World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 1
Page: 898-902

REVIEW OF SEMAGLUTIDE: AN OVERVIEW AND MECHANISM OF ACTION

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Article Received: 16 January 2025 | | Article Revised: 05 February 2025 | | Article Accepted: 27 February 2025

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DOI: https://doi.org/10.5281/zenodo.14966425

How to cite this Article: D. Bharathi, N. Deepa, J. Jaisudha, D. Gnanasekaran and T. Devi (2025). REVIEW OF SEMAGLUTIDE: AN OVERVIEW AND MECHANISM OF ACTION. World Journal of Pharmaceutical Science and Research, 4(1), 898-902. https://doi.org/10.5281/zenodo.14966425

ABSTRACT

A revolutionary treatment for type 2 diabetes mellitus (T2DM) and obesity is semaglutide, an agonist of the glucagon-like peptide-1 (GLP-1) receptor. Semaglutide was first created for glycemic management, but it has shown significant weight loss effectiveness, especially at higher dosages, making it a dual-purpose drug. Glycated hemoglobin (HbA1c), fasting plasma glucose levels, and body weight have all been demonstrated to significantly decrease in T2DM patients in clinical trials. Likewise, semaglutide promotes significant weight loss in non-diabetic individuals that are overweight or obese; in long-term studies, participants saw reductions of up to 17% of their starting body weight. It works by imitating endogenous GLP-1, which increases insulin secretion, postpones stomach emptying, and decreases hunger via pathways in the central nervous system. Although semaglutide is usually well tolerated, temporary gastrointestinal problems such nausea and diarrohea are frequent side effects. Careful patient selection and monitoring are necessary for uncommon but major side effects such pancreatitis and gallbladder disease. Evidence of better cardiovascular outcomes in high-risk populations supports semaglutide's usage in lowering cardiovascular risk, demonstrating its flexibility. Its effectiveness and good safety record highlight its potential as a mainstay treatment for metabolic diseases. In order to firmly establish semaglutide's place in contemporary pharmacotherapy, future studies will investigate long-term effects and innovative uses.

KEYWORDS: Semaglutide, glucagon-like peptide-1, Glycated hemoglobin (HbA1c), insulin, pancreatitis.

INTRODUCTION

A glucagon-like peptide-1 (GLP-1) receptor agonist, semaglutide was first created to treat type 2 diabetes mellitus (T2DM) before being authorized to treat chronic weight loss in people with obesity or overweight disorders. Its dual effectiveness in glycemic management and significant weight loss made its launch a major breakthrough in metabolic treatment. Numerous clinical trials have assessed semaglutide, showing that it can improve body weight, fasting glucose levels, and glycated hemoglobin (HbA1c) levels in addition to offering other cardiovascular advantages. Semaglutide works pharmacologically by imitating endogenous GLP-1, a hormone that increases glucose-dependent insulin secretion, inhibits glucagon release, slows stomach emptying, and controls hunger through pathways in the central nervous system. In order to achieve the clinical results seen in both diabetes patients, these combined effects have been essential. **(Wilding et al., 2021; Davies et al., 2021).**

Despite its relatively good tolerance, semaglutide can cause short-term gastrointestinal adverse effects like nausea, vomiting, and diarrhea, which usually go away with prolonged use. There have been reports of uncommon but dangerous side effects, like pancreatitis and gallbladder illness, which need for close patient observation **(Rubino et al., 2021).**

Semaglutide has emerged as a key treatment for these related disorders as obesity and type 2 diabetes become more common worldwide. Its effectiveness and good safety record highlight how crucial it is to tackling the escalating problems with metabolic health.

Semaglutide's Mode of Action

A glucagon-like peptide-1 (GLP-1) receptor agonist, semaglutide simulates the actions of endogenous GLP-1, a hormone implicated in appetite regulation and glucose management. Its effectiveness in glycemic control and weight management is attributed to a number of routes in its mechanism of action:

1. Induction of Insulin Secretion Dependent on Glucose Semaglutide increases glucose-dependent insulin production by binding to GLP-1 receptors on pancreatic beta cells. This lowers the risk of hypoglycemia by only taking place when blood glucose levels are high (Nauck et al., 2016).
2. Glucagon Secretion Inhibition Semaglutide inhibits the release of glucagon via interacting with the pancreatic alpha cells. This suppression lowers fasting and postprandial glucose levels because glucagon ordinarily increases hepatic glucose synthesis (Drucker et al., 2017).
3. Postponement of Gastric Emptying by slowing stomach emptying, semaglutide lowers the rate at which nutrients are absorbed and lessens the impact of postprandial glucose increases (Meier, 2012). Additionally, this action prolongs satiety.
4. The Central Nervous System Regulates Appetite Semaglutide works on GLP-1 receptors in the hypothalamus, a crucial region for hunger regulation, after crossing the blood-brain barrier. Hunger, calorie intake, and total body weight are all decreased by this action (Blundell et al., 2017).
5. Impact on the Heart in high-risk groups, semaglutide has demonstrated cardiovascular benefits, such as a decrease in major adverse cardiovascular events (MACE). Reduced inflammation, better glycemic management, and weight loss could all contribute to these outcomes (Marso et al., 2016).

Pharmacokinetics

Semaglutide has a half-life of roughly 165 hours and is designed to be administered subcutaneously once a week. Its prolonged action enables consistent therapeutic benefits and long-lasting GLP-1 receptor activation (Kapitza et al., 2015).

Safety Procedures for Semaglutide

A common glucagon-like peptide-1 (GLP-1) receptor agonist used to treat type 2 diabetes and obesity is semaglutide. Although it is usually well accepted, its safety profile needs to be closely watched, especially in patients who are prone to certain side effects or have pre-existing medical issues. The following are the main safety factors for semaglutide:

1. Typical Side Effects Gastrointestinal (GI) symptoms are the adverse events that are most commonly reported: Especially in the first several weeks of treatment, nausea, vomiting, diarrhea, constipation, and abdominal pain are frequent side effects. These effects are often temporary and dose-dependent.
2. Risk of Pancreatitis: Semaglutide and other GLP-1 receptor agonists have been linked to a small number of acute pancreatitis cases. Patients having a history of pancreatitis should be monitored.
3. Disease of the Gallbladder: There has been evidence of an elevated risk of gallbladder-related complications, such as gallstones (cholelithiasis) and gallbladder inflammation (cholecystitis). This could be related to the quick weight loss that semaglutide causes.
4. C-cell tumors of the thyroid: Although this risk has not been verified in humans, semaglutide has been linked in animal studies to an increased risk of thyroid C-cell cancers. Semaglutide should not be used by patients who have a personal or family history of multiple endocrine neoplasia syndrome type 2 (MEN2) or medullary thyroid cancer (MTC).
5. Low blood sugar: Because semaglutide secretes insulin through a glucose-dependent mechanism, it has a low intrinsic risk of hypoglycemia. However, the risk of hypoglycemia rises when used with insulin or sulfonylureas, requiring the co-administered medicines' doses to be changed.
6. Impairment of Renal Function: There have been isolated reports of acute kidney injury (AKI), mostly as a result of dehydration brought on by severe gastrointestinal adverse effects. Individuals who already have kidney disease should be properly watched.
7. Cardiovascular Safety: Studies have shown that semaglutide lowers major adverse cardiovascular events (MACE) in people with type 2 diabetes who are at high cardiovascular risk. One such study is the SUSTAIN-6 trial.

An analysis of semaglutide

The effectiveness and safety of semaglutide, an agonist of the glucagon-like peptide-1 (GLP-1) receptor, in the treatment of type 2 diabetes and obesity have been thoroughly examined. A selection of noteworthy review papers and studies is provided below:

1. "Semaglutide for the treatment of overweight and obesity: A review" The effectiveness of semaglutide 2.4 mg in causing notable weight loss in people without type 2 diabetes is examined in this study, which also highlights findings from the STEP clinical trial program.
2. "Efficacy of Semaglutide in Treating Obesity: A Systematic Review of Randomized Controlled Trials" This systematic review suggests that semaglutide is safe and effective for treating obesity, with gastrointestinal problems being the most common side effects.

3. "Safety of Semaglutide" This review focuses on semaglutide's adverse events, such as hypoglycemia, gastrointestinal side effects, and potential dangers to pancreatic and thyroid function.
4. "Once-Weekly Semaglutide in Adults with Overweight or Obesity" This study found that taking 2.4 mg of semaglutide once a week, along with lifestyle changes, resulted in long-term, clinically significant weight loss.
5. "Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial" This study shows that semaglutide medication causes significant, long-term weight loss in persons who are overweight or obese after 104 weeks.
6. "Efficacy and safety of semaglutide 2.4 mg for weight loss in patients with overweight or obesity: a systematic review and meta-analysis"

According to this meta-analysis, semaglutide provides a spectacular and long-lasting weight loss effect that is well-tolerated and safe in overweight or obese non-diabetics.

These evaluations underline semaglutide's strong impact on weight management and glycemic control, as well as its safety profile, reinforcing its position in the treatment of obesity and type 2 diabetes.

CONCLUSION

Semaglutide is a highly effective treatment for type 2 diabetes and obesity, with considerable improvements in glycemic control, weight loss, and cardiovascular risk reduction. Its mechanism of action as a GLP-1 receptor agonist enables it to treat both the metabolic and behavioral aspects of these diseases.

Clinical investigations and systematic reviews repeatedly indicate its efficacy:

- For Type 2 Diabetes, semaglutide can improve HbA1c readings, lower fasting and postprandial glucose, and reduce hypoglycemia when administered correctly.
- Semaglutide is a highly successful treatment for obesity, especially at larger doses, resulting in significant and persistent weight loss.
- Cardiovascular Health: It reduces the risk of major adverse cardiovascular events (MACE) for high-risk individuals.
- Despite these benefits, semaglutide has several safety issues that need to be addressed
- Common adverse effects include nausea and vomiting, which are dose-dependent and usually temporary.
- Rare but severe dangers include pancreatitis, gallbladder illness, and thyroid C-cell malignancies.
- Use with caution in those with pancreatitis, thyroid cancer, or severe gastrointestinal disorders.

Semaglutide offers a significant development in the treatment of chronic metabolic illnesses, providing both improved health outcomes and weight management. Ongoing research and real-world evidence are anticipated to refine its use and strengthen its position as a cornerstone therapy in the management of obesity and type 2 diabetes.

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