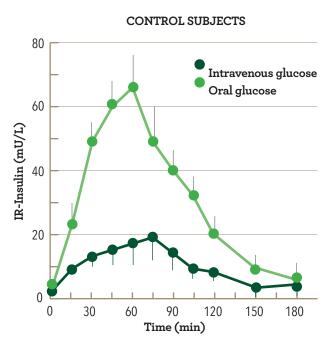
INTRODUCING INCRETINS

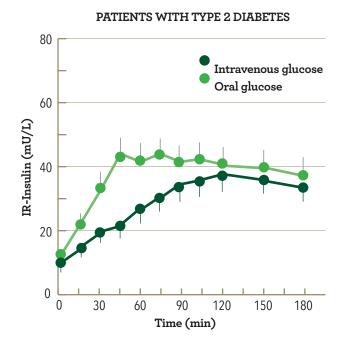
INTRODUCTION

- Incretins are a group of metabolic hormones that affect insulin secretion.
- Incretins account for 50-70% of insulin release following oral glucose stimulation.¹
- The gastrointestinal tract produces two incretins.²
 - GIP: Glucose-dependent insulinotropic peptide
 - GLP-1: Glucose-like peptide-1

THE INCRETIN EFFECT IS REDUCED IN T2D

■ The incretin response following an oral glucose load in people with type 2 diabetes (T2D) is reduced by 50% compared with those without T2D, probably reflecting defective GIP action and reduced GLP-1 secretion.³





* p ≥OS compared with respective value after oral load

Oral glucose induces greater insulin secretion than a glucose infusion that results in a similar plasma glucose concentration.3

GLP-1 HAS SEVERAL BIOLOGICAL ROLES THAT COULD CONTRIBUTE TO T2D2

- Increases insulin secretion and insulin sensitivity
- Increases beta-cell mass and maintains beta-cell function
- Increases glucose disposal
- Reduces glucagon secretion
- Delays gastric emptying
- Reduces appetite by increasing satiety

GLP-1 RA AS A T2D TREATMENT

- The half-life of intravenous GLP-1 is about 2 minutes, which makes the enzyme unsuitable as a T2D treatment.²
- Chemical modification of GLP-1 produced drugs that bind to the GLP-1 receptor (GLP-1 RA) and produce the same effects as the native protein but with a longer half-life.²
- Current GLP-1 RAs have similar mechanisms of action.
- Effects in T2D include reductions in HbA1c and weight. Some therapies also have cardiovascular benefits.
- All current GLP-1 RAs are injectable, but have different profiles that affects dosing frequency as shown in the table. Oral and implantable GLP-1 RAs are in development.

GLP-1 RA	INJECTION FREQUENCY	MAIN PHARMACOLOGICAL ACTION(S)	GLUCOSE TARGET
Exenatide	Twice daily	↓ Gastric emptying	Prandial
Liraglutide	Once daily	↑Insulin ↓Glucagon	Prandial and fasting
Lixisenatide	Once daily	↓ Gastric emptying	Prandial
Exenatide prolonged release	Weekly	↓ Gastric emptying	Prandial and fasting
Dulaglutide	Weekly	↑Insulin ↓Glucagon	Prandial and fasting
Semaglutide	Weekly	↑Insulin ↓Glucagon	Prandial and fasting

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Novo Nordisk has, through a sponsorship, fully funded all costs for the technical development and hosting of the hubs. Novo Nordisk has had no influence on the content of the hubs and full editorial control remains the sole responsibility of the Primary Care Diabetes Society.