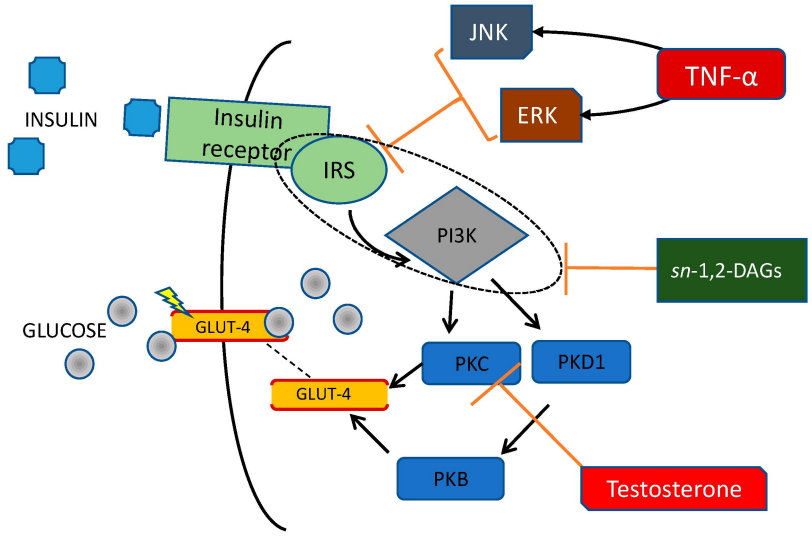

Figure 1 Alterations in the insulin receptor pathway, resulting from the activity of pro-inflammatory cytokines and androgens (Adopted from Bednarz et al., 2022)

Image caption: Tumour necrosis factor α (TNF-α) affects insulin signaling by phosphorylation of serine in insulin receptor substrate-1 (IRS-1) through activation of several serine kinases, including c-Jun-NH2-terminal kinase (JNK) and extracellular signal-regulated kinase (ERK). It inhibits insulin-induced tyrosine phosphorylation of IRS-1 and downregulates phosphoinositide 3-kinase (PI3K) activity; Decreased adiponectin concentration results in increased membrane sn-1,2-diacylglycerols (sn-1,2-DAGs) activity. It leads to impaired kinases activity and decreased insulin signaling; Testosterone induces insulin resistance in cells by affecting insulin-stimulated phosphorylation of protein kinase C (PKC); All these mechanisms contribute to decreased glucose transporter type 4 (GLUT-4) expression and decreased glucose transport into cells (Adopted from Bednarz et al., 2022)

4.2 Slow down gastric emptying and improve post-meal conditions

GLP-1 RAs can also help with weight loss by influencing gastric activity. Mainly, it slows down the speed at which food enters the small intestine from the stomach, prolongs post-meal satiety, slows down glucose absorption, and makes post-meal blood glucose changes more stable (Zhao et al., 2021; Bednarz et al., 2022; Fadel et al., 2025). Generally, short-acting GLP-1 RAs inhibits gastric emptying more significantly and controls postprandial blood glucose better. Long-acting drugs are more often used to regulate fasting blood glucose and maintain overall blood glucose stability (Moiz et al., 2025).

Slower gastric emptying can prolong the feeling of fullness and reduce snack and calorie intake between meals (Hamed et al., 2024; Ilias et al., 2025), but this is only an auxiliary effect. The main weight loss effect still comes from the brain's control of appetite (Zhao et al., 2021; Bednarz et al., 2022; Fadel et al., 2025). In addition, changes in gastric activity may increase the risk of gastrointestinal discomfort. Therefore, it is best to conduct an assessment before performing certain medical procedures or examinations (Urva et al., 2023; Nadeem et al., 2024).

4.3 Regulate glucagon and improve insulin resistance

In addition to influencing eating and gastric activity, GLP-1 RAs is also involved in the body's metabolic regulation, helping to control weight and blood sugar. The research by O Olukorode et al. (2024) and Bednarze et al. (2024) mentioned that when blood sugar is high, it can prompt pancreatic β cells to secrete more insulin and prevent α cells from secreting excessive glucagon, thereby improving fasting and postprandial blood sugar. When glucagon levels decrease, the process of glucose production in the liver is inhibited, which is more pronounced in patients with type 2 diabetes (Hamed et al., 2024; Moiz et al., 2025; Fadel et al., 2025).

Studies also suggest that GLP-1 RAs can enhance insulin sensitivity and reduce various chronic inflammatory indicators, such as C-reactive protein and interleukin-6, which are often elevated in obese and type 2 diabetic populations (Yao et al., 2024; Ren et al., 2025). Related metabolic improvements contribute to reducing visceral fat accumulation, optimizing lipid profiling and enhancing overall cardiometabolic health (Moiz et al., 2025;