



## Incretin-Based Therapies: Advances in the Management of Type 2 Diabetes

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### Introduction

Incretin-based therapies represent a significant advancement in the treatment of type 2 diabetes mellitus (T2DM), targeting the hormonal pathways that regulate postprandial glucose homeostasis. Incretins are gut-derived hormones, primarily glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), which enhance insulin secretion in a glucose-dependent manner, suppress glucagon release, and slow gastric emptying. These mechanisms make incretin-based therapies highly effective in improving glycemic control while minimizing the risk of hypoglycemia, offering an important alternative to traditional oral antidiabetic agents.

### Discussion

Two main classes of incretin-based therapies are currently in clinical use: GLP-1 receptor agonists (GLP-1 RAs) and dipeptidyl peptidase-4 (DPP-4) inhibitors. GLP-1 RAs, such as exenatide and liraglutide, mimic the effects of endogenous GLP-1 by activating GLP-1 receptors on pancreatic beta cells and other tissues. These agents enhance glucose-stimulated insulin secretion, suppress inappropriate glucagon secretion, delay gastric emptying, and promote satiety, often resulting in weight loss. GLP-1 RAs also exhibit cardiovascular benefits, reducing major adverse cardiovascular events in patients with established cardiovascular disease.

DPP-4 inhibitors, including sitagliptin and linagliptin, act by inhibiting the enzyme dipeptidyl peptidase-4, which rapidly degrades endogenous GLP-1 and GIP. By prolonging the half-life of these incretin hormones, DPP-4 inhibitors improve postprandial insulin secretion and reduce glucagon levels without causing significant weight change. They are generally well-tolerated and have a low risk of hypoglycemia, making them suitable for combination therapy with other antidiabetic agents.

Incretin-based therapies are particularly advantageous in patients with obesity, cardiovascular risk, or renal impairment. They provide dual benefits of glycemic control and weight management, while also offering organ-protective effects. However, these therapies

are not without limitations. GLP-1 receptor agonists may cause gastrointestinal side effects such as nausea and vomiting, and their injectable route can limit adherence. DPP-4 inhibitors are generally less potent in glycemic reduction compared to GLP-1 RAs, and long-term data on rare adverse effects continue to be monitored.

### Conclusion

Incretin-based therapies represent a paradigm shift in the management of type 2 diabetes, targeting physiological mechanisms to improve glucose homeostasis while minimizing hypoglycemia. GLP-1 receptor agonists and DPP-4 inhibitors offer distinct but complementary benefits, including improved insulin secretion, glucagon suppression, weight reduction, and cardiovascular protection. As research continues, these therapies hold promise for personalized diabetes management, optimizing treatment efficacy and safety while addressing comorbid metabolic and cardiovascular risks.

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