STM JOURNALS

Research & Reviews: A Journal of
Pharmacology

ISSN: 2321-2810
Volume 16, Issue 1, 2026
January–April
DOI (Journal): 10.37591/RRJoP

https://journals.stmjournals.com/rrjop

Review RRJoP

GLP-1 Receptor Agonists: A Dual Therapeutic Strategy for the Management of Type 2 Diabetes Mellitus and Obesity

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Abstract

For the treatment of obesity and type 2 diabetes mellitus (T2DM), glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have become a revolutionary class of pharmaceutical drugs. These drugs were first created as glucose-lowering treatments, but they have now shown other advantages, such as notable weight loss, better cardiovascular results, and general metabolic control. The objective of this narrative review is to assess the pharmacological mechanisms, clinical efficacy, safety profile, and therapeutic implications of GLP-1 receptor agonists, with a focus on their dual role in the management of obesity and diabetes. Randomized controlled trials, meta-analyses, and clinical guidelines published between 2010 and 2025 were all included in the extensive literature search that was carried out utilizing electronic databases like PubMed, Scopus, and Web of Science. There is evidence that GLP-1 RAs lead to sustained weight loss via improving glycemic control through glucose-dependent insulin secretion, delayed stomach emptying, and increased satiety. Moreover, significant clinical trials have shown decreases in mortality and cardiovascular events. These drugs are usually well tolerated, despite the frequent occurrence of moderate gastrointestinal side effects. In conclusion, GLP-1 receptor agonists offer a comprehensive strategy for successfully controlling type 2 diabetes and obesity and constitute a paradigm change in the treatment of metabolic illnesses.

Keywords: GLP-1 receptor agonists; Type 2 diabetes mellitus; Obesity; Semaglutide; Liraglutide; Pharmacotherapy; Clinical pharmacy

INTRODUCTION

Obesity and type 2 diabetes mellitus (T2DM) are long-term, progressive metabolic illnesses that pose severe hazards to public health. The International Diabetes Federation estimates that over 537 million people worldwide suffer from diabetes, with type 2 diabetes accounting for over 90% of cases. Obesity has become an epidemic on a global scale and is a significant risk factor for heart disease, type 2 diabetes, and many types of cancer (1-8).

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Received Date: March 22, 2026
Accepted Date: April 04, 2026
Published Date: April 05, 2026

Citation: Darshan G., Hamsa Priya M., Bharath B. GLP-1 Receptor Agonists: A Dual Therapeutic Strategy for the Management of Type 2 Diabetes Mellitus and Obesity. Research & Reviews: A Journal of Pharmacology. 2026; 16(1): 69–75p.

Even though conventional Antidiabetics medications like insulin and sulfonylureas effectively lower blood glucose levels, their adverse effects – such as weight gain and hypoglycemia – often make long-term adherence challenging. Treatments that address both glycemic control and weight management have consequently undergone a paradigm shift.

Endogenous GLP-1, an incretin hormone involved in glucose homeostasis and appetite regulation, is mimicked by glucagon-like peptide-1 receptor agonists (GLP-1 RAs). GLP-1 RAs have proven to be quite successful in enhancing glycemic control, encouraging weight loss, and lowering cardiovascular

risk during the last ten years, according to a wealth of clinical data. This review seeks to give a complete and structured examination of GLP-1 receptor agonists, focusing on their pharmacology, clinical results, and contribution to advancing knowledge in diabetes and obesity management. Obesity and type 2 diabetes mellitus (T2DM) are two of the most urgent global public health issues of the twenty-first century. The World Health Organization reports that while the prevalence of diabetes is continuously increasing worldwide, the prevalence of obesity has almost tripled since 1975 (7, 9, 10) (Figure1).

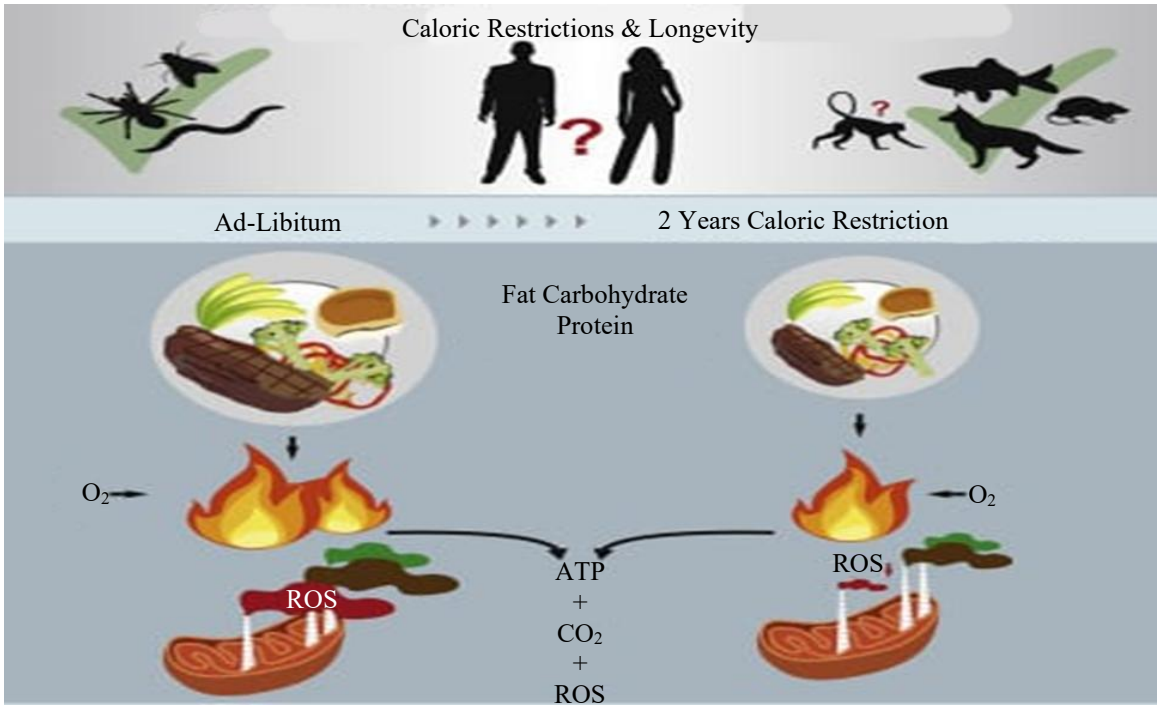

Figure 1. Impact of caloric restriction on oxidative stress, metabolic substrate utilization, and longevity.

These disorders often combine and work together to raise the risk of chronic renal disease, cardiovascular disease, and early death.

The main goal of traditional Antidiabetics treatments like insulin and sulfonylureas is to lower blood sugar levels, but they frequently cause weight gain and hypoglycemia, which makes long-term adherence difficult. The development of incretin-based medications has been prompted by the need for treatments that address both hyperglycemia and excess body weight (11-15).

Due to their glucose-dependent insulin secretion, appetite control, and positive cardiovascular effects, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have become a groundbreaking family of medications. GLP-1 RAs have become essential parts of contemporary diabetes and obesity therapy algorithms during the last ten years thanks to a wealth of clinical trial data and real-world research. Obesity and type 2 diabetes mellitus are two interconnected worldwide health issues that greatly increase morbidity, mortality, and healthcare costs. The prevalence of T2DM has risen substantially during the past three decades, paralleling the global obesity pandemic. Conventional Antidiabetics treatments frequently ignored weight control and cardiovascular risk in favor of glycemic control.

Diabetes treatment underwent a paradigm shift with the development of incretin-based treatments. Among these, GLP-1 receptor agonists have become more well-known because of their benefits for weight loss, good cardiovascular outcomes, and glucose-dependent insulin tropic actions. GLP-1 RAs have recently been approved as treatments for long-term weight control, including in people without diabetes, going beyond their initial indication (Figure2).

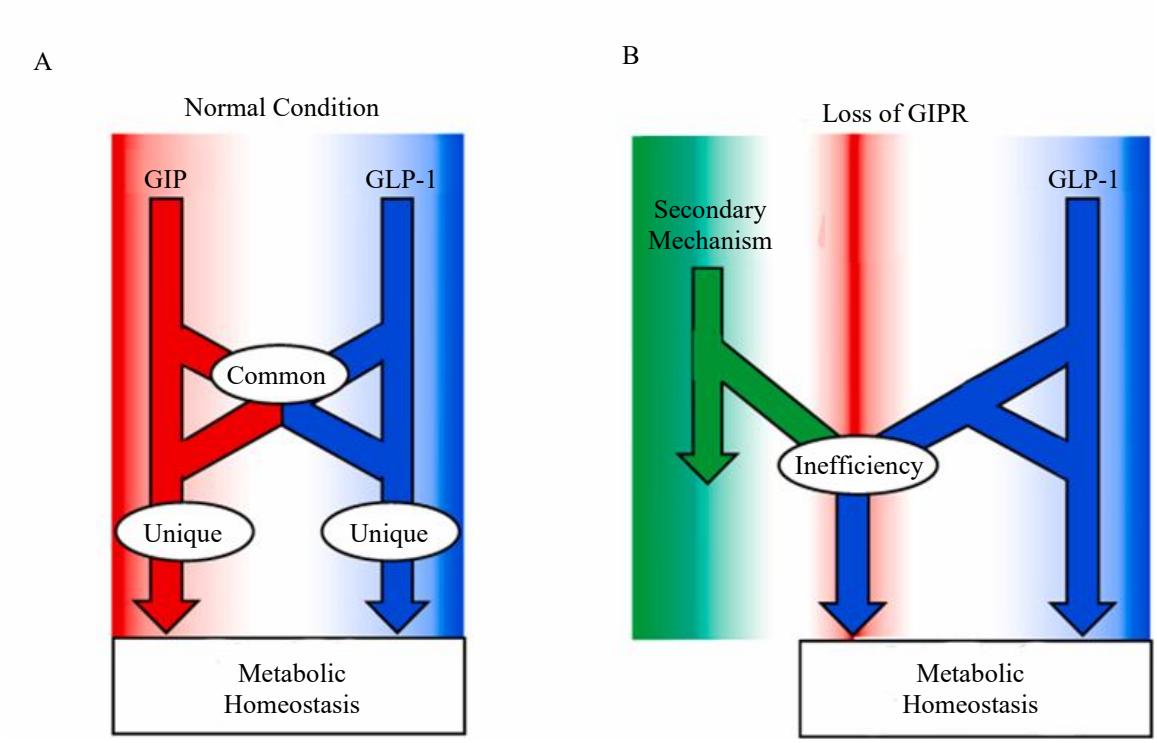

Figure 2. Metabolic inefficiency resulting from compensation.

This review aims to give an in-depth, publication-ready overview of GLP-1 receptor agonists, concentrating on their pharmacology, clinical efficacy, safety, and future developments, with special emphasis on the role of pharmacists in optimizing therapy.

METHODOLOGY

Design of the Study

This review was carried out as a thorough narrative analysis of published literature with an emphasis on the function of GLP-1 receptor agonists in the treatment of obesity and type 2 diabetes.

Data Sources

A thorough search was conducted for pertinent articles published between January 2010 and December 2025 using electronic databases such as PubMed, Scopus, Web of Science, and Google Scholar.

Method of Searching

"GLP-1 receptor agonists, " "type 2 diabetes mellitus, " "obesity, " "semaglutide, " "liraglutide, " "cardiovascular outcomes, " and "weight management" was among the keywords utilized. The search was narrowed down using Boolean operators.

Inclusion Criteria

- Controlled, randomized trials.
- Meta-analyses and systematic reviews.
- Real-world and observational research.

Exclusion Criteria

- Case reports.
- Opinions and editorials.
- Non-human research.

Study Selection and Data Extraction

A full-text review was conducted after pertinent papers were filtered by title and abstract. Study design, sample size, intervention specifics, results, and important conclusions were among the data that were retrieved.

Data Analysis

Qualitative synthesis was done using data from chosen research. Clinical outcomes were evaluated between studies, including HbA1c decrease, changes in body weight, cardiovascular events, and side effects. A narrative synthesis approach was used in place of quantitative meta-analysis due to the heterogeneity in study designs.

DETAILED ANALYSIS OF RESULTS

Expanded Analysis of Landmark Clinical Trials

LEADER Trial (Liraglutide)

Over 9, 300 individuals with type 2 diabetes mellitus at high cardiovascular risk were included in the LEADER trial, a multicenter, randomized, double-blind, placebo-controlled cardiovascular outcomes study. In addition to normal therapy, participants got either a placebo or liraglutide. The primary composite outcome was the first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [2].

The liraglutide group significantly reduced their relative risk of major adverse cardiovascular events (MACE) by 13% when compared to the placebo group. Liraglutide was also linked to decreased all-cause mortality, mild weight loss, and long-term HbA1c reduction. Liraglutide was one of the first glucose-lowering medications with a shown cardiovascular benefit, according to these studies [11–15].

SUSTAIN Clinical Trial Program (Semaglutide)

A number of phase III randomized controlled trials assessing the safety and effectiveness of once-weekly semaglutide in individuals with type 2 diabetes comprised the SUSTAIN program. Semaglutide continuously showed better reductions in HbA1c and body weight when compared to placebo and active comparators like insulin glargine and sitagliptin across the SUSTAIN-1 to SUSTAIN-10 trials [3].

A significant decrease in nonfatal stroke and total cardiovascular risk was found in the cardiovascular outcomes trial SUSTAIN-6. Semaglutide-treated patients obtained HbA1c reductions of up to 1.8% and weight loss reaching 10% in some study populations.

Semaglutide in Obesity: The STEP Clinical Trial Program

The STEP (Semaglutide Treatment Effect in People with Obesity) trials assessed semaglutide 2.4 mg once weekly in individuals with obesity, with and without type 2 diabetes. Over the course of 68 weeks, STEP-1 showed a mean weight decrease of 14.9% from baseline, far surpassing placebo.

Improvements in waist circumference, blood pressure, lipid profiles, and quality of life were verified by later STEP trials. GLP-1 receptor agonists are now the first-line treatments for long-term weight control thanks to these trials, which represented a paradigm change in obesity pharmacology “The key findings of these major clinical trials are summarized in (Table 1).”

Table 1. Summary of major landmark trials.

Trial	Drug	Population	Primary outcome	Key findings
Leader mortality	Liraglutide	T2DM + CVD	MACE	↓ CV death, ↓ all-cause mortality.
SUSTAIN 6	Semaglutide	T2DM	CV safety	↓ nonfatal stroke.
STEP 1 reduction	Semaglutide 2.4 mg	Obesity	Weight loss	~15% mean weight reduction.

Analysis of Comparative Effectiveness

Insulin vs. GLP-1 Receptor Agonists

GLP-1 receptor agonists offer similar or better glycemic control with a lower risk of hypoglycemia and substantial weight reduction when compared to basal insulin therapy. GLP-1 RAs and basal insulin combination therapy have demonstrated synergistic benefits that improve glycemic results while reducing insulin-associated weight gain.

GLP-1 Receptor Agonists versus SGLT2 Inhibitors

GLP-1 RAs had better results on weight loss and postprandial glucose management, but SGLT2 inhibitors provide advantages for the heart and kidneys. In order to optimize the cardiometabolic benefit, current guidelines increasingly suggest combination therapy.

Analysis of Adverse Effects and Safety

Effects on the Digestive System

The most often reported side effects include dose-dependent nausea, vomiting, and diarrhea. Tolerability is greatly enhanced by gradual dose titration.

Gallbladder Disease and Pancreatitis

Acute pancreatitis and gallbladder illness have been documented, however they are uncommon. Although there is currently insufficient evidence to demonstrate a clear causal association, clinical caution is advised "The common adverse effects and their management are presented in (Table 2)."

Table 2. Common adverse effects of GLP-1 receptor agonists.

Adverse effect	Frequency	Clinical management
Nausea	Common	Dose titration, dietary Counseling.
Vomiting	Moderate	Temporary dose reduction.
Hypoglycemia	Rare	Monitor with insulin/sulfonylureas.

Safety of the Thyroid

Human data have not supported the higher incidence of C-cell malignancies found in rodent research. Patients with a history of medullary thyroid cancer should not take GLP-1 RAs.

"The comparative cardiometabolic benefits of GLP-1 receptor agonists are illustrated in (Figure 3)."

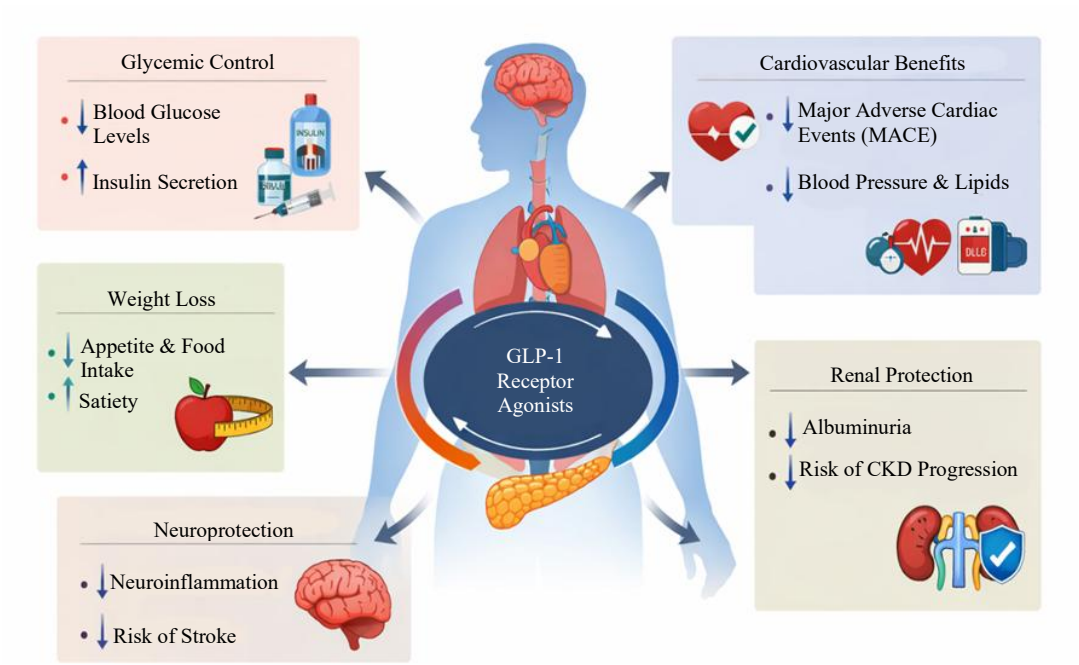

Figure 3. Comparative cardiometabolic benefits of GLP-1 Ras.

IMPROVEMENT OF STATE OF KNOWLEDGE

By providing an integrated assessment of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) as dual-purpose treatment agents for type 2 diabetes mellitus and obesity, this review adds to the body of existing literature. This paper highlights the interrelated pathophysiology of diabetes and obesity and shows how GLP-1 receptor agonists concurrently address hyperglycemia, excess body weight, and metabolic dysfunction, in contrast to previous evaluations that only concentrated on glycemic results. This study supports the emerging role of GLP-1 RAs as complete cardiometabolic therapy rather than just glucose-lowering medicines by combining data from seminal cardiovascular and obesity trials.

Additionally, by combining data on cardiovascular and renal outcomes related to GLP-1 receptor agonist medication, this review increases our understanding. The long-term advantages of these medications in lowering major adverse cardiovascular events, all-cause mortality, and obesity-related comorbidities are made clear by the inclusion of significant cardiovascular outcome trials like LEADER, SUSTAIN-6, and STEP. This combined analysis strengthens evidence-based clinical decision-making by supporting current guidelines that prioritize GLP-1 receptor agonists in individuals with obesity and high cardiovascular risk.

Lastly, by comparing GLP-1 receptor agonists with other Antidiabetics treatments and highlighting the role of clinical pharmacists in improving treatment outcomes, this review emphasizes the practical and therapeutic value of these drugs. This work bridges the gap between clinical trial evidence and practical application by addressing safety concerns, adherence issues, and combination therapy approaches. This contribution highlights the growing use of GLP-1 receptor agonists in contemporary clinical practice and is especially helpful in promoting interdisciplinary, patient-centered approaches to metabolic illness care.

SUMMARY AND CONCLUSION

Obesity and type 2 diabetes mellitus are closely related metabolic conditions that greatly raise the risk of heart disease, kidney problems, and early death. Glycemic control has been the main emphasis of traditional Antidiabetics treatments, frequently ignoring weight control and long-term cardiovascular risk. Because they target several aspects of metabolic disorder at once, glucagon-like peptide-1 receptor agonists have become a significant therapeutic development.

GLP-1 receptor agonists provide effective glycemic control, clinically relevant and sustained weight loss, and significant reductions in cardiovascular events, according to data from major randomized controlled trials and real-world research. Their glucose-dependent mode of action reduces the risk of hypoglycemia, and other advantages including delayed stomach emptying and appetite suppression enhance metabolic results. In individuals with type 2 diabetes and obesity, these medications have also demonstrated positive benefits on the kidneys and enhanced quality of life.

In conclusion, GLP-1 receptor agonists are a paradigm change in the treatment of obesity and type 2 diabetes. Their early and increased usage in clinical practice is supported by their dual efficacy, good safety profile, and cardiometabolic advantages. The standard of care for metabolic illnesses can be redefined and long-term outcomes greatly improved by incorporating GLP-1 receptor agonists into customized, interdisciplinary treatment plans.

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