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Unit-V/Part-A

Anti-diabetic Agent

Presented By;-

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Diabetes ?

1. **Diabetes** is a chronic metabolic disease characterized by high blood sugar (glucose) levels.
2. **Normally,** your body uses a hormone called **insulin** (made by the pancreas) to move glucose from the bloodstream into cells, where it's used for energy.
3. In diabetes, this process doesn't work properly — either because:
    a. Your body **doesn't make enough insulin**, or
    b. Your body **can't use insulin properly (insulin resistance)**

Types of Diabetes

Type of Diabetes	Cause	Key Features
Type 1 Diabetes	Autoimmune destruction of insulin-producing beta cells in pancreas	- Sudden onset- Usually in children/young adults- Requires insulin for life
Type 2 Diabetes	Insulin resistance and/or reduced insulin production	- Gradual onset- Often in adults- Strongly linked to obesity and lifestyle
Gestational Diabetes	Hormonal changes during pregnancy causing insulin resistance	- Occurs in pregnancy- Usually disappears after delivery- Risk of Type 2 later
Prediabetes	Impaired glucose regulation (not high enough to be diabetes)	- Often no symptoms- Reversible- Warning stage for developing Type 2
MODY (Rare)	Genetic mutations affecting insulin secretion	- Inherited (autosomal dominant)- Early onset (teens to 30s)- Not always insulin-dependent
Secondary Diabetes	Due to other medical conditions or medications (e.g., pancreatitis, steroids)	- Caused by another disease or drug- Often reversible if underlying issue is treated

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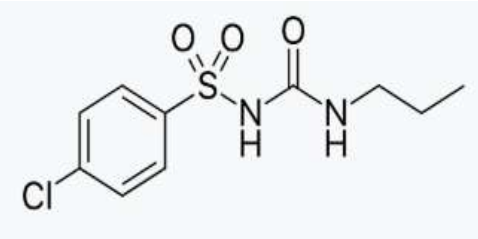
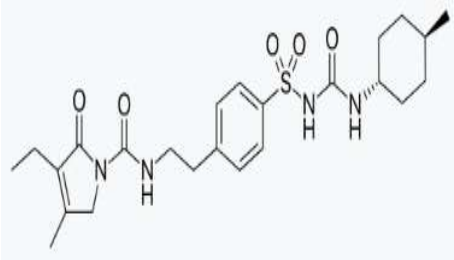
Classification of Anti-diabetic Agent

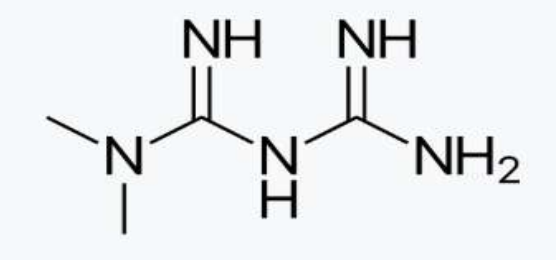
1. **Insulin and its Analog:-** Insulin, Insulin Lispro, Glargine
2. **Sulfonyl ureas:-** Tolbutamide*, Chlorpropamide, Glipizide, Glimepiride.
3. **Biguanides:-** Metformin.
4. **Thiazolidinediones:-** Pioglitazone, Rosiglitazone.
5. **Meglitinides:-** Repaglinide, Nateglinide.
6. **Glucosidase inhibitors:-** Acrabose, Voglibose.



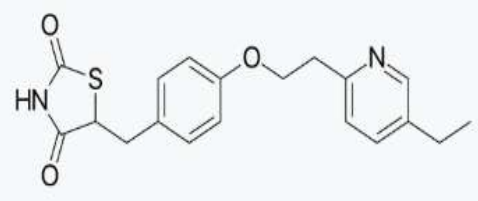
Chlorpropamide



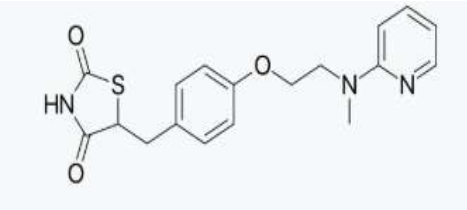
Glimepiride



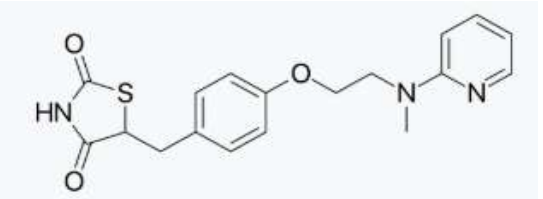
Metformin



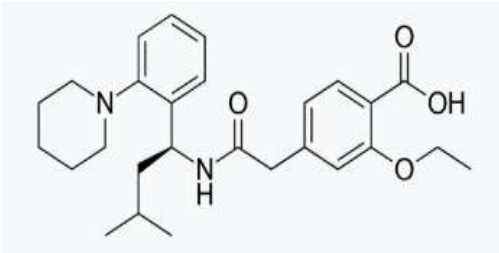
Pioglitazone



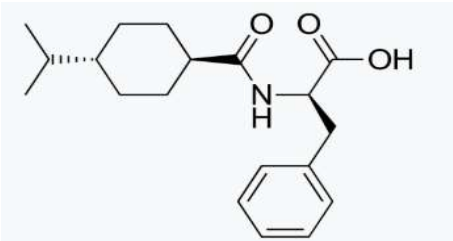
Rosiglitazone



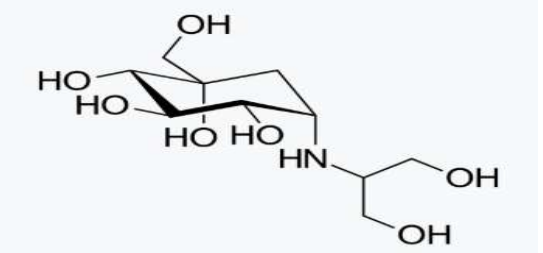
Rosiglitazone



Repaglinide



Nateglinide



Voglibose

MOA of Common Anti-diabetic Drugs

Drug	Class	Mechanism of Action (MOA)
Insulin	Insulin & analogs	Replaces/supplements natural insulin → promotes glucose uptake in muscle, fat, liver
Tolbutamide*	Sulfonylurea (1st gen)	Stimulates insulin secretion by blocking ATP-sensitive K^+ channels in pancreatic β-cells
Chlorpropamide	Sulfonylurea (1st gen)	Same as above: enhances insulin release via K^+-ATP channel blockade in β-cells
Glipizide	Sulfonylurea (2nd gen)	Same as above: more potent, faster onset than 1st gen
Glimepiride	Sulfonylurea (3rd gen)	Stimulates insulin secretion by enhancing β-cell depolarization and calcium influx
Metformin	Biguanide	Activates AMPK → ↓ hepatic gluconeogenesis, ↑ peripheral insulin sensitivity
Pioglitazone	Thiazolidinedione (TZD)	Activates PPAR-γ → ↑ insulin sensitivity in adipose, muscle tissues
Rosiglitazone	Thiazolidinedione (TZD)	Same as above: enhances glucose uptake via PPAR-γ activation
Repaglinide	Meglitinide	Stimulates rapid, short-acting insulin secretion by blocking β-cell K^+-ATP channels
Nateglinide	Meglitinide	Similar to Repaglinide: promotes quick insulin release in response to meals
Acarbose	α-Glucosidase inhibitor	Inhibits intestinal α-glucosidase → delays carbohydrate digestion and postprandial glucose rise
Voglibose	α-Glucosidase inhibitor	Same as Acarbose: slows glucose absorption in small intestine by enzyme inhibition

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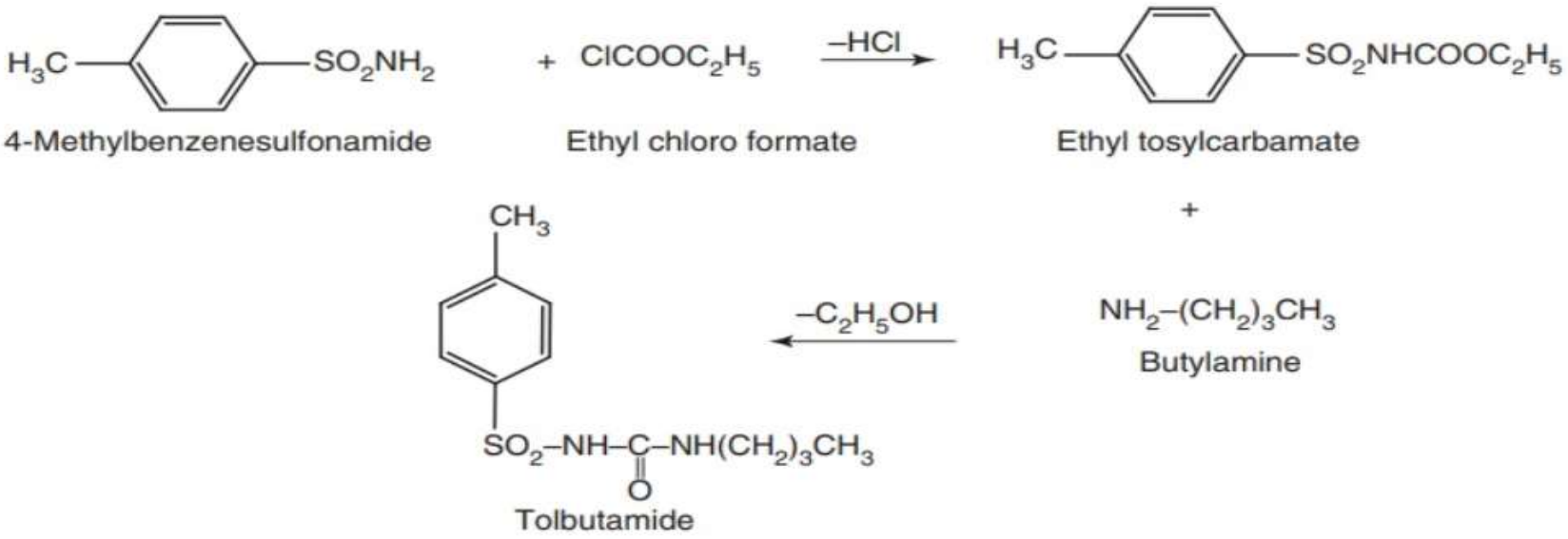
Synthesis of Tolbutamide



SAR of Tolbutamide

General structure - Ar–SO_2–NH–CO–R^1

Structural Feature	SAR Observation	Effect on Activity
Aryl (Ar) group	A para-substituted phenyl ring is essential (e.g., p-methyl in tolbutamide)	Enhances binding to the sulfonylurea receptor (SUR1)
Sulfonyl group (SO_2)	Must be directly attached to the aromatic ring	Required for hypoglycemic activity
Urea linkage (-NH-CO-)	Essential for activity	Maintains the correct conformation for receptor binding
R^1 group (on urea)	Usually a bulky aliphatic or cyclic group (e.g., butyl in tolbutamide)	Affects potency, duration, and binding affinity
Length of alkyl chain (R^1)	Increasing chain length up to a certain limit increases potency; tolbutamide has a butyl group	Too long chains reduce activity due to poor receptor binding
Electron-withdrawing groups on aromatic ring	Decrease activity	Reduce electron density needed for receptor interaction
Lipophilicity	Moderate lipophilicity improves membrane permeability and receptor binding	Very lipophilic drugs (e.g., second-gen) have higher potency

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THANK YOU