2017. Balancing herbal medicine and functional food for prevention and treatment of cardiometabolic diseases through modulating gut microbiota. *Front. Microbiol.*, 8, 2146. https://doi.org/10.3389/fmicb.2017.02146

McMurdie, P.J., Stoeva, M.K., Justice, N., Nemchek, M., Sieber, C.M.K., Tyagi, S., Gines, J., Skennerton, C.T., Souza, M., Kolterman, O. and Eid, J. 2022. Increased circulating butyrate and ursode-

oxycholate during probiotic intervention in humans with type 2 diabetes. *BMC Microbiol*., 22, 19. https://doi.org/10.1186/s12866-021-02419-9

Mendis, S., Graham, I., Branca, F., Collins, T., Tukuitonga, C., Gunawardane, A. and Narula, J. 2025. Alarming rise of obesity: The 4th United Nations High-Level Meeting on noncommunicable diseases and mental health should advance action to tackle obesity. *Glob. Heart*, 20(1), 70. https://doi.org/10.5334/gh.1459

Milano, W. and Capasso, A. 2018. Diseases and health risks associated with obesity. *Integr. Obes. Diabetes*, 4(1), 1–4. https://doi.org/10.15761/IOD.1000200

Min, Q., Wang, Y., Jin., T.C., Zhu, L., Wu, X.Y., Li, Y.K., Wang, Y.J. and Xu, N. 2022. Analysis of intestinal short-chain fatty acid metabolism profile after probiotics and GLP-1 treatment for type 2 diabetes mellitus. *Front. Endocrinol.*, 13, 892127. https://doi.org/10.3389/fendo.2022.892127

Müller, M., Hernández, M.A.G., Goossens, G.H., Reijnders, D., Holst, J.J., Jocken, J.W.E., van Eijk, H., Canfora, E.E. and Blaak, E.E. 2019. Circulating but not faecal short-chain fatty acids are related to insulin sensitivity, lipolysis and GLP-1 concentrations in humans. *Sci. Rep.*, 9, 12515. https://doi.org/10.1038/s41598-019-48775-0

Müller, T.D., Finan, B., Bloom, S.R., D'Alessio, D., Drucker, D.J., Flatt, P.R., Fritsche, A., Gribble, F., Grill, H.J., Habener, J.F., Holst J.J., Langhans, W., Meier, J.J., Nauck, M.A., Perez-Tilve, D., Pocai, A., Reimann, F., Sandoval, D.A., Schwartz, T.W., Seeley, R.J., Stemmer, K., Tang-Christensen, M., Woods, S.C., DiMarchi, R.D. and Tschöp, M.H. 2019. Glucagon-like peptide-1 (GLP-1). *Mol. Metab.*, 30, 72–130. https://doi.org/10.1016/j.molmet.2019.09.010

Oudat, Q. and Okour, A. 2025. The role of probiotics in modulating gut microbiota and metabolic health for weight management: A mini review. *Acta Microbiol. Hellenica*, 70(1), 5. https://doi.org/10.3390/amh70010005

Pizarroso, N.A., Fuciños, P., Gonçalves, C., Pastrana, L. and Amado, I.R. 2021. Food-derived bioactive molecules and the microbiota–gut–brain axis in satiety regulation: A review. *Nutrients*, 13(2), 632. https://doi.org/10.3390/nu13020632

Planes-Muñoz, D., López-Nicolás, R., González-Bermúdez, C.A., Ros-Berruezo, G. and Frontela-Saseta, C. 2018. In vitro effect of green tea and turmeric extracts on GLP-1 and CCK secretion: The effect of gastrointestinal digestion. *Food Funct.*, 9(10), 5245–5250. https://doi.org/10.1039/C8FO01334A

Poulain, J.P. 2024. Sociology of obesity: How to justify fighting against the development of the obesity epidemic. *Obesities*, 4(4), 389–398. https://doi.org/10.3390/obesities4040031

Qu, L., Ren, J., Huang, L., Pang, B., Liu, X., Liu, X., Li, B. and Shan, Y. 2018. Antidiabetic effects of Lactobacillus casei fermented yogurt through reshaping gut microbiota structure in type 2 diabetic rats. *J. Agric. Food Chem.*, 66(48), 12696–12705. https://doi.org/10.1021/acs.jafc.8b04874

Radziszewska, M., Ostrowska, L. and Smarkusz-Zarzecka, J. 2024. The impact of gastrointestinal hormones on human adipose tissue function. *Nutrients,* 16(19), 3245. https://doi.org/10.3390/nu16193245

Roshanravan, N., Mahdavi, R., Alizadeh, E., Jafarabadi, M.A., Hedayati, M., Ghavami, A., Alipour, S., Alamdari, N.M., Barati, M. and Ostadrahimi, A. 2017. Effect of butyrate and inulin supplementation on glycemic status, lipid profile and glucagon-like peptide-1 level in patients with type 2 diabetes: A randomized double-blind, placebo-controlled trial. *Horm. Metab. Res.*, 49(11), 886–891. https://doi.org/10.1055/s-0043-119089

Salvador, R., Moutinho, C.G., Sousa, C., Vinha, A.F., Carvalho, M. and Matos, C. 2025. Semaglutide as a GLP-1 agonist: A breakthrough in obesity treatment. *Pharmaceuticals,* 18(3), 399. https://doi.org/10.3390/ph18030399

Singh, A., Zapata, R.C., Pezeshki, A., Reidelberger, R.D. and Chelikani, P.K. 2018. Inulin fiber dose-dependently modulates energy balance, glucose tolerance, gut microbiota, hormones and diet preference in high-fat-fed male rats. *J. Nutr. Biochem.*, 59, 142–152. https://doi.org/10.1016/j.jnutbio.2018.05.017

Tolhurst, G., Heffron, H., Lam, Y.S., Parker, H.E., Habib, A.M., Diakogiannaki, E., Cameron, J., Grosse, J., Reimann, F. and Gribble, F.M. 2012. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. *Diabetes*, 61(2), 364–371. https://doi.org/10.2337/db11-1019

Tom Dieck, H., Schön, C., Wagner, T., Pankoke, H.C., Fluegel, M. and Speckmann, B. 2022. A synbiotic formulation comprising *Bacillus subtilis* DSM 32315 and L-alanyl-L-glutamine improves intestinal butyrate levels and lipid metabolism in healthy humans. Nutrients, 14(1), 143. https://doi.org/10.3390/nu14010143

Tomás-Barberán, F.A., Selma, M.V. and Espín, J.C. 2016. Interactions of gut microbiota with dietary polyphenols and consequences to human health. *Curr. Opin. Clin. Nutr. Metab. Care,* 19(6), 471–476. https://doi.org/10.1097/MCO.0000000000000314

vGüney-Coşkun, M. and Başaranoğlu, M. 2024. Interplay of gut microbiota, GLP-1 receptor agonists, and nutrition: New frontiers in metabolic dysfunction-associated steatotic liver disease therapy. *World J. Gastroenterol.*, 30(43), 4682–4688. https://doi.org/10.3748/wjg.v30.i43.4682

Vilarrasa, E., Nicolau, J., de la Cueva, P., Goday, A., Gallardo, F., Martorell-Calatayud, A. and Carrascosa, J.M. 2024. Glucagon-like peptide-1 agonists for treating obesity in patients with immune-mediated skin diseases [Translated article]. *Actas Dermo-Sifiliogr.*, 115(1), T56–T65. https://doi.org/10.1016/j.ad.2023.10.019

Wang, G., Li, X., Zhao, J., Zhang, H. and Chen, W. 2017. Lactobacillus casei CCFM419 attenuates type 2 diabetes via a gut-microbiota-dependent mechanism. *Food Funct.*, 8(9), 3155–3164. https://doi.org/10.1039/C7FO00593A

Wang, L., Su, Z., Li, Y.-C., Cao, B.-Y., Su, C. and Gong, C.-X. 2024. Relationship of glucagon-like peptide-1 and peptide YY

with catch-up growth in children born small for gestational age. *J. Clin. Res. Pediatr. Endocrinol*., 16(1), 69–75. https://doi.org/10.4274/jcrpe.galenos.2023.2023-5-21

Wang, Q., Farhadipour, M., Thijs, T., Ruilova Sosoranga, E., Van der Schueren, B., Ceulemans, L.J., Deleus, E., Lannoo, M., Tack, J. and Depoortere, I. 2024. Bitter-tasting drugs tune GDF15 and GLP-1 expression via bitter taste or motilin receptors in the intestine of patients with obesity. *Mol. Metab.*, 88, 102002. https://doi.org/10.1016/j.molmet.2024.102002

Wang, X., Lv, X., Qi, Y., Wang, S., Yang, M., Wang, B., Cao, H., Zhang, J. and Xu, X. 2025. *Lactobacillus rhamnosus* GG supernatant improves GLP-1 secretion through attenuating L-cell lipotoxicity and modulating gut microbiota in obesity. *Probiotics Antimicrob. Proteins.* 178(1), 876-891. https://doi.org/10.1007/s12602-025-10564-9

Wang, Y., Dilidaxi, D., Wu, Y., Sailike, J., Sun, X. and Nabi, X.-H. 2020. Composite probiotics alleviate type 2 diabetes by regulating intestinal microbiota and inducing GLP-1 secretion in db/db mice. *Biomed. Pharmacother.*, 125, 109914. https://doi.org/10.1016/j.biopha.2020.109914

Wang, Y., Wu, Y., Sailike, J., Sun, X., Abuduwaili, N., Tuoliuhan, H., Yusufu, M. and Nabi, X. 2020. Fourteen composite probiotics alleviate type 2 diabetes through modulating gut microbiota and modifying M1/M2 phenotype macrophage in db/db mice. *Pharmacol. Res.*, 161, 105150. https://doi.org/10.1016/j.phrs.2020.105150

World Health Organization. 2025, May 7. Obesity and overweight. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

Xu, Y. and Kuipers, O.P. 2025. Design and biosynthesis of ornithine-8-containing semaglutide variants with a click-chemistry-modifiable position 26. *ACS Synth. Biol.*, 14(5), 1790–1801. https://doi.org/10.1021/acssynbio.5c00132

Yadav, H., Lee, J.H., Lloyd, J., Walter, P. and Rane, S.G. 2013. Beneficial metabolic effects of a probiotic via butyrate-induced GLP-1 hormone secretion. *J. Biol. Chem.*, 288(35), 25088–25097. https://doi.org/10.1074/jbc.M113.452516

Yu, W., Sun, S. and Fu, Q. 2025. The role of short-chain fatty acid in metabolic syndrome and its complications: focusing on immunity and inflammation. *Front. Immunol.*, 16, 1519925. https://doi.org/10.3389/fimmu.2025.1519925

Zhang, C., Fang, B., Zhang, N., Zhang, Q., Niu, T., Zhao, L., Sun, E., Wang, J., Xiao, R., He, J., Li, S., Chen, J., Guo, J., Xiong, W. and Wang, R. 2024. The effect of *Bifidobacterium animalis* subsp. lactis MN-Gup on glucose metabolism, gut microbiota, and their metabolites in type 2 diabetic mice. Nutrients, 16(11), 1691. https://doi.org/10.3390/nu16111691

Zhu, M., Yang, L., Li, L., Bai, Y. and Zhao, B. 2025. Administration of *Bifidobacterium animalis* subsp. *lactis* BLa80 and *Lactobacillus acidophilus* LA85 improved hyperglycemia and modulated gut microbiota in type 2 diabetic mice. *Probiotics Antimicrob. Proteins*., 18(1), 822-836. https://doi.org/10.1007/s12602-025-10567-6

Zuñiga-Martínez, B.S., Domínguez-Avila, J.A., Montiel-Herrera, M., Villegas-Ochoa, M.A., Robles-Sánchez, R.M., Ayala-Zavala, J.F., Viuda-Martos, M. and González-Aguilar, G.A. 2024. Consumption of plant-derived phenolic acids modulates hunger and satiety responses due to chemical interactions with enteroendocrine mediators. *Foods*, 13(22), 3640. https://doi.org/10.3390/foods13223640