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MEDICINAL CHEMISTRY - II

UNIT 5

TOPIC :

- **Anti diabetic agents:**
Insulin and its preparations



Antidiabetic Agents

- Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia due to defective insulin secretion, insulin action, or both.
- Persistent hyperglycemia leads to microvascular and macrovascular complications.
- Antidiabetic agents are drugs used to control blood glucose levels.

Classified as:

- + Insulin and insulin analogs
- + Oral hypoglycemic agents (for Type 2 DM)
- + Adjunctive agents

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Insulin and Its Preparations

- Insulin is a peptide hormone produced by the β -cells of the islets of Langerhans in the pancreas.
- It regulates glucose, protein, and lipid metabolism by promoting uptake of glucose into cells, glycogen formation, and inhibition of gluconeogenesis.
- Used therapeutically in diabetes mellitus, particularly Type 1 diabetes and sometimes in Type 2 diabetes when oral hypoglycemic agents fail.

Structure of Insulin

- Composed of two polypeptide chains (A & B) linked by disulfide bonds.
- A chain: 21 amino acids
- B chain: 30 amino acids
- Proinsulin: Precursor $\rightarrow$ cleaved to active insulin + C-peptide

Mechanism of Action

1. Insulin binds to insulin receptors (tyrosine kinase receptor) on target cells.
2. Activates intracellular signaling $\rightarrow$ GLUT-4 translocation to cell membrane $\rightarrow$ glucose uptake.
3. Metabolic effects:
 - Carbohydrates: $\uparrow$ glycogenesis, $\downarrow$ gluconeogenesis, $\downarrow$ glycogenolysis
 - Lipids: $\uparrow$ lipogenesis, $\downarrow$ lipolysis, $\downarrow$ ketogenesis
 - Proteins: $\uparrow$ amino acid uptake and protein synthesis, $\downarrow$ proteolysis

Types of Insulin Preparations

Insulin preparations differ in onset, peak, and duration, allowing basal and bolus coverage.

Type	Onset	Peak	Duration	Examples	Clinical Use
Rapid-acting	10–30 min	30–90 min	3–5 hrs	Lispro, Aspart, Glulisine	Postprandial glucose control
Short-acting (Regular insulin)	30–60 min	2–4 hrs	6–8 hrs	Humulin R, Novolin R	Meal coverage, DKA, IV infusion
Intermediate-acting	1–2 hrs	4–12 hrs	18–24 hrs	NPH, Lente	Basal insulin, twice-daily dosing
Long-acting	1–2 hrs	Minimal	~24 hrs	Glargine, Detemir, Degludec	Basal insulin, once daily
Premixed	Varies	Varies	12–24 hrs	70/30 NPH/Regular, 75/25 Lispro Mix	Convenience, basal + bolus coverage

Routes of Administration

- Subcutaneous (SC): Most common
- Intravenous (IV): Regular insulin in emergencies (DKA, hyperosmolar states)
- Intramuscular (IM): Rarely used
- Inhalational insulin: Rapid-acting forms for prandial use

Clinical Uses

1. Type 1 Diabetes Mellitus: Lifelong insulin therapy
2. Type 2 Diabetes Mellitus: When oral agents are insufficient
3. Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS)
4. Hyperkalemia: IV insulin with glucose shifts potassium into cells
5. Gestational Diabetes: When diet and exercise fail

Adverse Effects

- Hypoglycemia: Most common, can cause tremors, sweating, confusion, coma
- Allergic reactions: Local (rash, lipodystrophy) or systemic (rare)
- Weight gain: Due to increased anabolic effects
- Lipodystrophy: At injection site if repeated injections at same site
- Edema: Rare with high doses

Storage and Handling

- Store unopened vials at 2–8°C (refrigerator)
- Do not freeze
- Once opened, can be stored at room temperature ($\leq 30^{\circ}\text{C}$) for 28 days
- Protect from direct sunlight and heat

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