



Gut Hormone Modulation for Glycemic Control: Exploring the Role of the Gut–Pancreatic Axis in the Regulation of Glucose Homeostasis and Metabolic Health

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Introduction

Effective glycemic control is fundamental to the prevention and management of metabolic disorders, particularly type 2 diabetes mellitus (T2DM). Traditionally, glucose regulation has been attributed mainly to insulin and glucagon; however, growing evidence highlights the critical influence of gut-derived hormones in maintaining glucose homeostasis. These hormones, secreted by enteroendocrine cells in response to nutrient intake, act through the gut–pancreatic axis to regulate insulin secretion, appetite, gastric emptying, and energy balance. Understanding and modulating gut hormone activity has therefore emerged as a promising strategy for improving glycemic control and metabolic outcomes [1,2].

Discussion

Among the most important gut hormones involved in glycemic regulation are glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), peptide YY (PYY), and ghrelin. GLP-1 and GIP, known as incretin hormones, enhance glucose-dependent insulin secretion following meals. GLP-1 also suppresses glucagon release, slows gastric emptying, and promotes satiety, thereby reducing postprandial glucose spikes. In individuals with T2DM, the incretin effect is often impaired, contributing to chronic hyperglycemia [3,4].

Pharmacological modulation of gut hormones has transformed diabetes management. GLP-1 receptor agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors prolong or enhance incretin action, leading to improved glycemic control with a low risk of hypoglycemia. Newer multi-agonist therapies targeting GLP-1, GIP, and glucagon receptors demonstrate enhanced efficacy by exploiting complementary

hormonal pathways.

Lifestyle factors also play a significant role in gut hormone modulation. Diets high in dietary fiber and protein stimulate the release of GLP-1 and PYY, improving insulin sensitivity and appetite regulation. The gut microbiota further contributes by fermenting fibers into short-chain fatty acids, which activate enteroendocrine cells and enhance incretin secretion. Bariatric surgery exemplifies the powerful impact of gut hormone modulation, as rapid postoperative increases in GLP-1 and PYY are associated with marked improvements in glycemic control, often before significant weight loss occurs [5].

Despite these advances, variability in individual hormonal responses and long-term safety considerations highlight the need for continued research and personalized treatment approaches.

Conclusion

Gut hormone modulation represents a critical and evolving approach to glycemic control. By targeting the complex hormonal networks linking the gut and pancreas, both pharmacological and lifestyle interventions can significantly improve glucose regulation. Future research integrating gut hormone biology, nutrition, and microbiome science will be essential for optimizing therapies and advancing personalized metabolic care.

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