

INSULIN ANALOGS

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Insulin is very important armamentarium in the management of diabetes mellitus.

Why insulin analogs -

- Insulin therapy should mimic physiological insulin secretion (Basal & Bolus). Conventional insulins don't mimic physiological secretion, often resulting in mismatch between requirement and availability with inadequate glycaemic control & late hypoglycaemia.
- An insulin analog mimics physiological endogenous insulin secretion
- An insulin analog is an altered form of insulin, different from the conventional insulin, but performing the same action in terms of glycemic control . Through genetic engineering of the underlying DNA, the amino acid sequence of insulin can be changed to alter its ADME (**absorption, distribution, metabolism and excretion**) characteristics.

Bolus analogs	Basal analogs
Lispro : Pro ^{B28} Lys ^{B29} Pro Aspart : Pro ^{B28} Asp Glulisine : Asn ^{B3} Lys ^{B29} Glu	Glargine : Arg ^{B31} Arg ^{B32} tag Arg ²¹ Gly Determir : Modification of Lys ^{B29} by a tethered fatty acid.

Pharmacokinetic Classification -

Bolus analogs

Lispro , aspart, Glulisine

Onset of action 5-15 minutes , peak in 1 hr and duration 2 hrs

Basal analogs (Peakless insulin) :

Glargine – onset of action in 1-4 hrs, duration 24 hrs

Determir – onset of action 2-4 hours with duration 20 hrs

Premix analogs -

- Premix analogues of NPL with Lispro (50/50 & 75/25)
- Premix analogues of NPA with Aspart (70/30)

Pharmacokinetic mechanism -

Bolus analogs – slightly modified amino acid sequences prevent aggregation in solution, dissociating very quickly in monomers in subcutaneous tissue.

Basal analogs

- Glargine – At pH 4, as in the supply injection solution is completely soluble and stable. After injection into subcutaneous tissue, the acidic solution is neutralized, leading to formation of microprecipitates from which small amounts of insulin glargine are slowly released, resulting in a relatively constant concentration/time profile over 24 hours with no pronounced peaks. This profile allows once-daily dosing as patient's basal insulin.
- Determir – Following subcutaneous injection, insulin determir binds to albumin via fatty acid chain , thereby providing slow absorption and prolonged metabolic effect.