

Anti-Diabetic Agents

Antidiabetic agents (Hypoglycemic Agents)

- Antidiabetic agents are medications used to manage blood glucose levels in individuals with diabetes mellitus.
- These agents work through various mechanisms to enhance insulin action, increase insulin secretion, reduce hepatic glucose production, or decrease glucose absorption from the gastrointestinal tract.
- Proper classification of antidiabetic agents is essential for selecting appropriate therapy based on the patient's specific needs, type of diabetes, and potential side effects.

Classification of Antidiabetic agents



Classification of Hypoglycemic Agents

1. Biguanides

- **Metformin***
- Decreases hepatic glucose production and increases insulin sensitivity.

2. Sulfonylureas (2nd Generation)

- **Glibenclamide*** (also known as *Glyburide*)
- **Glimepiride**
- Stimulate pancreatic β -cells to release insulin.

3. Thiazolidinediones (Glitazones)

- **Pioglitazone**
- Improve insulin sensitivity in adipose tissue, muscle, and liver by activating PPAR- γ .

4. Meglitinides (Glinides)

- **Repaglinide**
- Stimulates rapid, short-duration insulin secretion from pancreatic β -cells.

5. SGLT-2 Inhibitors (Gliflozins)

- **Gliflozins** (e.g., *Dapagliflozin*, *Canagliflozin*, *Empagliflozin*)

- Inhibit sodium-glucose co-transporter-2 in the kidneys → increase urinary glucose excretion.

6. DPP-4 Inhibitors (Gliptins)

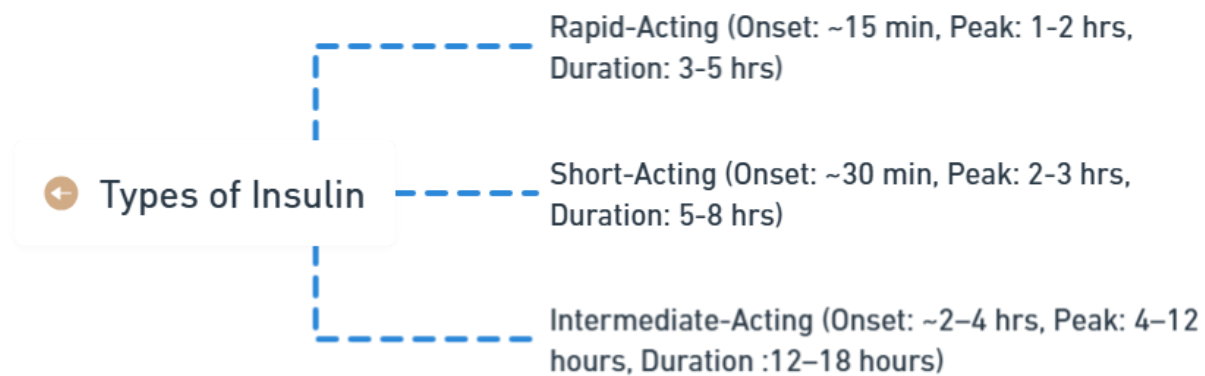
- **Gliptins** (e.g., *Sitagliptin*, *Vildagliptin*, *Saxagliptin*)
- Inhibit DPP-4 enzyme → prolong action of incretin hormones → increase insulin secretion and suppress glucagon.

Insulin

Introduction:

- Insulin is a peptide hormone produced by beta cells in the pancreas.
- It regulates blood glucose levels by facilitating glucose uptake into cells (liver, fat, and muscle tissues) and aids in the metabolism of carbohydrates, fats, and proteins.
- In diabetes, impaired insulin production or function necessitates external administration.

Types of Insulin



1. **Rapid-Acting** (Onset: ~15 min, Peak: 1-2 hrs, Duration: 3-5 hrs)
 - **Examples:** Lispro, Aspart, Glulisine
 - **Uses:** Mealtime glucose control.
2. **Short-Acting** (Onset: ~30 min, Peak: 2-3 hrs, Duration: 5-8 hrs)
 - **Examples:** Regular Insulin (Humulin R, Novolin R)
 - **Uses:** Pre-meal and basal needs.
3. **Intermediate-Acting** (Onset: ~2-4 hrs, Peak: 4-12 hrs, Duration: 12-18 hrs)
 - **Examples:** NPH Insulin (Humulin N, Novolin N)
 - **Uses:** Basal coverage.
4. **Long-Acting** (Onset: ~1-2 hrs, Peak: Minimal, Duration: ~24 hrs)
 - **Examples:** Glargine, Detemir, Degludec
 - **Uses:** Basal insulin, once/twice daily.

5. **Ultra-Long-Acting** (Onset: ~30-90 min, Peak: None, Duration: >24 hrs)

- **Examples:** Degludec
- **Uses:** Extended basal needs.

Mechanism of Action

- **Insulin lowers blood glucose by:**
 - **Facilitating Glucose Uptake:** Promotes entry of glucose into muscle and fat cells.
 - **Inhibiting Gluconeogenesis:** Reduces glucose production in the liver.
 - **Promoting Glycogen Synthesis:** Enhances storage of glucose as glycogen in the liver and muscles.
 - **Stimulating Lipogenesis:** Encourages fat storage and inhibits lipolysis.

Uses

- **Type I Diabetes Mellitus:** Essential for survival due to absolute insulin deficiency.
- **Type II Diabetes Mellitus:** Used when oral antidiabetics are insufficient to control blood glucose levels.
- **Gestational Diabetes:** Manages elevated blood sugar levels during pregnancy.
- **Hyperkalemia:** Insulin shifts potassium into cells, lowering blood potassium levels.

Side Effects

1. **Hypoglycemia:** Low blood sugar levels, presenting as dizziness, sweating, confusion, and in severe cases, loss of consciousness.
2. **Weight Gain:** Increased fat storage due to insulin's anabolic effects.
3. **Injection Site Reactions:** Redness, swelling, or itching at the injection site.
4. **Allergic Reactions:** Rare but may include rash or anaphylaxis.
5. **Lipodystrophy:** Changes in fat tissue at injection sites from repeated use.

Preparation of Insulin

1. Formation of Preproinsulin:

- Insulin synthesis begins with preproinsulin (110 amino acids), synthesized in the rough endoplasmic reticulum.

2. Conversion to Proinsulin:

- Preproinsulin is processed in the Golgi apparatus to form proinsulin, an inactive precursor.

3. Folding and Bond Formation:

- Proinsulin folds to form three disulfide bonds, linking the A-chain and B-chain.

4. Packaging into Vesicles:

- Folded proinsulin is packaged into secretory vesicles for further processing.

5. Cleavage by Enzymes:

- Enzymes (Proprotein Convertase 1/3 and Proprotein Convertase 2) cleave the C-peptide from proinsulin.

6. Final Processing:

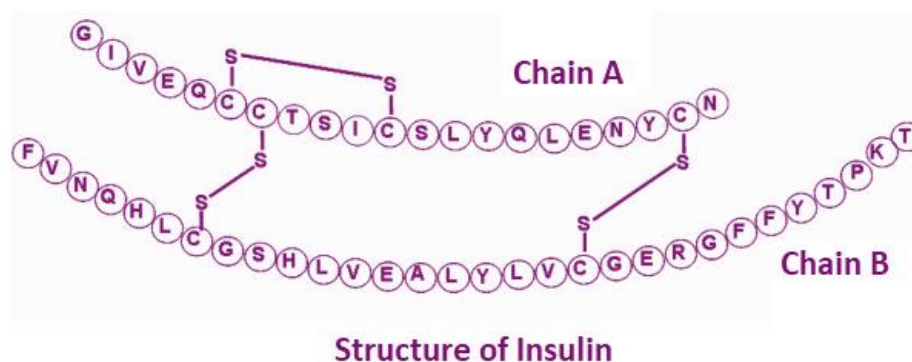
- Carboxypeptidase E removes terminal amino acids, yielding active insulin.

7. Active Insulin:

- Active insulin consists of:
 - **Chain A:** 21 amino acids.
 - **Chain B:** 30 amino acids.
- Chains are connected by two disulfide bonds.

8. Secretion:

- Active insulin is secreted into the bloodstream to regulate blood sugar and metabolic processes.



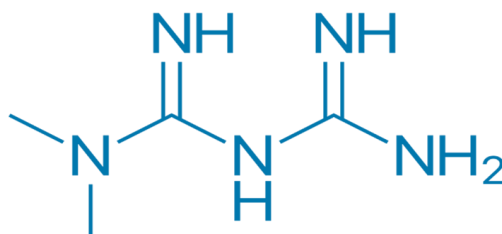
Various Anti-Diabetic Agents

1. Metformin*

Chemical Name:

- 1,1-Dimethylbiguanide hydrochloride

Chemical Structure:



- **Marked:** Biguanide core* with two methyl groups on the terminal nitrogen



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