

[illegible]

Diabetes mellitus (DM)

► Characteristics:

Biochemical criteria	Normal	Prediabetic	Diabetic
FBS	< 100 mg/dL	100-125 mg/dL	>126 mg/dL
2h BS	<140 mg/dL	140-199 mg/dL	>200 mg/dL
A1C	<5.6%	5.7-6.4%	>6.5%

Classification of DM

- DM type I
 - An autoimmune disease
 - Onset during childhood
 - Destruction of β -cells
 - Treatment with insulin
- DM type II
 - A progressive disorder
 - Onset in adulthood
 - Insulin resistance + progressive destruction of β -cells
 - Early stages controlled with non-insulin antidiabetic drugs
 - Later stages often require addition of insulin to drug regimen

Antihyperglycemic Agents

Class	Available Agents
Insulin	Several forms
Sulfonylurea	Glibenclamide, Gliclazide
Biguanide	Metformin
Thiazolidinedione	Pioglitazone
α -Glucosidase inhibitors	Acarbose

Antihyperglycemic Agents

- Mechanisms of action

Augment Insulin Supply	Enhance Insulin Action	Delay Carbohydrate Absorption
Insulins	Biguanides	α -Glucosidase inh.
Sulfonylureas	Thiazolidinediones	

A simple line drawing of a medical syringe and an insulin bottle. The bottle is on the left, labeled 'INSULIN' with a wavy line below it. The syringe is on the right, angled upwards, with a needle pointing towards the bottom left. Both are rendered in a minimalist, sketchy style.

Insulin indications

- DM I
- DM II
- DM emergencies
- Diabetic pregnant women



Insulin Preparations

Pharmacokinetic aspects

1. Rapid acting

- ✓ Lispro, Aspart, Glulisine

2. Short acting

- ✓ Regular (or crystal , natural)

3. Intermediate acting

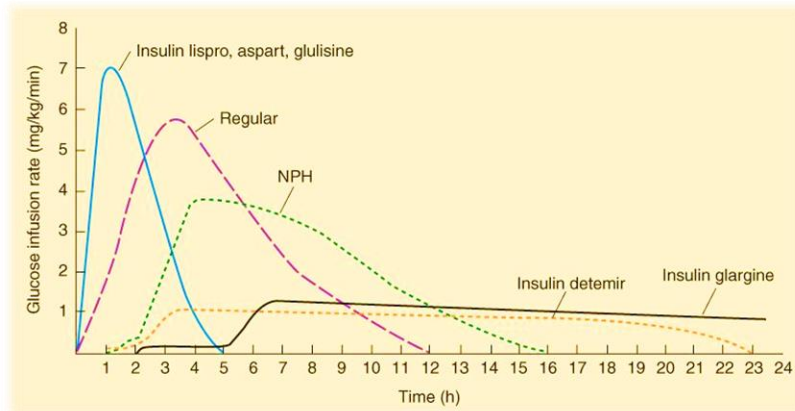
- ✓ Protamine insulin (NPH), Insulin zinc suspension

4. Long acting

- ✓ Glargine, Detemir, Ultralente, Degludec

Insulin Preparations

Pharmacokinetic (onset & duration of action)



Rapid-acting insulin

Lispro, Aspart, Glulisine

- Onset: <15 min
- Duration: 3-4 h
- Rapid onsets and early peaks of activity



Rapid-acting insulin

Lispro, Aspart, Glulisine

- Indications:
 - Control of postprandial glucose (immediately before a meal)
 - Emergency treatment of diabetic ketoacidosis
 - Continuous subcutaneous infusion devices



Short-acting insulin

Regular

- Onset: 0.5-1 h
- Duration: 4-6 h



Short-acting insulin

Regular

- Indications:
 - Emergencies of hyperglycemia (IV)
 - Ordinary maintenance regimens (SC)
- Alone or mixed with intermediate- or long-acting preparations.



Intermediate-acting insulin

Neutral Protamine Hagedorn (NPH) Or Isophane Insulin

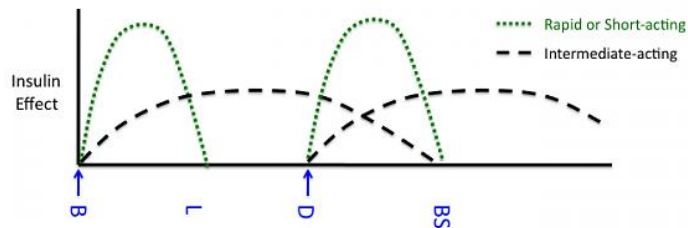
- Onset: 1-4 h
- Duration : 10-16 h



Intermediate-acting insulin

NPH insulin:

- A combination of regular insulin and protamine that exhibits a delayed onset and peak of action
- NPH insulin is often combined with regular or rapid-acting insulins



Long-acting insulin

Glargine, Detemir, Ultralente, Degludec

- Gradual release pattern from injection site
- Onset: 4 h
- Duration: 12-24 h



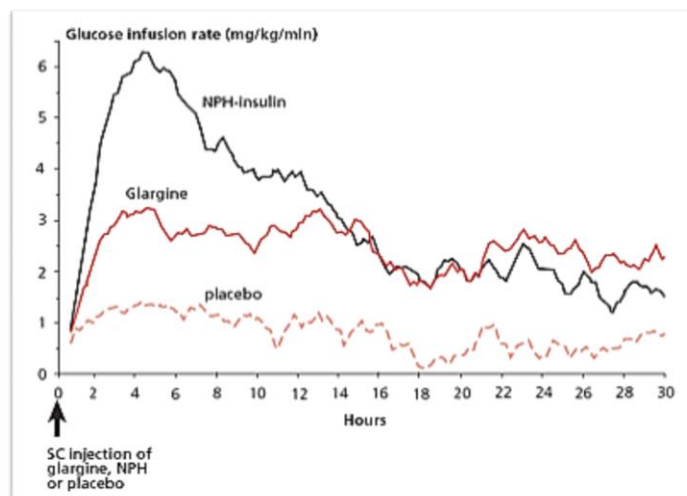
Long-acting insulin

Glargine, Detemir, Ultralente, Degludec



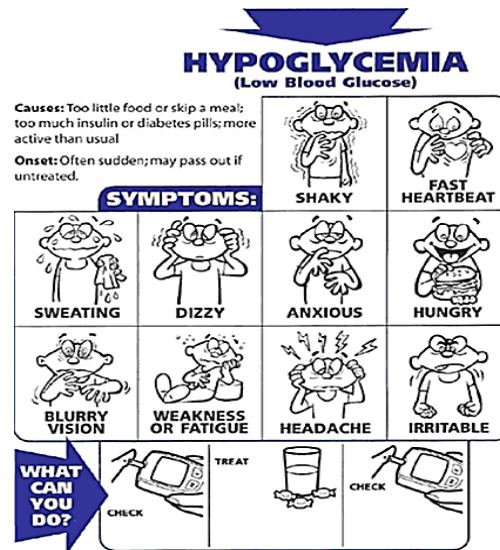
- Effects:
 - Provide a peakless basal insulin level lasting more than 20 h
- Indication:
 - Control basal glucose levels without producing hypoglycemia

Glargine vs NPH Insulin



Insulin side effects

- Hypoglycemia
- Injection pain
- Weight Gain
- Worsening Insulin Resistance



Insulin Delivery Systems

- The standard mode of insulin therapy is SC injection with conventional needles and syringes
- Portable pen-sized injectors:
 - replaceable cartridges
 - disposable
- Continuous SC insulin infusion devices
- Programmable pumps
 - manual adjustments in the rate of delivery can be made to accommodate changes in insulin requirements

NON INSULIN ANTIDIABETIC DRUGS

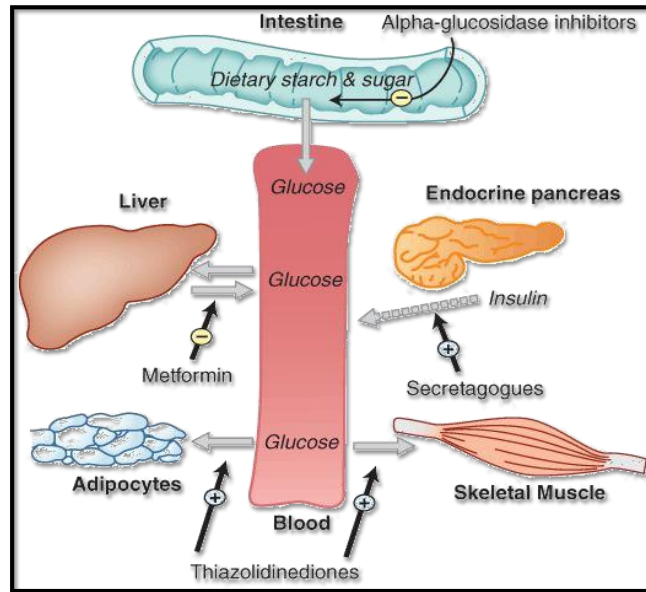
Oral antidiabetic drugs

1. **Sulfonylureas and Glinides**
2. **Biguanides**
3. **Thiazolidinediones**
4. **α -glucosidase inhibitors**

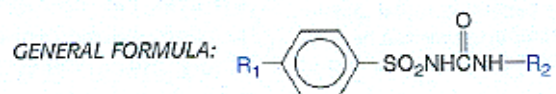
Most commonly for DM II treatment



Major actions of oral antidiabetic drugs



SULFONYLUREAS



Sulfonylureas (SUs)

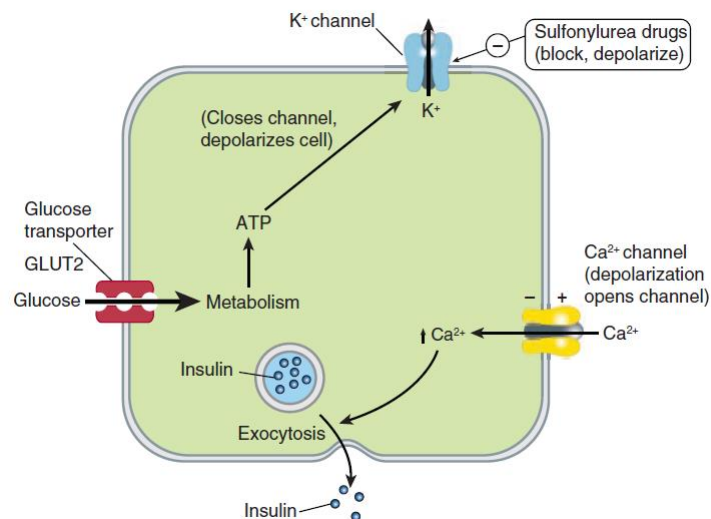
MOA:

- Insulin secretagogues
- Blockade of ATP-dependent K^+ channels (K_{ATP}) in B-cells of pancreas
- → membrane depolarization → ↑ release of insulin

Effects:

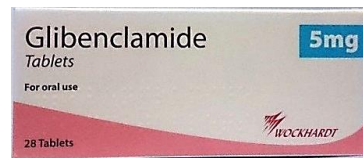
- ↑ Basal and postprandial insulin secretion
- No effect in patients with non-functional pancreatic B-cells

SUs



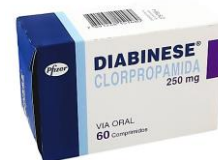
SUs

- The most common drugs:
 - Glibenclamide (Glyburide)
 - Glipizide
 - More potent
 - Use more commonly than the older agents

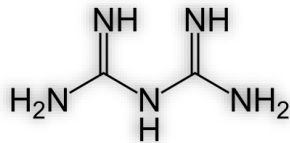


SUs

- **Indication:**
 - Type 2 DM
- **Dosing:**
 - Once, twice or three time daily
- **Side effects:**
 - Hypoglycemia
 - Weight gain
 - GI irritation
- **Contraindications:**
 - DM I
 - Pregnancy
 - Lactation



BIGUANIDES



Biguanides (Metformin)

MOA:

- ↑ Peripheral tissue sensitivity to insulin
- ↑ Peripheral glucose uptake & utilization
- ↓ Glycogenolysis
- ↓ Gluconeogenesis

Effects:

- Enhancement of insulin action, decrease weight
- Its action depends on presence of insulin
- Metformin is an antihyperglycemic agent (and not hypoglycemic)
- Slower action



Metformin

Indications:

- Type 2 DM
- Gestational DM
- Polycystic ovary syndrome

Dosing:

- Two to three times daily

Side effects:

- Gastrointestinal disturbances (anorexia, diarrhea, nausea)
- ↓ Appetite & weight loss
- Vitamin B12 deficiency (in long-term use)
- Lactic acidosis



THIAZOLIDINEDIONES

Thiazolidinediones (glitazones)

Pioglitazone, Rosiglitazone



Pioglitazone

MOA:

- ▶ Activation of nuclear receptors important for insulin action
 - ▶ peroxisome proliferator-activated receptor- γ (PPAR- γ receptor)
- ▶ Tissue sensitivity to insulin ($\uparrow$ Glut-4 expression)
 - ▶ skeletal muscle and adipose tissues

Effects:

- ▶ $\uparrow$ Glucose uptake in muscle and adipose tissue
- ▶ $\downarrow$ Gluconeogenesis
- ▶ $\downarrow$ Both fasting and postprandial hyperglycemia

Pioglitazone

- Indications:
 - Type 2 DM
 - ↓ Risk of Type 2 DM in high-risk patients
- Dosing:
 - Once daily
- Side effects:
 - Fluid retention
 - ↑ Risk of bone fractures
 - Headache, fatigue and GI disturbances



ALPHA GLUCOSIDASE INHIBITORS

α -glucosidase inhibitors

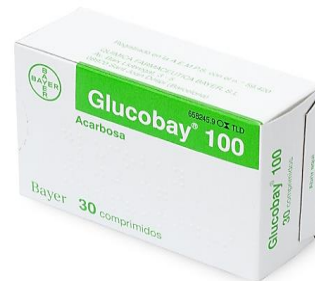
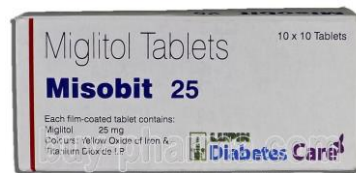
α -glucosidase:

- Breaks down starch and disaccharides to glucose

Acarbose

Miglitol

Voglibose



α -glucosidase inhibitors

MOA:

- Carbohydrate analogs
- → α -glucosidase inhibition within the intestine
- → ↓ Fiber digestion → ↓ glucose liberation
- → ↓ Intestinal glucose absorption → ↓(mild) BG

Effects:

- Delays carbohydrate absorption
- ↓ Postprandial hyperglycemia
- No effect on fasting blood sugar and insulin release

α -glucosidase inhibitors

Indications:

- Both type 1 & 2 DM
- Prevent type 2 DM in prediabetics

Dosing:

- Three times daily (with each meal)
- Must be taken just before a meal
- Can be used with or without other agents

α -glucosidase inhibitors

Side effects

- Flatulence
- Diarrhea
- Abdominal pain





Any question?