World Journal of Multidisciplinary Research and Development
www.worldsubjectjournal.com
Online ISSN: 3107-9598
Received: 14-05-2026, Accepted: 13-06-2026, Published: 28-06-2026
Volume 2, Issue 2, 2026, Page No. 12-20

Targeting endogenous GLP-1 through functional foods: Mechanisms, clinical evidence, and therapeutic potential in type 2 diabetes mellitus

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Abstract
Type 2 diabetes mellitus (T2DM) is a rapidly increasing global health challenge characterized by insulin resistance, progressive β-cell dysfunction, and chronic hyperglycemia. While pharmacological therapies such as glucagon-like peptide-1 (GLP-1) receptor agonists have revolutionized diabetes management, growing evidence suggests that dietary interventions capable of stimulating endogenous GLP-1 secretion represent a promising complementary strategy. Functional foods—foods that provide health benefits beyond basic nutrition—contain bioactive compounds capable of enhancing incretin secretion, improving insulin sensitivity, delaying gastric emptying, modulating gut microbiota, and reducing inflammation. Dietary fibres, resistant starch, prebiotics, probiotics, polyphenols, omega-3 fatty acids, and fermented foods have all demonstrated the capacity to stimulate intestinal L-cells, leading to increased endogenous GLP-1 production. These nutritional approaches offer a safe, cost-effective, and sustainable means of improving glycemic control while reducing dependence on pharmacological therapies. This review summarizes the physiology of endogenous GLP-1, mechanisms by which functional foods enhance incretin secretion, current evidence from clinical and experimental studies, and future perspectives for personalized nutrition in T2DM management.

Keywords: GLP-1, type 2 diabetes mellitus, functional foods, Incretins, Gut microbiota, Dietary fibre, polyphenols, resistant starch, prebiotics, nutrition therapy

Introduction

Type 2 diabetes mellitus (T2DM) accounts for approximately 90–95% of all diabetes cases worldwide and continues to rise due to sedentary lifestyles, unhealthy dietary habits, obesity, and population aging (Sanyaolu *et al*., 2023) [61]. Persistent hyperglycemia contributes to both microvascular and macrovascular complications, including nephropathy, retinopathy, neuropathy, and cardiovascular disease (Cole & Florez, 2020) [11].

Current diabetes management combines lifestyle modification with pharmacological therapies aimed at improving insulin secretion, reducing hepatic glucose production, and enhancing insulin sensitivity. Among these, GLP-1 receptor agonists have emerged as highly effective agents due to their ability to stimulate glucose-dependent insulin secretion, suppress glucagon release, promote satiety, delay gastric emptying, and induce weight loss (Wang *et al*., 2023) [65].

Despite their effectiveness, GLP-1 receptor agonists are expensive, injectable in many cases, and may cause gastrointestinal side effects. Consequently, increasing attention has focused on nutritional strategies capable of enhancing endogenous GLP-1 secretion naturally. Functional foods rich in fermentable fibres, resistant starches, polyphenols, probiotics, and bioactive peptides can stimulate intestinal enteroendocrine L-cells, increasing physiological GLP-1 release (Moran-Ramos *et al*., 2016) [46]. Such dietary approaches may complement pharmacotherapy and contribute to long-term metabolic health.

Physiology of Endogenous GLP-1

Glucagon-like peptide-1 (GLP-1) is an incretin hormone predominantly synthesized and secreted by enteroendocrine L-cells located in the distal ileum and colon in response to nutrient ingestion (Makrilakis, 2019; Mullur *et al*., 2024) [40, 49]. The secretion of endogenous GLP-1 is stimulated through direct sensing of dietary carbohydrates, fats, and proteins by intestinal L-cells, as well as indirectly by short-chain fatty acids and other metabolites produced through the fermentation of dietary fibre by the gut microbiota. Following its release into the circulation, GLP-1 exerts multiple physiological actions that are essential for maintaining glucose homeostasis (Müller *et al*., 2019). It enhances glucose-dependent insulin secretion from pancreatic -cells while suppressing glucagon release from -cells, thereby reducing hepatic glucose output and preventing excessive postprandial hyperglycemia (Gilbert & Pratley, 2020; Makrilakis, 2019) [25, 40].

Additionally, GLP-1 delays gastric emptying, prolonging nutrient absorption and promoting satiety, which contributes to reduced appetite and lower energy intake (Gilbert & Pratley, 2020 [25]; Müller *et al*., 2019). Beyond its glycemic effects, GLP-1 supports pancreatic -cell survival by promoting cell proliferation and reducing apoptosis, thereby helping preserve insulin secretory capacity (Ferhatbegović *et al*., 2023; Müller *et al*., 2019) [21, 40]. Emerging evidence also indicates that GLP-1 exerts cardioprotective effects through improvements in endothelial function, reductions in oxidative stress and inflammation, and favorable effects on blood pressure and lipid metabolism (Ferhatbegović *et al*., 2023 [21]; Ma *et al*., 2021).

Despite its potent metabolic benefits, endogenous GLP-1 has a very short plasma half-life of approximately 1–2 minutes because it is rapidly degraded by the enzyme dipeptidyl peptidase-4 (DPP-4), limiting its biological activity and providing the rationale for the development of GLP-1 receptor agonists and DPP-4 inhibitors in the treatment of type 2 diabetes mellitus (Ferhatbegović *et al*., 2023; Gilbert & Pratley, 2020) [21, 25].

Regulation of Endogenous GLP-1 Secretion

1. Carbohydrates

Carbohydrates are among the primary dietary stimuli for endogenous GLP-1 secretion. Following ingestion, glucose is absorbed by enteroendocrine L-cells through the sodium-glucose cotransporter-1 (SGLT-1), a key glucose-sensing transporter located on the apical membrane of these cells. Glucose uptake leads to membrane depolarization, which subsequently opens voltage-dependent calcium channels, resulting in an influx of calcium ions that triggers the exocytosis of GLP-1-containing secretory granules (Cui *et al*., 2026) [13]. This rapid postprandial release of GLP-1 enhances glucose-dependent insulin secretion, suppresses glucagon release, and contributes to the regulation of postprandial blood glucose levels. The extent of GLP-1 secretion is influenced by the type and amount of carbohydrate consumed, with slowly digestible carbohydrates and low-glycemic-index foods often promoting a more sustained incretin response than rapidly absorbed sugars (Balakumar *et al*., 2026) [3].

2. Dietary Fat

Dietary fats are potent stimulators of endogenous GLP-1 secretion, particularly long-chain unsaturated fatty acids (Rasheed, 2026) [58]. After digestion, free fatty acids interact with G-protein-coupled receptors (GPCRs), mainly GPR40 (FFAR1) and GPR120 (FFAR4), located on the surface of intestinal L-cells. Activation of these receptors initiates intracellular signaling pathways involving phospholipase C, protein kinase C, and increased intracellular calcium concentrations, ultimately promoting GLP-1 secretion (Vogt *et al*., 2026) [64]. In addition to enhancing incretin release, activation of GPR120 exerts anti-inflammatory effects and improves insulin sensitivity, further contributing to metabolic homeostasis. Healthy dietary fats derived from sources such as olive oil, nuts, seeds, avocados, and fatty fish have been shown to effectively stimulate GLP-1 secretion while providing additional cardiometabolic benefits (Mozaffarian *et al*., 2026) [47].

3. Proteins and Amino Acids

Dietary proteins and their constituent amino acids also play an important role in stimulating endogenous GLP-1 secretion (Cui *et al*., 2026) [13]. During protein digestion, amino acids such as glutamine, arginine, leucine, phenylalanine, and tryptophan activate calcium-sensing receptors (CaSR), G-protein-coupled receptors, and peptide transporters such as peptide transporter-1 (PepT1) expressed on intestinal L-cells. These signaling pathways increase intracellular calcium levels and promote the exocytosis of GLP-1. Protein-induced GLP-1 secretion contributes to improved postprandial insulin release, enhanced satiety, delayed gastric emptying, and better glycemic control (Presenza *et al*., 2026) [55]. High-quality protein sources, including dairy products, legumes, soy, eggs, fish, and lean meats, have demonstrated favorable effects on incretin secretion and are increasingly incorporated into dietary strategies for managing type 2 diabetes (Comerford and Pasin, 2016) [12].

4. Microbial Metabolites

The gut microbiota plays a crucial role in regulating endogenous GLP-1 secretion through the production of microbial metabolites, particularly short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate (Gofron *et al*., 2025) [20]. These metabolites are generated during the fermentation of dietary fibres and resistant starches by beneficial intestinal bacteria in the colon. SCFAs stimulate enteroendocrine L-cells by activating free fatty acid receptors FFAR2 (GPR43) and FFAR3 (GPR41), leading to increased intracellular signaling and enhanced GLP-1 release (Elsayed, 2025) [20]. In addition to promoting incretin secretion, SCFAs improve intestinal barrier integrity, reduce systemic inflammation, enhance insulin sensitivity, and support the growth of beneficial gut microorganisms. Consequently, diets rich in fermentable fibres, prebiotics, and whole plant foods indirectly enhance endogenous GLP-1 secretion through microbiota-mediated mechanisms, highlighting the importance of the gut microbiome in metabolic health and diabetes management (Irfan *et al*., 2026) [34].

Functional Foods Targeting Endogenous GLP-1

Functional foods are foods that provide health-promoting benefits beyond their basic nutritional value due to the presence of physiologically active compounds capable of modulating metabolic processes (Debri *et al*., 2026) [14]. In recent years, these foods have gained considerable attention as natural dietary approaches for enhancing endogenous glucagon-like peptide-1 (GLP-1) secretion and improving glycemic control in individuals with type 2 diabetes mellitus. Functional foods stimulate intestinal enteroendocrine L-cells either directly through nutrient-sensing mechanisms or indirectly by modifying the composition and metabolic activity of the gut microbiota, resulting in increased GLP-1 release, improved insulin secretion, enhanced satiety, delayed gastric emptying, reduced appetite, and better glucose homeostasis (Su Khin *et al*., 2026) [62]. The principal categories of functional foods with demonstrated GLP-1-stimulating potential include dietary fibre, resistant starch, whole grains, polyphenol-rich fruits and vegetables, fermented foods, prebiotics, probiotics, synbiotics, omega-3 fatty acids, and bioactive peptides derived from plant and animal proteins. These functional ingredients also exert complementary metabolic benefits, such as improving insulin sensitivity, reducing oxidative stress and chronic inflammation, enhancing intestinal barrier function, and promoting a healthier gut microbiome. Consequently, incorporating GLP-1-promoting functional foods into daily dietary patterns represents a safe, sustainable, and cost-effective nutritional strategy that may complement pharmacological therapies in the prevention and management of type 2 diabetes (Patel and Niazi, 2025) [54].

Dietary Fibre and GLP-1 Secretion

Dietary fibre is one of the most effective nutritional modulators of endogenous glucagon-like peptide-1 (GLP-1) secretion and plays a central role in the dietary management

of type 2 diabetes mellitus (Cui *et al*., 2026) [34]. Soluble and fermentable fibres escape digestion in the upper gastrointestinal tract and reach the colon, where they are fermented by beneficial gut microorganisms to produce short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate (Modasia *et al*., 2026) [44]. These SCFAs activate free fatty acid receptors FFAR2 (GPR43) and FFAR3 (GPR41) expressed on intestinal enteroendocrine L-cells, initiating intracellular signaling pathways that stimulate GLP-1 synthesis and secretion (Brockmann *et al*., 2025) [7]. Increased endogenous GLP-1 enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and promotes satiety, thereby improving overall glucose homeostasis. In addition to stimulating incretin release, dietary fibre slows gastric emptying and carbohydrate digestion, resulting in a lower glycemic response after meals. Regular consumption of high-fibre foods has been associated with improved insulin sensitivity, reduced postprandial blood glucose excursions, enhanced appetite control, greater weight management, and increased microbial diversity within the gut. Furthermore, dietary fibre contributes to improved intestinal barrier integrity and reduced systemic inflammation, both of which are important in the pathophysiology of insulin resistance. Rich dietary sources of fermentable fibre include oats and barley, which are abundant in β-glucan; psyllium husk; legumes such as beans, lentils, and chickpeas; a wide variety of fruits and vegetables; and flaxseed, which provides both soluble fibre and bioactive lignans. Increasing daily dietary fibre intake through these functional foods represents a practical, economical, and evidence-based strategy for naturally enhancing endogenous GLP-1 secretion and improving metabolic health in individuals with type 2 diabetes (Hu *et al*., 2026) [34].

Resistant Starch

Resistant starch (RS) is a unique type of dietary carbohydrate that resists digestion by human digestive enzymes in the small intestine and reaches the colon intact, where it undergoes fermentation by beneficial gut microbiota (Pandey *et al*., 2026) [53]. Unlike rapidly digestible starches, resistant starch functions similarly to dietary fibre by serving as a substrate for microbial metabolism, leading to the production of short-chain fatty acids (SCFAs), particularly butyrate, along with acetate and propionate. These SCFAs activate free fatty acid receptors FFAR2 (GPR43) and FFAR3 (GPR41) expressed on enteroendocrine L-cells, stimulating the secretion of endogenous glucagon-like peptide-1 (GLP-1) (Hirdaramani *et al*., 2026) [64]. Increased GLP-1 release enhances glucose-dependent insulin secretion, suppresses glucagon production, delays gastric emptying, and promotes satiety, thereby improving postprandial glucose regulation (Dimitriadis *et al*., 2021) [17]. Among the SCFAs, butyrate plays a particularly important role in maintaining intestinal health by serving as the primary energy source for colonocytes, strengthening gut barrier integrity, reducing intestinal permeability, and suppressing chronic low-grade inflammation associated with insulin resistance and type 2 diabetes mellitus. Resistant starch also positively influences gut microbial composition by promoting the growth of beneficial bacteria such as *Bifidobacterium* and *Faecalibacterium prausnitzii*, thereby enhancing microbial diversity and metabolic health (Fineman *et al*., 2012) [24]. Natural food sources rich in resistant starch include green bananas, cooked and cooled potatoes, brown rice, lentils, beans, peas, oats, barley, and whole grains, as well as cooled pasta and other retrograded starch-containing foods (Sajilata, 2006) [60]. Numerous randomized clinical trials have demonstrated that regular resistant starch consumption improves insulin sensitivity, lowers fasting and postprandial blood glucose concentrations, reduces glycated hemoglobin (HbA1c), enhances endogenous GLP-1 secretion, and supports body weight management. Owing to these multiple physiological benefits, resistant starch has emerged as a promising functional food component for the nutritional prevention and adjunctive management of type 2 diabetes through modulation of the gut microbiota–GLP-1 axis (Liu *et al*., 2020) [25].

Polyphenols and GLP-1

Polyphenols are a diverse group of naturally occurring phytochemicals widely distributed in fruits, vegetables, tea, cocoa, herbs, and spices, and are recognized for their potent antioxidant, anti-inflammatory, and antidiabetic properties (Rana *et al*., 2022) [57]. Increasing evidence suggests that dietary polyphenols play a significant role in enhancing endogenous glucagon-like peptide-1 (GLP-1) secretion through multiple complementary mechanisms. Certain polyphenols directly stimulate intestinal enteroendocrine L-cells, promoting GLP-1 release in response to nutrient intake, while others inhibit the activity of the enzyme dipeptidyl peptidase-4 (DPP-4), thereby prolonging the biological activity of circulating GLP-1 (Dominguez Avila *et al*., 2017) [18]. Additionally, polyphenols reduce oxidative stress by scavenging reactive oxygen species and enhancing endogenous antioxidant defenses, which helps preserve pancreatic β-cell function and insulin secretory capacity. Their anti-inflammatory effects further improve insulin sensitivity by suppressing pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). Polyphenols also beneficially modulate the gut microbiota by increasing the abundance of beneficial bacterial species that produce short-chain fatty acids, indirectly enhancing GLP-1 secretion through activation of enteroendocrine L-cells. Major dietary sources of polyphenols include green tea, cocoa, berries, grapes, apples, turmeric, pomegranate, cinnamon, olives, and numerous colorful fruits and vegetables. Among the various classes of polyphenols, flavonoids such as quercetin, catechins, anthocyanins, and resveratrol have demonstrated significant incretin-enhancing activity in experimental and clinical studies by improving GLP-1 secretion, preserving β-cell function, reducing postprandial hyperglycemia, and enhancing insulin sensitivity. Collectively, these findings highlight polyphenol-rich functional foods as promising dietary interventions for naturally targeting the GLP-1 pathway and improving metabolic control in individuals with type 2 diabetes mellitus.

Prebiotics

Prebiotics are non-digestible dietary substrates that are selectively utilized by beneficial intestinal microorganisms, thereby promoting gut health and improving metabolic function. Unlike probiotics, which introduce live microorganisms into the gastrointestinal tract, prebiotics serve as fermentable substrates that stimulate the growth

and activity of resident beneficial bacteria, particularly *Bifidobacterium* and *Lactobacillus* species. The most extensively studied prebiotics include inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS), which are naturally present in foods such as chicory root, garlic, onions, leeks, asparagus, bananas, and whole grains (Guarino *et al*., 2020) [29]. Upon reaching the colon, these compounds undergo bacterial fermentation, leading to the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. These microbial metabolites activate free fatty acid receptors FFAR2 (GPR43) and FFAR3 (GPR41) on enteroendocrine L-cells, stimulating endogenous glucagon-like peptide-1 (GLP-1) secretion. Increased GLP-1 enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and promotes satiety, thereby improving glycemic control and reducing energy intake (Camilleri and Lupianez-Merly, 2024) [9]. In addition to enhancing incretin secretion, prebiotics strengthen intestinal barrier integrity, reduce endotoxin-induced inflammation, improve insulin sensitivity, and favorably modulate the composition and diversity of the gut microbiota (Joshi *et al*., 2026) [68]. Numerous clinical studies have demonstrated that regular prebiotic supplementation is associated with significant improvements in glycated hemoglobin (HbA1c), fasting blood glucose, insulin resistance, body weight, and appetite regulation in individuals with obesity and type 2 diabetes mellitus. Consequently, incorporating prebiotic-rich functional foods into daily dietary patterns represents an effective nutritional strategy for targeting the gut microbiota–GLP-1 axis and supporting long-term metabolic health (R. Dias *et al*., 2017) [56].

Probiotics

Prebiotics are non-digestible dietary substrates that are selectively utilized by beneficial intestinal microorganisms, thereby promoting gut health and improving metabolic function. Unlike probiotics, which introduce live microorganisms into the gastrointestinal tract, prebiotics serve as fermentable substrates that stimulate the growth and activity of resident beneficial bacteria, particularly *Bifidobacterium* and *Lactobacillus* species (Yoo *et al*., 2024) [66]. The most extensively studied prebiotics include inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS), which are naturally present in foods such as chicory root, garlic, onions, leeks, asparagus, bananas, and whole grains (Ballini *et al*., 2023) [4]. Upon reaching the colon, these compounds undergo bacterial fermentation, leading to the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate (Fernández *et al*., 2016) [22]. These microbial metabolites activate free fatty acid receptors FFAR2 (GPR43) and FFAR3 (GPR41) on enteroendocrine L-cells, stimulating endogenous glucagon-like peptide-1 (GLP-1) secretion. Increased GLP-1 enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and promotes satiety, thereby improving glycemic control and reducing energy intake (Oteng and Liu, 2023) [52]. In addition to enhancing incretin secretion, prebiotics strengthen intestinal barrier integrity, reduce endotoxin-induced inflammation, improve insulin sensitivity, and favorably modulate the composition and diversity of the gut microbiota (Brown, 2017) [8]. Numerous clinical studies have demonstrated that regular prebiotic supplementation is associated with significant improvements in glycated hemoglobin (HbA1c), fasting blood glucose, insulin resistance, body weight, and appetite regulation in individuals with obesity and type 2 diabetes mellitus. Consequently, incorporating prebiotic-rich functional foods into daily dietary patterns represents an effective nutritional strategy for targeting the gut microbiota–GLP-1 axis and supporting long-term metabolic health (Kellow *et al*., 2014) [35].

Synbiotics

Synbiotics are functional food formulations that combine probiotics (beneficial live microorganisms) with prebiotics (non-digestible substrates that selectively nourish these microorganisms) to produce synergistic effects on gut health and metabolic function (Tewari *et al*., 2021) [63]. The prebiotic component enhances the survival, colonization, and activity of the probiotic strains within the gastrointestinal tract, resulting in greater microbial stability and improved fermentation efficiency (You *et al*., 2022) [67]. This synergistic interaction promotes the production of short-chain fatty acids (SCFAs), particularly acetate, propionate, and butyrate, which activate FFAR2 (GPR43) and FFAR3 (GPR41) receptors on enteroendocrine L-cells, thereby stimulating endogenous glucagon-like peptide-1 (GLP-1) secretion (Martin-Gallausiaux *et al*., 2021) [42]. Elevated GLP-1 levels enhance glucose-dependent insulin secretion, suppress glucagon release, delay gastric emptying, and increase satiety, contributing to improved glycemic control and appetite regulation (Moiz *et al*., 2025) [45]. In addition, synbiotics improve intestinal barrier integrity, reduce intestinal permeability, suppress systemic inflammation, and positively modulate the composition and diversity of the gut microbiota, thereby alleviating insulin resistance and metabolic dysfunction. Clinical studies have demonstrated that synbiotic supplementation can improve fasting blood glucose, glycated hemoglobin (HbA1c), insulin sensitivity, lipid profiles, and inflammatory biomarkers while supporting healthy body weight management in individuals with type 2 diabetes mellitus. Owing to their combined microbiota-modulating and incretin-enhancing effects, synbiotics represent a promising nutritional strategy for targeting the gut microbiota–GLP-1 axis and complementing conventional dietary and pharmacological interventions in diabetes management (Nikolaidis *et al*., 2025) [51].

Fermented Foods

Fermented foods are functional foods produced through the action of beneficial microorganisms such as lactic acid bacteria, yeasts, and fungi, which transform food substrates into products enriched with probiotics, bioactive peptides, organic acids, vitamins, and other health-promoting metabolites (Feroz *et al*., 2023) [23]. These foods have gained considerable attention for their beneficial effects on gut health and metabolic regulation, particularly in the management of type 2 diabetes mellitus (Nie *et al*., 2019) [40]. Common fermented foods include yogurt, kefir, kimchi, sauerkraut, fermented soy products such as tempeh, miso, and natto, as well as other traditional fermented dairy and vegetable products (Dimidi *et al*., 2019) [16]. Regular consumption of fermented foods enhances the diversity and abundance of beneficial gut microorganisms, leading to improved microbial balance and increased production of short-chain fatty acids (SCFAs), which stimulate

enteroendocrine L-cells to enhance endogenous glucagon-like peptide-1 (GLP-1) secretion (Markowiak-Kopeć and Śliżewska, 2020) [41]. In addition, bioactive peptides generated during the fermentation process may exert direct antidiabetic effects by improving insulin sensitivity, inhibiting dipeptidyl peptidase-4 (DPP-4) activity, and reducing oxidative stress and inflammation (Li *et al*., 2026). Fermented foods also strengthen intestinal barrier integrity by enhancing tight junction protein expression and reducing intestinal permeability, thereby limiting metabolic endotoxemia and chronic low-grade inflammation associated with insulin resistance (Zang *et al*., 2026) [34]. Through these complementary mechanisms—including increased microbial diversity, enhanced gut barrier function, improved SCFA production, and greater endogenous GLP-1 secretion—fermented foods contribute to better glycemic control, improved insulin action, enhanced satiety, and overall metabolic health. Consequently, incorporating fermented foods into a balanced dietary pattern represents a practical and sustainable nutritional approach for supporting the gut microbiota–GLP-1 axis in individuals with type 2 diabetes mellitus (Martin-Gallausiaux *et al*., 2021) [42].

Omega-3 Fatty Acids

Omega-3 fatty acids are essential polyunsaturated fatty acids that possess potent anti-inflammatory, cardioprotective, and antidiabetic properties, making them valuable functional food components in the management of type 2 diabetes mellitus (Bayram and Kızıltan, 2024) [5]. The long-chain marine-derived omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), exert their metabolic benefits through multiple mechanisms, including activation of the G-protein-coupled receptor GPR120 (free fatty acid receptor-4, FFAR4), which plays a crucial role in regulating inflammation, insulin sensitivity, and incretin secretion (Zheng *et al*., 2026) [69]. Activation of GPR120 suppresses inflammatory signaling pathways by inhibiting nuclear factor-kappa B (NF-κB) and reducing the production of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), thereby improving insulin signaling in peripheral tissues (Du *et al*., 2022) [26]. Omega-3 fatty acids have also been shown to stimulate endogenous glucagon-like peptide-1 (GLP-1) secretion from intestinal enteroendocrine L-cells, leading to enhanced glucose-dependent insulin secretion, delayed gastric emptying, improved satiety, and better postprandial glucose regulation. Furthermore, they protect pancreatic β-cells from oxidative stress and inflammatory damage, preserving insulin secretory function and delaying β-cell dysfunction associated with diabetes progression. In addition to their direct metabolic effects, omega-3 fatty acids favorably modulate gut microbiota composition and improve endothelial function, contributing to reduced cardiovascular risk, which is a major concern in individuals with type 2 diabetes. Rich dietary sources of omega-3 fatty acids include oily fish such as salmon, sardines, mackerel, herring, and tuna, while plant-based sources of alpha-linolenic acid (ALA) include flaxseed, chia seeds, walnuts, hemp seeds, and canola oil. Regular consumption of omega-3-rich foods has been associated with improvements in insulin sensitivity, glycemic control, lipid metabolism, systemic inflammation, and endogenous GLP-1 secretion, highlighting their therapeutic potential as part of a comprehensive nutritional strategy for the prevention and management of type 2 diabetes mellitus (Dias *et al*., 2025) [51].

Bioactive Peptides

Bioactive peptides are short sequences of amino acids released from dietary proteins during gastrointestinal digestion, food processing, or microbial fermentation, and they have emerged as promising functional food components for improving metabolic health and glycemic control (Antony and Vijayan, 2021) [2]. These peptides exhibit a wide range of biological activities, including antihypertensive, antioxidant, anti-inflammatory, immunomodulatory, and antidiabetic effects (Jakubczyk *et al*., 2020) [33]. Recent evidence indicates that specific protein-derived peptides can enhance endogenous glucagon-like peptide-1 (GLP-1) secretion by directly stimulating enteroendocrine L-cells through activation of calcium-sensing receptors (CaSR) and other nutrient-sensing pathways. Increased intracellular calcium signaling promotes the exocytosis of GLP-1-containing secretory granules, thereby enhancing glucose-dependent insulin secretion and suppressing glucagon release (Adriaenssens *et al*., 2018) [1]. In addition, several bioactive peptides have been shown to inhibit the activity of dipeptidyl peptidase-4 (DPP-4), the enzyme responsible for the rapid degradation of GLP-1, resulting in prolonged incretin activity and improved glycemic regulation. Bioactive peptides may also protect pancreatic β-cells against oxidative stress and inflammation, improve insulin sensitivity, and contribute to better appetite regulation through enhanced satiety signaling. Major dietary sources of these peptides include dairy proteins such as casein and whey, soy proteins, fish proteins, egg proteins, and fermented protein-rich foods, where enzymatic hydrolysis during fermentation increases peptide bioavailability (Chakrabarti *et al*., 2018) [10]. Numerous experimental and clinical studies have demonstrated that peptides derived from milk, soybeans, fish, and eggs possess significant incretin-enhancing and DPP-4 inhibitory activities, making them attractive natural alternatives or complementary dietary strategies for supporting endogenous GLP-1 secretion. Consequently, the incorporation of bioactive peptide-rich functional foods into daily diets represents a promising nutritional approach for improving glucose homeostasis and managing type 2 diabetes mellitus through multiple complementary mechanisms.

Gut Microbiota–GLP-1 Axis

The intestinal microbiota plays a central role in regulating incretin secretion.

Healthy microbiota
↓
Fibre fermentation
↓
SCFA production
↓
FFAR2/FFAR3 activation
↓
L-cell stimulation
↓
GLP-1 secretion
↓
Improved glucose homeostasis

Dysbiosis reduces SCFA production and weakens endogenous GLP-1 secretion, contributing to insulin resistance (Grasset *et al*., 2017) [28].

Table 1: Functional Foods Influencing Endogenous GLP-1 (Bodnaruc *et al*., 2016) [22]

Functional Food	Bioactive Components	Mechanism	GLP-1 Effect
Oats	β-glucan	SCFA production	↑ GLP-1
Barley	β-glucan	Fermentation	↑ GLP-1
Legumes	Resistant starch	Butyrate formation	↑ GLP-1
Green banana	Resistant starch	Colon fermentation	↑ GLP-1
Flaxseed	Fibre + lignans	SCFA production	↑ GLP-1
Green tea	Catechins	DPP-4 inhibition	↑ GLP-1
Berries	Anthocyanins	L-cell stimulation	↑ GLP-1
Cocoa	Flavanols	Antioxidant activity	↑ GLP-1
Yogurt	Probiotics	Gut microbiota modulation	↑ GLP-1
Kefir	Probiotics	SCFA production	↑ GLP-1

Clinical Evidence

Clinical trials have shown that diets rich in soluble fibre, resistant starch, and prebiotic ingredients significantly increase endogenous GLP-1 concentrations while improving insulin sensitivity and glycemic control (Giuntini *et al*., 2022) [26]. Mediterranean dietary patterns, characterized by high intakes of whole grains, legumes, fruits, vegetables, nuts, and olive oil, have been associated with increased postprandial GLP-1 responses and improved metabolic outcomes (Ruiz-Pozo *et al*., 2024) [59]. Supplementation with inulin, resistant starch, β-glucan, and probiotic formulations has demonstrated reductions in fasting glucose, HbA1c, body weight, and inflammatory markers in individuals with T2DM (Kim *et al*., 2018 [36]). Although the magnitude of GLP-1 elevation varies among studies, these interventions consistently support the role of functional foods as effective adjuncts to conventional diabetes therapy.

Table 2: Advantages of Functional Foods Compared with Pharmacological GLP-1 Therapy (Dias *et al*., 2025) [15]

Functional Foods	GLP-1 Receptor Agonists
Natural	Synthetic
Low cost	Expensive
Minimal side effects	Gastrointestinal adverse effects
Improve gut microbiota	Limited microbiota effects
Multiple metabolic benefits	Primarily receptor activation
Sustainable long-term use	Lifelong medication often required

Challenges and Future Perspectives

Despite encouraging evidence, several challenges remain. Interindividual variability in gut microbiota composition influences responsiveness to functional food interventions. The bioavailability and stability of bioactive compounds differ among food sources and processing methods, and there is a lack of standardized dosages for many functional ingredients. Furthermore, most studies are short-term and involve relatively small sample sizes. Future research should focus on large, well-designed randomized controlled trials, the development of personalized nutrition strategies based on microbiome profiling, and the identification of novel bioactive compounds capable of stimulating endogenous GLP-1 secretion. Advances in nutrigenomics, metabolomics, and microbiome science are expected to facilitate precision nutrition approaches for T2DM prevention and management.

Conclusion

Targeting endogenous GLP-1 secretion through functional foods represents a promising nutritional strategy for the prevention and management of type 2 diabetes mellitus. Functional foods rich in dietary fibre, resistant starch, polyphenols, prebiotics, probiotics, synbiotics, omega-3 fatty acids, and bioactive peptides stimulate intestinal L-cells through nutrient-sensing pathways and gut microbiota-derived metabolites, leading to enhanced physiological GLP-1 release. These mechanisms improve insulin secretion, suppress glucagon, enhance satiety, reduce postprandial glycemia, and support long-term metabolic health. Although functional foods cannot replace pharmacological GLP-1 receptor agonists in patients requiring intensive treatment, they offer a safe, affordable, and sustainable complementary approach that addresses multiple aspects of metabolic dysfunction. Integrating functional foods into evidence-based dietary recommendations may enhance diabetes care, improve patient outcomes, and reduce the global burden of T2DM.

Future Research Directions

Despite the growing body of evidence supporting the role of functional foods in enhancing endogenous glucagon-like peptide-1 (GLP-1) secretion and improving metabolic health, several important research gaps remain. Future investigations should prioritize well-designed, long-term randomized controlled trials to establish the efficacy, optimal dosage, and safety of GLP-1-targeting functional foods across diverse populations with type 2 diabetes mellitus. Additional research is needed to evaluate the synergistic effects of combining prebiotics, probiotics, synbiotics, polyphenols, resistant starch, and other bioactive food components, as these combinations may produce greater improvements in incretin secretion and glycemic control than individual interventions. Advances in nutrigenomics, metabolomics, and gut microbiome profiling offer opportunities to develop personalized nutrition strategies that account for interindividual differences in microbial composition, metabolic responses, and genetic variability. Furthermore, the discovery and characterization of novel food-derived bioactive peptides, phytochemicals, and other naturally occurring compounds with incretin-enhancing or dipeptidyl peptidase-4 (DPP-4)-inhibitory properties may expand the range of dietary interventions available for diabetes management. Research should also investigate how food processing techniques, cooking methods, fermentation, and formulation influence the stability, bioavailability, and GLP-1-stimulating activity of functional food ingredients. Another important area of investigation is the integration of functional foods with conventional GLP-1 receptor agonists and other antidiabetic medications to determine whether combined nutritional and pharmacological approaches provide additive or synergistic metabolic benefits while minimizing drug dosage and adverse effects. Finally, future studies should evaluate the long-term cost-effectiveness, feasibility, patient adherence, and real-world implementation of GLP-1-targeted dietary interventions in different healthcare settings and socioeconomic populations to facilitate their translation into evidence-based clinical practice and public health nutrition guidelines.

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