Tirzepatide

By MSc Student

Mazin Wafi Abdulrazzaq

15 April 2025

Overview

- Diabetes and obesity are chronic diseases leading to substantial morbidity and high mortality worldwide, especially in developed countries. They are considered the twin epidemics of the21st century. Neither disorder is a simple problem; rather, both are complex health issues combining genetic, epigenetic, and lifestyle factors, including socioeconomic and environmental impacts

Overview

- Type 2 diabetes happens when the body cannot use insulin correctly and sugar builds up in the blood. It was once called adult-onset diabetes.
- **Causes**
- Type 2 diabetes is mainly the result of two issues:

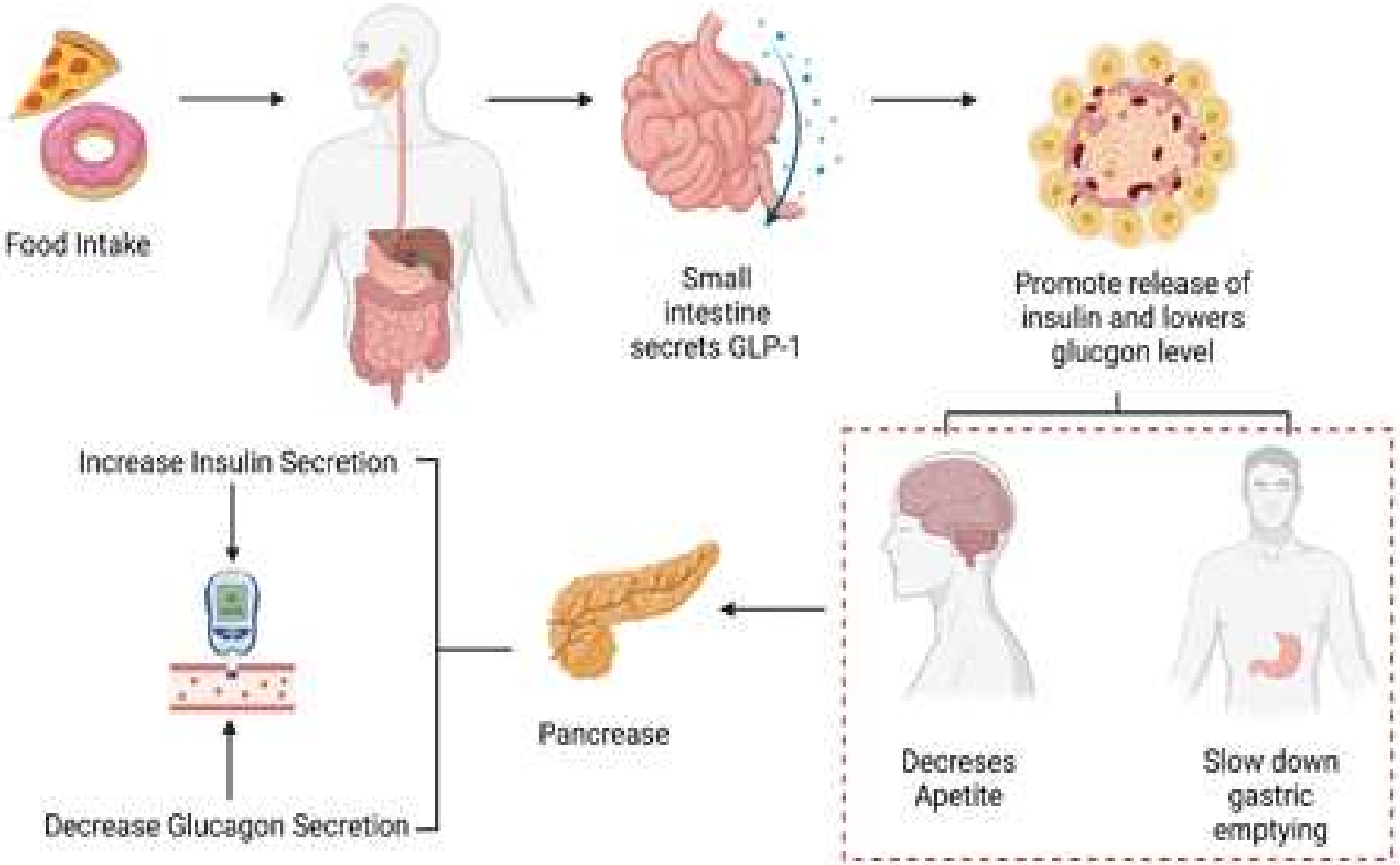
- Cells in muscle, fat and the liver don't respond to insulin as they should. As a result, the cells don't take in enough sugar.
- The gland that makes insulin, called the pancreas, can't make enough to keep blood sugar levels within a healthy range.

Overview

- Treatment of T2D includes lifestyle changes such as diet, exercise, and nutraceuticals, as well as administration of medications such as metformin. Various synthetic moieties and herbal preparations have been developed to support the functioning of beta cells and suppress harmful inflammatory responses. The majority of these agents have unwanted effects pertaining to the route of administration and various other factors.

Overview

- Products generated in the human body that stimulate beta cells to release insulin, termed as ‘Incretins’, also known as ‘Incretin hormones’, were discovered in the early 1970s. These products are secreted in the intestine, affecting the functioning of beta cells (Figure 1). The most commonly known incretins include glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)


Food Intake
Small intestine secrets GLP-1
Promote release of insulin and lowers glucgon level
Decreses Apetite
Slow down gastric emptying
Pancrease
Increase Insulin Secretion
Decrease Glucagon Secretion

Tirzepatide

- Tirzepatide is a synthetic linear peptide molecule containing 39 amino acids. Residues derive from GLP-1, GIP and semaglutide
- Tirzepatide is as the first dual GLP-1 and GIP receptor agonist as a promising therapeutic agent for the treatment of either diabetes or obesity and to highlight its superiority to other similar agents.

Tirzepatide (Mounjaro)

- Used for type 2 diabetes to help improve blood sugar levels. In type 2 diabetes, tirzepatide decreases blood sugar levels by helping release insulin when blood sugar levels are high, lowering the amount of sugar the liver makes, and slowing food movement through the intestines. Mounjaro should be used together with diet and exercise.

Tirzepatide (Zepbound brand)

- Used for weight loss, to help lose weight and keep weight off. Tirzepatide works for weight loss by decreasing appetite and slowing the movement of food from the stomach into the small intestine, which may make you feel full more quickly and for a longer period. The Zepbound brand of tirzepatide is also used for moderate to severe obstructive sleep apnea (OSA) in adults with obesity. Tirzepatide is a once-weekly injection given under the skin using a pen (autoinjector).

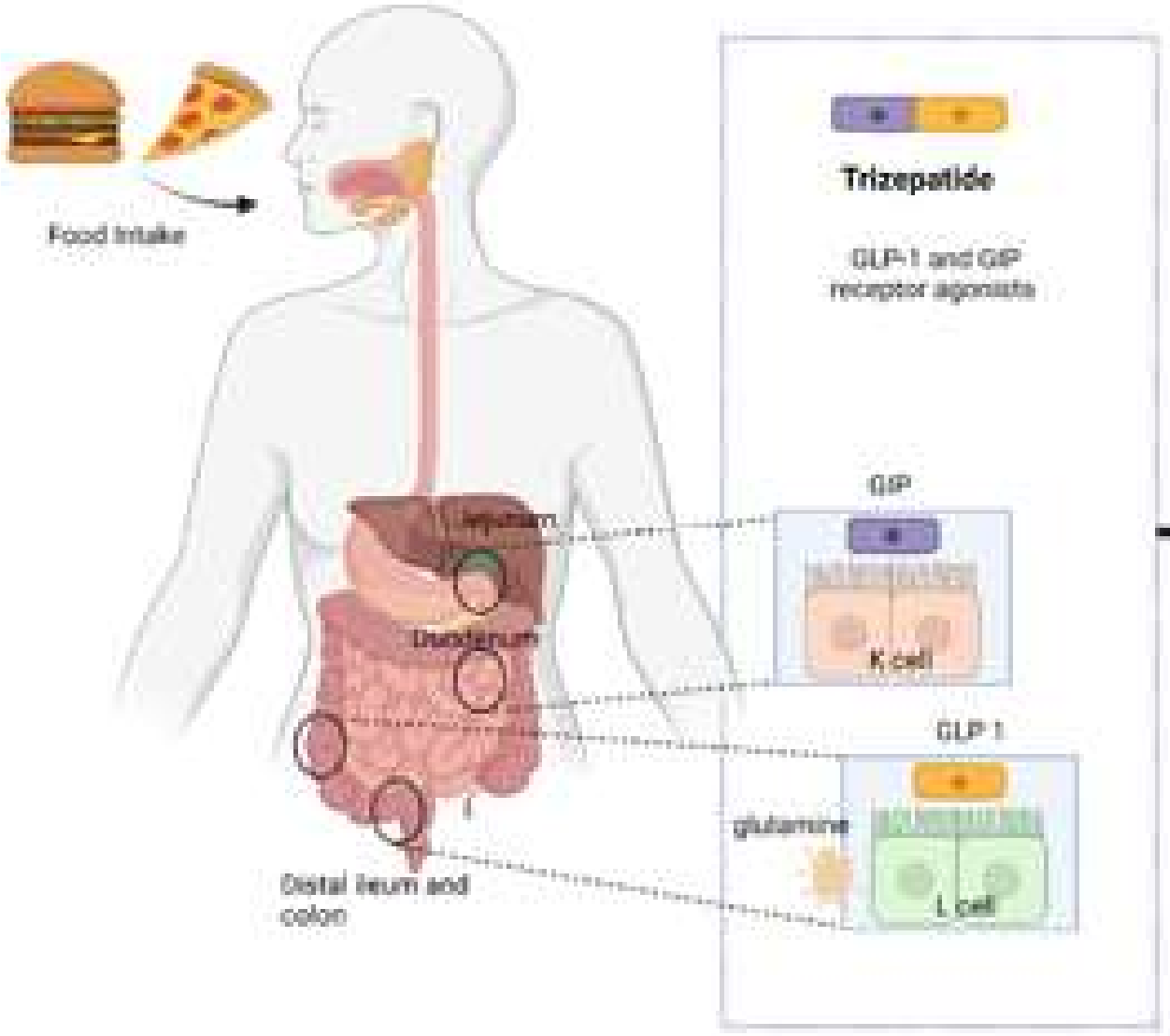

mounjaro™
(tirzepatide) injection
15 mg 0.5 mL
mounjaro™
(tirzepatide) injection
10 mg 0.5 mL
mounjaro™
(tirzepatide) injection
5 mg 0.5 mL


2.5 mg 0.5 mL
Maintenance
5 mg 0.5 mL
7.5 mg 0.5 mL
Maintenance
10 mg 0.5 mL
12.5 mg 0.5 mL
Maintenance
15 mg 0.5 mL
zepbound
NEEDLE END

Mechanism of action

- Normally, when we eat, natural hormones called GIP and GLP-1 are released by the gut. These hormones increase insulin release, suppress appetite, slow gastric emptying, and increase the feeling of fullness. Tirzeptide works like our natural hormones GIP and GLP-1 by activating the GIP and GLP-1 receptors.

- Tirzepatide is a GIP and GLP-1 receptor agonist. Tirzepatide works (mechanism of action) by activating both GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) hormone receptors.



Decrese Food Intake

Decrese Appetite

Increase Weight Loss

Increases insuling secretion and Synthesis

Increase Lipolysis (GLP-1)

Increase Lipogenesis (GIP)

Increase beta cell survival

Increase cardioprotection (GLP-1)

Decrease Bone reabsorption (GIP)

Dose

Type 2 Diabetes Mellitus

Mounjaro only

- Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- 2.5 mg SC qWeek x 4 weeks initially; THEN increase to 5 mg SC qWeek
- If additional glycemic control needed, increase by 2.5-mg increments after at least 4 weeks at current dose
- Maximum dose: 15 mg SC qWeek
- Note: 2.5-mg dose is intended for treatment initiation and is not effective for glycemic control

Weight Management

- Zepbound only

Initial dose

- Initiate with low dose and gradually escalate to maintenance dose of 2.5 mg/week SC to minimize GI adverse reactions
- Note: 2.5-mg dose is intended for treatment initiation and not for chronic weight management

Maintenance dose

- After 4 weeks, increase to 5 mg SC qWeek
- May increase in 2.5-mg increments, after at least 4 weeks on current dose
- Recommended maintenance dosages are 5 mg, 10 mg, or 15 mg SC qWeek
- Consider treatment response and tolerability when selecting maintenance dosage
- If maintenance dosage not tolerated, consider lower maintenance dosage

Common tirzepatide side effects

- The most common tirzepatide side effects include abdominal pain, burping, constipation, diarrhea, dyspepsia, fatigue, gastroesophageal reflux disease, hair loss, hypersensitivity reactions, injection site reactions, nausea, and vomiting, which affects 5% or more patients.

Side effects

- The adverse drug reaction profile of tirzepatide is comparable to GLP-1 agonists, as it is a dual GIP/GLP-1 agonist. The most common side effects associated with tirzepatide are related to gastrointestinal tract like nausea, vomiting and diarrhea . The incidence of hypoglycemia is low, based on phase 2 trials.

Serious tirzepatide side effects

- Serious tirzepatide side effects include severe stomach problems, acute kidney damage, gallbladder disease, inflamed pancreas (acute pancreatitis), serious allergic reactions, low blood sugar levels (hypoglycemia), diabetic retinopathy issues in type 2 diabetics, suicidal behavior or thoughts, and food or liquid getting into the lungs during anesthesia or deep sedation.
- Stop using this medicine and get emergency medical help if you have:
- Signs of an allergic reaction: hives; difficulty breathing; feeling light-headed; swelling of your face, lips, tongue, or throat; or
- Pancreatitis with symptoms of severe pain in your upper stomach spreading to your back, nausea, and vomiting.

Contraindications

- Tirzepatide is contraindicated in patients with medullary thyroid cancer. Tirzepatide is also contraindicated in multiple endocrine neoplasia syndrome type-2 (MEN-2). For further information, refer to the boxed warning below. Furthermore, the use is contraindicated in patients with known severe hypersensitivity to tirzepatide or any excipients, as it has been associated with severe hypersensitivity reactions, including anaphylaxis and angioedema.In patients who have experienced angioedema or anaphylaxis due to GLP-1 receptor agonists, it is important to use tirzepatide cautiously.

Tirzepatide vs Semaglutide in DM

- A study about Subcutaneously administered tirzepatide vs semaglutide for adults with type 2 diabetes showed that s.c. tirzepatide had a more pronounced effect on HbA1c and weight reduction compared with s.c. semaglutide in people with type 2 diabetes. Both drugs, particularly higher doses of tirzepatide, increased gastrointestinal adverse events.

Tirzepatide vs Semaglutide in obesity

- Another study about Semaglutide vs Tirzepatide for Weight Loss in Adults With Overweight or Obesity showed that individuals with overweight or obesity treated with Tirzepatide were significantly more likely to achieve clinically meaningful weight loss and larger reductions in body weight compared with those treated with semaglutide

Tirzepatide vs Semaglutide

- A systematic review of Phase 3 clinical trials to compare efficacy and safety of Semaglutide 2.4 mg and Tirzepatide 5–15 mg in obesity with or without type 2 diabetes showed that Tirzepatide 10 and 15 mg appear to cause additional weight loss and HbA1c reduction with less frequent GI side effects compared with semaglutide 2.4 mg in people with obesity with or without T2D. Only an appropriately powered head-to-head randomized trial comparing semaglutide 2.4 mg and tirzepatide 5, 10, and 15 mg in people with obesity with or without T2D can conclusively answer the superiority or non-inferiority of either agent. To this end, the final results from the recently concluded

References

1- Frias, J.P.; Nauck, M.A.; Van, J.; Kutner, M.E.; Cui, X.; Benson, C.; Urva, S.; Gimeno, R.E.; Milicevic, Z.; Robins, D.; et al. Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: A randomised, placebo-controlled and active comparator-controlled phase 2 trial. Lancet 2018, 392, 2180–2193. [CrossRef]

2- Frias, J.P.; Nauck, M.A.; Van, J.; Benson, C.; Bray, R.; Cui, X.; Milicevic, Z.; Urva, S.; Haupt, A.; Robins, D.A. Efficacy and tolerability of tirzepatide, a dual glucose-dependent insulinotropic peptide and glucagon-like peptide-1 receptor agonist in patients with type 2 diabetes: A 12-week, randomized, double-blind, placebo-controlled study to evaluate different dose-escalation regimens. Diabetes Obes. Metab. 2020, 22, 938–946.

3- Apostolopoulos, V.; Bojarska, J.; Chai, T.-T.; Elnagdy, S.; Kaczmarek, K.; Matsoukas, J.; New, R.; Parang, K.; Lopez, O.P.; Parhiz, H.; et al. A Global review on short peptides: Frontiers and perspectives. Molecules 2021, 26, 430. [CrossRef]

4- Nauck, M.A.; Meier, J.J. The incretin effect in healthy individuals and those with type 2 diabetes: Physiology, pathophysiology, and response to therapeutic interventions. Lancet Diabetes Endocrinol. 2016, 4, 525–536. [CrossRef]

5-Müller, T.D.; Finan, B.; Bloom, S.R.; D'Alessio, D.; Drucker, D.J.; Flatt, P.R.; Fritsche, A.; Gribble, F.; Grill, H.J.; Habaner, J.F.; et al. Glucagon-like peptide 1 (GLP-1). Mol. Metab. 2019, 30, 72–130


Thank you
for listening