Clinical Case Reports and Studies
2026 Volume 12, Issue 5
DOI: 10.59657/2837-2565.brs.26.324

BioRes Scientia
Value your Research

Review Article

Open Access

GLP-1 Therapy Through a Microbiome Lens

Swarup K. Chakrabarti *

H. P. Ghosh Research Center, New Town, Kolkata, West Bengal 700161, India.

**Corresponding author: Swarup K. Chakrabarti.*

Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have transformed the management of obesity and type 2 diabetes by improving glycemic control, promoting weight loss, and reducing cardiovascular risk. Traditionally, their effects have been interpreted through a host-centric metabolic framework, largely overlooking the gut microbiome's role. Emerging evidence positions the microbiome as a systems-level mediator of GLP-1RA efficacy, integrating metabolic, immune, and neuroendocrine outcomes. Preclinical and clinical studies show that GLP-1 RAs remodel gut microbial composition, enriching beneficial taxa such as Akkermansia, Bacteroides, Lactobacillus, and SCFA-producing Roseburia and Faecalibacterium prausnitzii. These shifts enhance intestinal barrier function, reduce systemic inflammation, and stimulate endogenous GLP-1 secretion, establishing feedback loops that amplify therapeutic effects. Individual baseline microbial profiles affect treatment response, while GLP-1RAs also exert direct immunomodulatory and cytoprotective actions in the gut. By linking microbial metabolites to host metabolic and neuroendocrine pathways, this framework highlights the gut microbiome as an active participant rather than a passive responder. Integrating microbiome dynamics into GLP-1RA biology offers a foundation for precision medicine approaches, providing strategies to optimize therapeutic outcomes and broaden clinical benefits beyond glycemic control.

Keywords: GLP-1 receptor agonists; gut microbiome; obesity; type 2 diabetes; short-chain fatty acids; gut-brain axis

Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as a cornerstone in the management of obesity and type 2 diabetes, demonstrating robust efficacy in glycemic control, weight reduction, and cardiovascular risk mitigation [1-3]. Their rapid clinical adoption reflects the growing burden of metabolic disease and the limitations of conventional lifestyle and surgical interventions. Mechanistically, GLP-1 RAs mimic endogenous incretin signaling to regulate satiety, glucose homeostasis, and central appetite pathways, enabling sustained weight loss of approximately 15-25% within the first year of treatment [4-6]. Despite these advances, challenges remain, including gastrointestinal adverse effects, potential lean mass loss, and weight regain following discontinuation [7]. These limitations highlight the need to better define the biological determinants of therapeutic response. Conventional frameworks have largely interpreted GLP-1RA efficacy through a host-centric metabolic lens [8]. In contrast, this review advances a conceptual shift by positioning the gut microbiome as a systems-level mediator that integrates peripheral metabolic regulation with central neuroendocrine outcomes. Emerging evidence indicates that GLP-1 RAs reshape microbial composition and function, while microbiome-derived metabolites reciprocally influence host signaling pathways [9,10]. However, current findings remain predominantly associative, with limited mechanistic resolution. Variability in microbial signatures across studies, compounded by differences in diet, treatment duration, and baseline metabolic status, further limits interpretability [11,12]. Establishing causality between microbiome remodeling and therapeutic outcomes, therefore, remains a central challenge. These gaps underscore the need for a systems-level framework integrating host-microbiome interactions to more precisely define GLP-1-mediated responses.

Gut Microbiome as a Mediator of GLP-1 Therapy

The gut microbiome plays a central role in regulating host metabolism, immune function, and neuroendocrine signaling [13,14]. Increasing evidence suggests that it functions as an active mediator of GLP-1 RA efficacy rather than a passive bystander. GLP-1 RAs promote shifts in microbial composition that enrich beneficial taxa and suppress potentially pathogenic communities [15,16]. These compositional changes are accompanied by functional remodeling, including enhanced intestinal barrier integrity, reduced systemic inflammation, and

increased production of short-chain fatty acids. Metabolites such as butyrate and propionate contribute to improved insulin sensitivity, appetite regulation, and modulation of inflammatory responses [17,18]. Notably, microbial metabolites stimulate enteroendocrine L-cells to increase endogenous GLP-1 secretion, establishing a bidirectional feedback loop between host physiology and microbial ecology [19,20]. Collectively, these findings support a model in which therapeutic outcomes arise from an integrated host–microbiome system rather than from isolated pharmacological effects.

Impact of GLP-1 Analogs on Gut Microbiota: Preclinical and Clinical Insights

GLP-1RAs, including liraglutide, semaglutide, and dulaglutide, are increasingly recognized for their capacity to modulate the gut microbiota alongside their established roles in glycemic control and weight reduction [21,22]. Preclinical studies consistently demonstrate that these agents promote microbial configurations enriched in beneficial taxa such as Akkermansia muciniphila, Bacteroides, Lactobacillus, Roseburia, and Faecalibacterium prausnitzii [23,24]. These taxa are prominent producers of short-chain fatty acids (SCFAs), including butyrate and propionate, which contribute to improved insulin sensitivity, enhanced intestinal barrier integrity, and reduced systemic inflammation [25,26]. Mechanistically, GLP-1RAs may influence gut motility, luminal pH, and bile acid metabolism, thereby creating a favorable niche for beneficial microbes and reinforcing the gut–brain-microbiome axis [9,10,27].

Liraglutide, in particular, has been extensively studied in rodent models and demonstrates consistent microbiome remodeling [28,29]. It increases the relative abundance of Akkermansia, Bacteroides, Lactobacillus, Parabacteroides, and Oscillospira. In methionine- and choline-deficient (MCD) diet models, liraglutide restores Bacteroides populations and shifts Erysipelotrichaceae composition from Allobaculum to Turicibacter, suggesting a role in mitigating diet-induced dysbiosis in liver disease contexts [30,31]. In db/db mice, enrichment of SCFA-producing taxa (Parabacteroides, Oscillibacter, Prevotellaceae) is accompanied by a reduction in pro-inflammatory genera (Anaerotruncus, Lachnospiraceae) and improvements in alanine aminotransferase/aspartate aminotransferase (ALT/AST) levels, linking microbial remodeling to both metabolic and hepatic benefits [32,33].

High-resolution taxonomic analyses further indicate that liraglutide stabilizes SCFA-producing communities across major phyla, including Bacteroidota (Bacteroides, Alistipes, Parabacteroides, Butyricimonas) and Bacillota (Lactobacillus, Allobaculum, Clostridium, Oscillospira), while reducing potentially pathogenic taxa such as Staphylococcus, Anaerotruncus, and Flavonifractor [34,35]. Notably, reductions in Prevotella_9 are of particular interest given the association of Prevotella-dominated microbiota with insulin resistance, underscoring the metabolic relevance of GLP-1RA-induced microbial shifts [36,37].

Beyond metabolic regulation, GLP-1 signaling exerts direct anti-inflammatory and cytoprotective effects within the gut. Activation of GLP-1 receptors on intraepithelial lymphocytes (IELs) reduces pro-inflammatory cytokine production, suppresses interferon-stimulated gene (ISG) expression, and limits epithelial cell death [38,39]. In anti-CD3-treated mice, exenatide significantly reduces interferon gamma (IFNG) and ISG expression in intestinal epithelial cells (IECs), along with decreased crypt cell death-effects absent in GLP-1R knockout models-highlighting the critical role of GLP-1R signaling in maintaining intestinal immune homeostasis [40,41]. In colitis models, liraglutide attenuates inflammation, preserves crypt architecture, and limits leukocyte infiltration, further supporting its protective role in intestinal integrity [42,43].

Semaglutide exhibits distinct microbial signatures, including enrichment of Akkermansia, Faecalibaculum, and Allobaculum, alongside improvements in glucose tolerance and gut barrier function [44,45]. Interestingly, some studies report reduced microbial diversity following treatment, suggesting that functional remodeling may be more relevant than diversity metrics in determining therapeutic benefit. 46 In polycystic ovary syndrome (PCOS) models, microbiome alterations are associated with weight loss, while neurobehavioral studies demonstrate reduced hippocampal inflammation and enhanced neurogenesis, supporting a role for GLP-1RAs in modulating the gut-brain axis [47-49].

Clinical findings largely mirror these preclinical observations. Short-term liraglutide treatment induces favorable microbiome shifts, whereas long-term dulaglutide therapy leads to gradual microbial

restructuring, paralleling sustained improvements in glycemic control, weight loss, and systemic inflammation [50,51]. Importantly, baseline microbiome composition appears to influence therapeutic outcomes. Higher abundances of Bacteroides dorei and Roseburia inulinivorans are associated with greater reductions in HbA1c, while increased Prevotella copri may attenuate treatment efficacy [52,53]. Across studies, enrichment of key SCFA-producing taxa such as Faecalibacterium prausnitzii and Roseburia consistently correlates with improvements in fasting glucose and lipid profiles [54,55].

Retrospective clinical analyses further suggest that GLP-1RA therapy improves quality of life in patients with inflammatory bowel disease (IBD), particularly those with coexisting type 2 diabetes, highlighting the dual metabolic and immunomodulatory effects of these agents [56,57]. In murine inflammation models, GLP-1RAs promote the expansion of SCFA-producing Firmicutes associated with IL-22 production while suppressing pathogenic taxa such as Staphylococcus, coinciding with reduced epithelial damage and modulation of interferon signaling pathways [58,59]. Table 1 summarizes the effects of GLP-1RAs on gut microbiota, including the types of analogs used, study models, microbial alterations, and associated functional and metabolic outcomes.

Table 1: GLP-1 Analog Effects on Gut Microbiota.

GLP-1 Analog	Model / Study Type	Microbiota Changes (Composition / Diversity)	Functional / Metabolic Outcomes
Liraglutide	Animal (rodent models)	↑ Beneficial genera (e.g., *Akkermansia*, *Bacteroides*, *Lactobacillus*, *Parabacteroides*, *Oscillospira*); ↓ harmful taxa; ↓ *Firmicutes: Bacteroidetes* ratio in some models	Enhanced glucose metabolism, reduced weight gain, improved lipid profiles [34,35]
	Animal (MCD diet: methionine-choline deficient)	Restored normal *Bacteroides* levels; shifted *Erysipelotrichaceae* from *Allobaculum* → *Turicibacter*; overall altered gut microbiota disrupted by MCD diet	Potential mitigation of diet-induced dysbiosis; supports metabolic homeostasis in liver disease model [30]
	Animal (Male db/db mice)	↑ SCFA-producing/anti-inflammatory taxa (*Parabacteroides*, *Oscillibacter*, *Prevotellaceae*); ↓ *Anaerotruncus*, *Lachnospiraceae*; correlated with ALT/AST	Anti-inflammatory effects via SCFAs; improved liver markers [15,60]
	Human (T2D patients)	↑ *Akkermansia* vs metformin; no consistent alpha/beta diversity change in RCTs	Correlate with improved gut-barrier taxa; clinical significance unclear [61-63]
Semaglutide	Animal (obesity / high-fat diet)	↑ *Akkermansia*, *Faecalibaculum*, *Allobaculum*; restored dysbiotic taxa; often times reduced diversity	Reduced weight gain, enhanced glucose tolerance, improved gut-barrier integrity [64,65]
	Animal (PCOS model)	↑ *Helicobacter* (negatively correlated with body weight)	Weight loss correlated with microbiome shift [66]
	Animal (C57BL/6 mice, neurobehavioral model)	Modulates gut microbiota	Reduces hippocampal neuroinflammation; promotes neurogenesis via insulin/GLP-1 pathway; potential antidepressant and anxiolytic effects [67,68]
Dulaglutide	Animal models	↑ *Bacteroides*, *Akkermansia*, *Ruminococcus*	Improved metabolic patterns (SCFA, gut barrier support) [59]
	Human studies	Limited data; some ↑ *Lactobacillus*; no significant changes after 1 week, but microbial abundance decreased after 48 weeks in newly diagnosed T2D patients	Metabolic effects observed; microbial effects underpowered; long-term microbiota modulation [53,59]
Exenatide / Exendin-4	Animal models	↑ *Akkermansia*, *Barnesiella*, *Ruminococcus*; ↓ dysbiotic taxa	Improved metabolic parameters correlated with microbiota shifts [69]

	Human observations	↑ *Coprococcus*, *Bifidobacterium* in small cohorts; otherwise, inconsistent	Limited clinical evidence for direct microbiota mediation [15]
GLP-1RAs (general)	Mixed clinical observations	Some ↑ *Akkermansia*, *Roseburia*, *Faecalibacterium*; SCFA-producing genera enriched; human diversity often unchanged	Suggestive links to glucose tolerance and inflammation regulation; causality not confirmed [70]
	Observational (Human patients)	Increased abundance of *Faecalibacterium prausnitzii*, negatively correlated with fasting blood glucose levels.	Improved glycemic control; suggests microbiota influences drug responsiveness [70-72]
	Observational (Human cohort)	Higher abundance of *Roseburia* associated with reduced obesity and dyslipidemia; *Prevotella/Bacteroides* ratio positively associated with obesity, with *Prevotella* linked to insulin resistance.	Highlights specific taxa as biomarkers of metabolic health and potential predictors of GLP-1 responsiveness [73-75]
Inflammatory / extra-metabolic models	Animal inflammatory models	Shifts toward more beneficial taxa (SCFA-producing *Firmicutes*); ↓ pathogenic taxa like Staphylococcus	Enhanced anti-inflammatory activity (IL-22), improved gut barrier; causality in humans unproven to date [76,77]

Abbreviations: GLP-1: Glucagon-Like Peptide-1; HFD: High-Fat Diet; T2D: Type 2 Diabetes; MCD: Methionine-Choline Deficient; SCFA: Short-Chain Fatty Acids; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; PCOS: Polycystic Ovary Syndrome; IL-22: Interleukin-22.

Collectively, GLP-1RAs engage a bidirectional regulatory network linking host metabolism, intestinal immunity, and microbial ecology. Microbial-derived SCFAs stimulate endogenous GLP-1 secretion, while GLP-1RAs reshape gut physiology and microbial composition, reinforcing feedback loops that amplify therapeutic effects. These findings support the concept that the gut microbiome is not merely a passive responder but an active biological mediator of GLP-1RA efficacy, providing a strong rationale for microbiome-informed precision therapies in metabolic and inflammatory diseases.

Significance of The Review

This review establishes a systems-level framework that incorporates the gut microbiome into GLP-1 RA biology. It positions the microbiome as an active mediator of therapeutic responses, highlights bidirectional interactions between microbial metabolites and host signaling pathways, and underscores agent-specific microbial signatures. By linking microbiome dynamics to metabolic and neuroendocrine outcomes, this framework broadens the clinical relevance of GLP-1 therapies beyond glycemic control. This integrative perspective provides a conceptual foundation for microbiome-informed precision medicine.

Limitations and Potential Biases

Despite growing interest, current evidence remains largely associative and does not establish causality. Variability in microbial signatures across studies, coupled with differences in diet, treatment duration, and baseline metabolic status, complicates interpretation and limits reproducibility. Integration of microbiome data with neuroendocrine outcomes remains limited, and longitudinal, multi-omics investigations are scarce. These constraints hinder mechanistic insight and restrict the ability to delineate the temporal dynamics underlying therapeutic responses. The absence of causal human data remains the primary barrier to clinical translation.

Future Directions

Future research must move beyond associative observations toward longitudinal, multi-omics frameworks capable of capturing dynamic host–microbiome interactions during GLP-1 RA therapy. Identification of predictive microbial and metabolite signatures will be critical to addressing inter-individual variability and enabling microbiome-informed precision medicine. The gut–brain–microbiome axis represents a key integrative pathway through which therapeutic responses may be coordinated. In particular, the extent to which GLP-1 RAs restore central insulin and leptin signaling and how microbial metabolites modulate neuroinflammation and brain function remain to be elucidated. These priorities support the development of integrated therapeutic strategies that combine GLP-1 RAs with microbiome-targeted interventions within a unified systems-level framework.

Conclusions

GLP-1 RAs have redefined the management of obesity and type 2 diabetes by extending their effects beyond glycemic control to encompass immune, neuroendocrine, and microbiome-mediated processes. The gut microbiome emerges as a central mediator of these effects, challenging traditional host-centric models and supporting a systems-level understanding of therapeutic responses. However, current evidence remains largely associative, and mechanistic links to clinical outcomes have yet to be fully established. Addressing these gaps will be critical for translating microbiome insights into more effective and precise therapeutic strategies.

Declarations

Conflict of Interest

The author does have anything to declare.

Funding

None.

Generative AI statement

The authors confirm that no content in this manuscript was generated by artificial intelligence (AI) tools without appropriate oversight. Any use of AI-assisted technologies (e.g., for language editing or formatting) has been transparently acknowledged, and the authors have reviewed and verified all content for accuracy, originality, and compliance with ethical standards. The authors take full responsibility for the work, including any errors or inaccuracies.

References

1. Westermeier F, Fisman EZ. (2025). Glucagon like peptide-1 (GLP-1) agonists and cardiometabolic protection: historical development and future challenges. *Cardiovasc Diabetol*. 24(1):44.
2. Aristizábal-Colorado D, Corredor-Rengifo D, Sierra-Castillo S, López-Corredor C, Vernaza-Trujillo DA, et al. (2025). A decade of progress in type 2 diabetes and cardiovascular disease: advances in SGLT2 inhibitors and GLP-1 receptor agonists - a comprehensive review. *Front Endocrinol (Lausanne)*. 16:1605746.
3. Seremet OC, Puşcaşu C, Andrei C, Niţulescu G, Zbârcea CE, et al. (2025). Small-Molecule GLP-1 Receptor Agonists: A Promising Pharmacological Approach. *Medicina (Kaunas)*. 61(11):1902.
4. Liu Z, Yu S, Jin X, Sheng L, YanMu MR, et al. (2025). The Clinical Application of GLP-1RAs and GLP-1/GIP Dual Receptor Agonists Based on Pharmacological Mechanisms: A Review. *Drug Des Devel Ther*. 19:10383-10409.
5. Fadel LP, Thao G, Chitre T, Rojas ED, Nguyen Fricko M, et al. (2025). A System-Based Review on Effects of Glucagon-Like Peptide-1 Receptor Agonists: Benefits vs Risks. *Cureus*. 17(2):e78575.
6. Moiz A, Filion KB, Tsoukas MA, Yu OHY, Peters TM, et al. (2025). The expanding role of GLP-1 receptor agonists: a narrative review of current evidence and future directions. *EClinicalMedicine*. 86:103363.
7. Kim JA, Yoo HJ. (2025). Exploring the Side Effects of GLP-1 Receptor Agonist: To Ensure Its Optimal Positioning. *Diabet Meta*. 49(4):525-541.
8. Chen Q, Chen T, Lin W, Chen X. (2026). A Clinical Comprehensive Evaluation of Long-Acting GLP-1 Receptor Agonists in Type 2 Diabetes Management. *Diabetes Meta*. 19:585436.
9. Kamath S, Chan NSL, Joyce P. (2026). GLP-1 agonists and the gut microbiome: A bidirectional relationship. *Br J Clin Pharmacol*.
10. Kanbay M, Al-Shiab R, Shah E, Ozbek L, Guldan M, et al. (2025). Gut microbiota modulation in GLP-1RA and SGLT-2i therapy: clinical implications and mechanistic insights in type 2 diabetes. *Clin Kidney J*. 18(12):sfaf351.
11. Cano RJ, García Menéndez G. (2026). Why Clinical Trials of Microbiome-Targeted Interventions Often Fail to Support Health Claims: A Commentary on Probiotics and Translational Design. *Microorganisms*. 14(2):470.
12. Zeng Q, Feng X, Hu Y, Su S. (2025). The human gut microbiota is associated with host lifestyle: a comprehensive narrative review. 16:1549160.
13. O'Riordan KJ, Moloney GM, Keane L, Clarke G, Cryan JF. (2025). The gut microbiota-immune-brain axis: Therapeutic implications. 6(3):101982.
14. Rowland I, Gibson G, Heinken A, Scott K, Swann J, et al. (2018). Gut microbiota functions: metabolism of nutrients and other food components. *Eur J Nutr*. 57(1):1-24.
15. Gofron KK, Wasilewski A, Małgorzewicz S. (2025). Effects of GLP-1 Analogues and Agonists on the Gut Microbiota: A Systematic Review. *Nutrients*. 17(8):1303.
16. Zeng Y, Wu Y, Zhang Q, Xiao X. (2024). Crosstalk between glucagon-like peptide 1 and gut microbiota in metabolic diseases. 15(1):e0203223.
17. Yan K, Sun X, Wang X, Zheng J, Yu H. (2025). Gut Microbiota and Metabolites: Biomarkers and

Therapeutic Targets for Diabetes Mellitus and Its Complications. *Nutrients*. 17(16):2603.
18. Ahmad S, Assaf M, Thomas B, Ibrahim H, Muppuri G, et al. (2025). Fecal Short-Chain Fatty Acids (SCFAs) and Their Role in Metabolic Disorders: A Systematic Review. 17(9):e91579.
19. Grundeken E, El Aidy S. (2025). Enteroendocrine cells: the gatekeepers of microbiome-gut-brain communication. *NPJ Biofilms Microb*.11(1):179.
20. Gong B, Li C, Shi Z, Wang F, Dai R, et al. (2025). GLP-1 receptor agonists: exploration of transformation from metabolic regulation to multi-organ therapy. *Front Pharmacol*. 16:1675552.
21. Karimi MA, Gholami Chahkand MS, Dadkhah PA, Sheikhzadeh F, Yaghoubi S, et al. (2025). A. Comparative effectiveness of semaglutide versus liraglutide, dulaglutide or tirzepatide: a systematic review and meta-analysis. *Fron Ph*. 16:1438318.
22. Alkhatib M, Almasri N, Alshwayyat S, Almahariq H, Hammadeh BM, et al. (2025). The multifaceted effects of semaglutide: exploring its broad therapeutic applications. *Future Sci OA*. 11(1):2483607.
23. Singh K, Aulakh SK, Nijjar GS, Singh S, Sandhu APS, et al. (2024). Rebalancing the Gut: Glucagon-Like Peptide-1 Agonists as a Strategy for Obesity and Metabolic Health. *Cureus*. 16(7):e64738.
24. Kumar S, Mukherjee R, Gaur P, Leal É, Lyu X, et al. (2025). Unveiling roles of beneficial gut bacteria and optimal diets for health. *Front Microbiol*. 16:1527755.
25. Facchin S, Calgaro M, Savarino EV. (2025). Rethinking Short-Chain Fatty Acids: A Closer Look at Propionate in Inflammation, Metabolism, and Mucosal Homeostasis. 14(15):1130.
26. Ottria R, Mirmajidi S, Ciuffreda P. (2026). Gut Microbiota-Derived Short-Chain Fatty Acids in Inflammatory Bowel Disease: Mechanistic Insights into Gut Inflammation, Barrier Function, and Therapeutic Potential. 27(2):1095.
27. Beutler LR. (2026). GLP-1 physiology and pharmacology along the gut-brain axis. *J Clin Invest*. 136(2):e194744.
28. Shang J, Liu F, Zhang B, Dong K, Lu M, et al. (2021). Liraglutide-induced structural modulation of the gut microbiota in patients with type 2 diabetes mellitus. *PeerJ*. 9:e11128.
29. Moreira GV, Azevedo FF, Ribeiro LM, Santos A, Guadagnini D, et al. (2018). Liraglutide modulates gut microbiota and reduces NAFLD in obese mice. *J Nutr Biochem*. 62:143-154.
30. Somm E, Montandon SA, Loizides-Mangold U, Gaïa N, Lazarevic V, et al. (2021). The GLP-1R agonist liraglutide limits hepatic lipotoxicity and inflammatory response in mice fed a methionine-choline deficient diet. *Transl Res*. 227:75-88.
31. Wang L, Li P, Tang Z, Yan X, Feng B. (2016). Structural modulation of the gut microbiota and the relationship with body weight: compared evaluation of liraglutide and saxagliptin treatment. *Sci Rep*. 6:33251.
32. Zhang Q, Xing W, Wang Q, Tang Z, Wang Y, et al. (2022). Gut microbiota-mitochondrial intertalk in non-alcoholic fatty liver disease. 9:934113.
33. Bahitham W, Alghamdi S, Omer I, Alsudais A, Hakeem I, et al. (2024). Double Trouble: How Microbiome Dysbiosis and Mitochondrial Dysfunction Drive Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis. *Biomedicines*. 12(3):550.
34. Zhang Y, Yang X, Yang P, Sun H, Chen L, et al. (2025). Effect of liraglutide on the dysglycemia, inflammation, and gut microbiota in prediabetic KKay mice. *Front Pharmacol*. 16:1714859.
35. Zhao L, Qiu Y, Zhang P, Wu X, Zhao Z, et al. (2022). Gut microbiota mediates positive effects of liraglutide on dyslipidemia in mice fed a high-fat diet. *Front Nutr*. 9:1048693.
36. Gong J, Zhang Q, Hu R, Yang X, Fang C, et al. (2024). Effects of Prevotella copri on insulin, gut microbiota and bile acids. *Gut Microbes*. 16(1):2340487.
37. Jin JY, Yang XY, Feng R, Ye ML, Xu H, et al. (2025). Gut Microbiota-Derived Metabolites Orchestrate Metabolic Reprogramming in Diabetic Cardiomyopathy: Mechanisms and Therapeutic Frontiers. *FASEB J*. 39(17):e71004.
38. Deng S, Chen Z, Shi Y. (2025). Roles of glucagon-like peptide 1 receptor agonists in immune cell biology and autoimmune/autoinflammatory diseases. *Cell Biosci*. 15(1):137.
39. Kumar V. (2025). GLP-1/GLP-1R axis: from metabolism (obesity and T2DM) to immunity. *Open Biol*. 15(7):240303.
40. Wong CK, Drucker DJ. (2025). Antiinflammatory actions of glucagon-like peptide-1-based therapies beyond metabolic benefits. *J Clin Invest*. 135(21):e194751.
41. Abdalqadir N, Adeli K. (2022). GLP-1 and GLP-2 Orchestrate Intestine Integrity, Gut Microbiota, and Immune System Crosstalk. *Microorganisms*. 10(10):2061.

42. Saadoun AA, Abdelsattar AH, Elsaid AH, Abdelaleam EA, Abdelkader HK, et al. (2025). Repurposing liraglutide to the management of DSS-induced colitis: a potential for promoting autophagy. *Naunyn Schmiedebergs Arch Pharmacol*. 398(12):17173-17185.
43. Thin L, Teh WL. (2025). GLP-1R Agonists and Their Therapeutic Potential in Inflammatory Bowel Disease and Other Immune-Mediated Inflammatory Diseases, a Systematic Review of the Literature. *Biomedicines*. 13(5):1128.
44. Feng J, Teng Z, Yang Y, Liu J, Chen S. (2024). Effects of semaglutide on gut microbiota, cognitive function and inflammation in obese mice. *PeerJ*. 12:e17891.
45. Qi L, Kang H, Zeng F, Zhan M, Huang C, et al. (2025). Gut microbiota mediates semaglutide attenuation of diabetes-associated cognitive decline. *Neurotherapeutics*. 22(5):e00615.
46. Barrea L, Annunziata G, Verde L, Galasso M, Savastano S, et al. (2025). A Multidisciplinary Perspective on Semaglutide Treatment and Medical Nutrition Therapy in Obesity Management. *Curr Obes Rep*. 14(1):73.
47. Liu M, Guo S, Li X, Tian Y, Yu Y, et al. (2024). Semaglutide Alleviates Ovary Inflammation via the AMPK/SIRT1/NF-κB Signaling Pathway in Polycystic Ovary Syndrome Mice. *Drug Des Devel Ther*. 18:3925-3938.
48. Sun Y, Gao S, Ye C, Zhao W. (2023). Gut microbiota dysbiosis in polycystic ovary syndrome: Mechanisms of progression and clinical applications. *Front Cell Infect Microbiol*. 13:1142041.
49. Senthilkumar H, Arumugam M. (2025). Gut microbiota: a hidden player in polycystic ovary syndrome. *J Transl Med*. 23(1):443.
50. Kim HS, Kim MJ, Kim HS, Cho YK, Jung CH, et al. (2025). Real-World Evidence of Long-Term Dulaglutide Use: Sustained Glycemic and Weight Improvements Beyond Three Years. *Clin Endocrinol (Oxf)*.
51. Ruda AI, Ciobanu DM, Inceu G, Rusu A, Roman G. (2023). The effect of Dulaglutide on glycemic and weight control in patients with type 2 diabetes. *Med Pharm Rep*. 96(1):52-57.
52. Tian J, Yang Y, Yu Z, Gao Y, Zong X, et al. (2025). Comparative evaluation of dulaglutide alone vs. dulaglutide combined with probiotics on cardiovascular risk factors in T2DM. *Hormones (Athens)*. 24(3):643-650.
53. Liang L, Su X, Guan Y, Wu B, Zhang X, et al. (2024). Correlation between intestinal flora and GLP-1 receptor agonist dulaglutide in type 2 diabetes mellitus treatment-A preliminary longitudinal study. *iScience*. 27(5):109784.
54. Alqahtani MS. (2025). The Gut Microbiota-Metabolic Axis: Emerging Insights from Human and Experimental Studies on Type 2 Diabetes Mellitus-A Narrative Review. *Medicina (Kaunas)*. 61(11).
55. Liu SH, Yang XF, Liang L, Song BB, Song XM, et al. (2025). Regulatory mechanisms of the gut microbiota-short chain fatty acids signaling axis in slow transit constipation and progress in multi-target interventions. *Front Microbiol*. 16:1689597.
56. Colwill M, Povlsen S, Pollok R, Patel K, Goodhand J, et al. (2025). Glucagon-like peptide-1 (GLP-1) receptor agonists in inflammatory bowel disease: mechanisms, clinical implications, and therapeutic potential. *J Crohns Colitis*. 19(9):jjaf167.
57. Yen FS, Wang SI, Hung YM, Hsu CC, Hwu CM, et al. (2025). Impact of glucagon-like peptide-1 receptor agonists on the incidence of inflammatory bowel disease in people with type 2 diabetes. *Diabetes Obes Metab*. 6403-6415.
58. Gaudino SJ, Singh A, Huang H, Padiadpu J, Jean-Pierre M, et al. (2024). Intestinal IL-22RA1 signaling regulates intrinsic and systemic lipid and glucose metabolism to alleviate obesity-associated disorders. *Nat Commun*. 15(1):1597.
59. Gofron KK, Wasilewski A, Małgorzewicz S. (2025). Effects of GLP-1 Analogues and Agonists on the Gut Microbiota: A Systematic Review. *Nutrients*. 17(8):1303.
60. Liu Q, Cai BY, Zhu LX, Xin X, Wang X, et al. (2020). Liraglutide modulates gut microbiome and attenuates nonalcoholic fatty liver in db/db mice. *Life Sci*. 261:118457.
61. Wang Z, Saha S, Van Horn S, Thomas E, Traini C, et al. (2017). Gut microbiome differences between metformin- and liraglutide-treated T2DM subjects. *Endocrinol Diabetes Metab*. 1(1):e00009.
62. Glaros SB, Mishra SP, Jain S, Davis FS, Gabel SA, et al. (2025). Systemic and gut microbiome changes with metformin and liraglutide in youth-onset type 2 diabetes: the MIGHTY study. Gut Microbes. 17(1):2558071.
63. Long XF, Fang YQ, Li YH, Li JY, Wang XP, et al. (2025). Combination metformin and liraglutide

in PCOS: clinical efficacy in women and preclinical insights from gut microbiome modulation in rats. *Front Endocrinol (Lausanne)*. 16:1599879.
64. Sun L, Shang B, Lv S, Liu G, Wu Q, et al. (2025). Effects of semaglutide on metabolism and gut microbiota in high-fat diet-induced obese mice. *Front Pharmacol*. 16:1562896.
65. Duan X, Zhang L, Liao Y, Lin Z, Guo C, et al. (2024). Semaglutide alleviates gut microbiota dysbiosis induced by a high-fat diet. *Eur J Pharmacol*. 969:176440.
66. Xiong C, Wu J, Ma Y, Li N, Wang X, et al. (2024). Effects of Glucagon-Like Peptide-1 Receptor Agonists on Gut Microbiota in Dehydroepiandrosterone-Induced Polycystic Ovary Syndrome Mice: Compared Evaluation of Liraglutide and Semaglutide Intervention. *Diabetes Metab Syndr Obes*. 17:865-880.
67. Zhai Y, Lu K, Yuan Y, Zhang Z, Xue L, et al. (2025). Semaglutide improves cognitive function and neuroinflammation in APP/PS1 transgenic mice by activating AMPK and inhibiting TLR4/NF-κB pathway. *J Alzheimers Dis*. 105(2):416-432.
68. Tipa RO, Balan DG, Georgescu MT, Ignat LA, Vacaroiu IA, et al. (2024). A Systematic Review of Semaglutide's Influence on Cognitive Function in Preclinical Animal Models and Cell-Line Studies. *Int J Mol Sci*. 25(9):4972.
69. Chen Y, Shu A, Jiang M, Jiang J, Du Q, et al. (2023). Exenatide improves hypogonadism and attenuates inflammation in diabetic mice by modulating gut microbiota. *Int Immunopharmacol*. 120:110339.
70. Ganamurali N, Sabarathinam S. (2026). Bidirectional interplay between the gut microbiota and GLP-1 receptor agonists: towards Microbiome-Mediated therapeutics in type 2 diabetes mellitus. *J Diabetes Metab Disord*. 25(1):44.
71. Liang L, Rao E, Zhang X, Wu B, Su X, et al. (2023). GLP-1 receptor agonists modulate blood glucose levels in T2DM by affecting Faecalibacterium prausnitzii abundance in the intestine. *Medicine (Baltimore)*. 102(35):e34978.
72. Craciun CI, Neag MA, Catinean A, Mitre AO, Rusu A, et al. (2022). The Relationships between Gut Microbiota and Diabetes Mellitus, and Treatments for Diabetes Mellitus. *Biomedicines*. 10(2):308.
73. Masi D, Watanabe M, Clément K. (2026). Gut microbiome and obesity care: Bridging dietary, surgical, and pharmacological interventions. *Cell Rep Med*. 7(2):102573.
74. Dong TS, Guan M, Mayer EA, Stains J, Liu C, et al. (2022). Obesity is associated with a distinct brain-gut microbiome signature that connects Prevotella and Bacteroides to the brain's reward center. *Gut Microbes*. 14(1):2051999.
75. Singh K, Aulakh SK, Nijjar GS, Singh S, Sandhu APS, et al. (2024). Rebalancing the Gut: Glucagon-Like Peptide-1 Agonists as a Strategy for Obesity and Metabolic Health. *Cureus*. 16(7):e64738.
76. Münte E, Hartmann P. (2025). The Role of Short-Chain Fatty Acids in Metabolic Dysfunction-Associated Steatotic Liver Disease and Other Metabolic Diseases. *Biomolecules*. 15(4):469.
77. Wu X, Mu B, Li G, Du R, Park S. (2026). Gut Microbial Composition, Oxidative Stress, and Immunity in Metabolic Disease: Toward Personalized Interventions. *Antioxidants (Basel)*. 15(2):175.

Cite this article: Chakrabarti SK. (2026). GLP-1 Therapy Through a Microbiome Lens, *Clinical Case Reports and Studies*, BioRes Scientia Publishers. 12(5):1-8. DOI: 10.59657/2837-2565.brs.26.324

Article History: **Received:** April 01, 2026 | **Accepted:** April 20, 2026 | **Published:** April 28, 2026