

# HYPOGLYCEMIC AGENTS

## ❑ HYPOGLYCEMIC AGENT

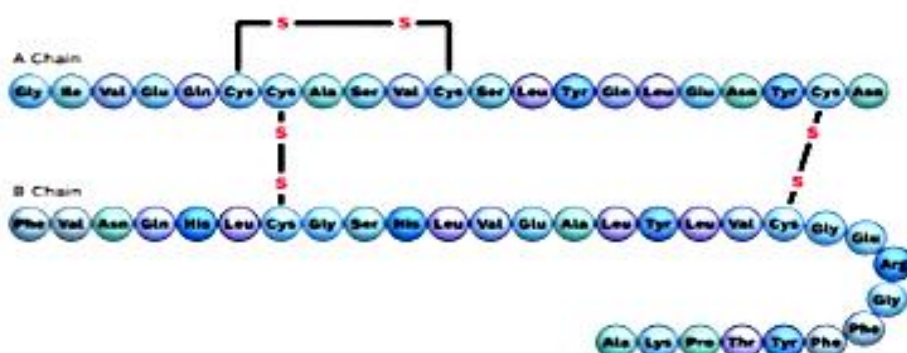
- Hypoglycemic agents are synthetic drugs that **lower the blood glucose levels** and are **used to treat type-2 diabetes mellitus**.
- It is also called antidiabetic agents.
- They may stimulate the **synthesis of insulin** by pancreatic beta cells, **inhibit glucose production**, **facilitate transport of glucose to muscle cells** and sometimes increase the number of receptor sites where insulin can be bound and can **initiate the process of breaking down glucose**.

## ❑ DIABETES

- Diabetes is a chronic, metabolic disease **characterized by elevated levels of blood glucose** (or blood sugar), which leads to serious damage to the heart, blood vessels, eyes, kidneys and nerves over time.
- The normal blood sugar level is 80-100 mg/dL and the normal fasting blood glucose levels are  $\leq 100$ mg/dl.
- Hypoglycemia is a condition in which your blood sugar (glucose) level is lower ( $\leq 70$ mg/dL) than the standard range
- Hyperglycemia is a condition in which your blood sugar (glucose) level is higher ( $\geq 126$ mg/dL) than the standard range.

## ❑ INSULIN AND ITS PREPARATION

- Insulin is a protein hormone secreted by  $\beta$  cells of pancreatic islets of Langerhans of pancreas.
- It consists of 51 amino acids arranged in two chains, A (21 Amino acid) and B (30 Amino acid).
- These chains are joined through disulphide bridges. Commercially insulin is extracted from pork and beef pancreas.



### ❖ Properties

- It is a white powder.
- It is slightly soluble in water.
- It dissolves in dilute solution of mineral acids.
- It is inactivated by proteolytic enzymes.

### ❖ Stability and Storage

- It is sensitive to heat and light.
- It is stored at a temperature between 2°C and 8°C and should not be allowed to freeze.
- Insulin injection is stored in a multidose container.

### ❖ Uses

- It is used to control diabetes mellitus.
- It is used to regulate carbohydrate metabolism
- To treat hyperkalemia.
- To treat severe ketosis or diabetic coma.

## PARENTERAL (BY INJECTION)

### ❑ TYPES OF INSULIN

TYPE	INSULIN
Rapid acting	Insulin lispro, Insulin aspart, Insulin glulisine
Short acting	Regular (soluble) insulin
Intermediate acting	Insulin zinc suspension or Lente, Natural Protamine Hagedorn (NPH) or isophane insulin
Long acting	Insulin glargine, Insulin detemir

### ❑ INSULIN INJECTION I.P.

- It is a sterile clear solution. Insulin is dissolved in water for injection and pH is adjusted to 3 (acidic).
- It contains glycerin as a preservative. It's Action from 2- 8 hours.

### ❖ Pharmaceutical Formulation

- This drug is formulated form of injection.



### ❖ Stability and storage

- It is sensitive to heat and light.
- It is stored at a temperature between 2°C - 8°C and should not be allowed to freeze.

### ❖ Popular Brand Names

- Humulin R
- Novolin R
- Actrapid

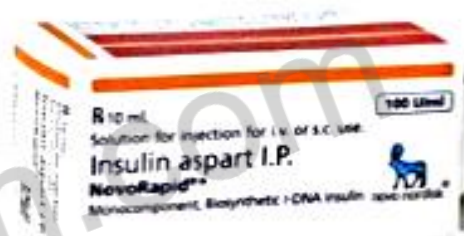


### ❖ Medicinal Uses

- It is used to control diabetes mellitus.
- It is used to regulate carbohydrate metabolism
- To treat hyperkalemia.
- To treat severe ketosis or diabetic coma

### ❑ GLOBIN ZINC INSULIN INJECTION I.P.

- It is a sterile clear solution. Its pH is 3 and contains 40 or 80 units/ml.
- It contains insulin, globin, zinc chloride and glycerin. It's Action from 4 - 12 hours.



### ❑ PROTAMINE ZINC INSULIN INJECTION I.P.

- It is a sterile suspension. It contains insulin, globin, zinc, chloride and glycerin.
- Its pH is 3 and contains 40 or 80 units/ml. It's Action from 12 hours or more



### ❑ ISOPHANE INSULIN INJECTION I.P.

- It is a sterile suspension. It contains insulin, globin, chloride, glycerin, less zinc, and more protamine sulphate.
- Its pH is 3 and contains 40 or 80 units/ml. It's Action from 12 hours or more



## ORAL ANTI-DIABETIC DRUGS

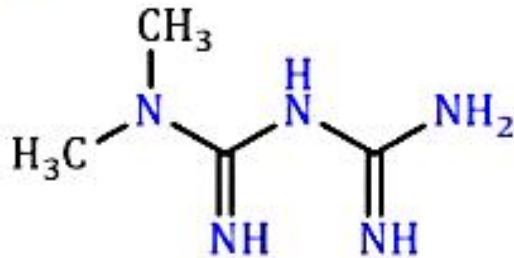
- Oral antihyperglycemic agent's lower glucose levels in the blood.
- They are commonly used in the treatment of diabetes mellitus.

CLASSES	SUB-CLASS		DRUGS
Enhanced insulin secretion	K <sup>+</sup> channel blocker	Sulfonylurea	1st generation - Tolbutamide, Chlorpropamide 2nd generation- Glibenclamide (glyburide), Glipizide, Gliclazide, Glimepiride.
		Meglitinide/ Phenylalanine analogues	Repaglinide, Nateglinide
Overcome insulin resistance	Repaglinide, Nateglinide		Repaglinide, Nateglinide
	Thiazolidinediones (PPAR $\gamma$ activators)		Pioglitazone
Miscellaneous drugs	DPP-4 inhibitors		Sitagliptin, Saxagliptin
	GLP-1 analogue		Exenatide
	Sod. Glucose cotransporter -2 (SGLT-2) inhibitor		Dapagliflozin, Canagliflozin
	Dopamine D <sub>2</sub> agonist		Bromocriptine
	Amylin Analogues		Pramlintide
Retard carbohydrate absorption	Retard carbohydrate absorption		Acarbose, Miglitol, Voglibose



## ❑ **METFORMIN**

- It is a biguanide derivative.
- ❖ **Chemical Formula**  $C_4H_{11}N_5$
- ❖ **Structure**



### ❖ **IUPAC Nomenclature**

- N,N-Dimethylimidodicarbonimidic diamide

### ❖ **Physiochemical Properties**

- Its hydrochloride salt has an odorless, bitter flavor and is a white, crystalline powder.
- It dissolves well in water but becomes insoluble in chloroform.

### ❖ **Pharmaceutical Formulation**

- This drug is formulated from of tablet.

### ❖ **Stability and storage**

- Store it at room temperature (15°C -30°C) and away from light, excess heat, and moisture.

### ❖ **Popular Brand Names**

- Glucophage
- Galzomet - M forte
- Salumate

### ❖ **Dose**

- 0.5-2.5 g/day in OD/BD.

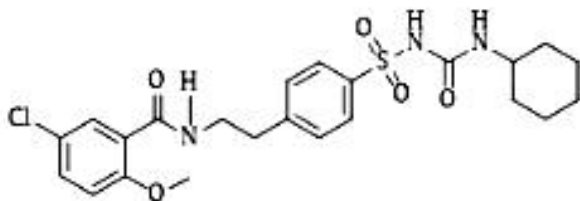
### ❖ **Medicinal Uses**

- It is used in the treatment of type 2 diabetes.
- It is also used in the treatment of polycystic ovary syndrome.
- It is sometimes used as an off-label adjunct to lessen the risk of metabolic syndrome in people who take antipsychotics.

## ❑ **GLIBENCLAMIDE (GLYBURIDE)**

❖ **Chemical Formula** -  $C_{23}H_{28}ClN_3O_5S$

❖ **Structure**



❖ **IUPAC Nomenclature**

• 5-chloro-N-[2-[4-(cyclohexylcarbamoylsulfamoyl)phenyl]ethyl]-2-methoxybenzamide

❖ **Physiochemical Properties**

- It is white crystalline powder and odourless.
- It is slightly soluble in water and sparingly soluble in chloroform.

❖ **Pharmaceutical Formulation**

- This drug is formulated from of tablet.

❖ **Stability and storage**

- Store it at room temperature ( $20^{\circ}\text{C}$  -  $25^{\circ}\text{C}$ ) and away from light, excess heat, and moisture.

❖ **Popular Brand Names**

- Diabeta
- Glynase
- Micronase

❖ **Dose**

- 2.5–15 mg/day in 1–2 doses.

❖ **Medicinal Uses**

- It is used in the treatment of type 2 diabetes.

## ❑ **GLIMEPIRIDE**

❖ **Chemical Formula** -  $C_{24}H_{34}N_4O_5S$

❖ **Structure**

❖ **Dose**

- 2.5–15 mg/day in 1–2 doses.

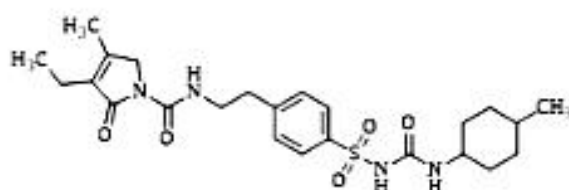
❖ **Medicinal Uses**

- It is used in the treatment of type 2 diabetes.

## ❑ **GLIMEPIRIDE**

❖ **Chemical Formula** -  $C_{24}H_{34}N_4O_5S$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 3-Ethyl-4-methyl-N-[2-(4-[[[(trans-4-methylcyclohexyl)carbamoyl]sulfamoyl]phenyl]ethyl]-2-oxo-2,5-dihydro-1H-pyrrole-1-carboxamide

❖ **Physiochemical Properties**

- It is practically insoluble in water.
- It has been reported that Glimepiride has melting point of 207°C.

❖ **Pharmaceutical Formulation**

- This drug is formulated from of tablet.

❖ **Stability and storage**

- Store it at room temperature (20°C -25°C) and away from light, excess heat, and moisture.

❖ **Popular Brand Names**

- Amaryl
- Glyride-1

❖ **Dose**

- 1-6 mg per day in 1-2 doses

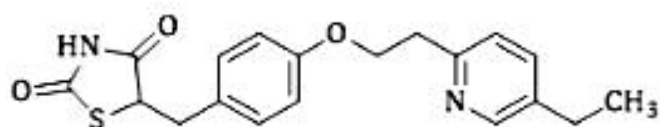
❖ **Medicinal Uses**

- It is used in the treatment of only type 2 diabetes.

## ❑ **PIOGLITAZONE**

❖ **Chemical Formula** -  $C_{19}H_{20}N_2O_3S$

❖ **Structure**





### ❖ IUPAC Nomenclature

- (RS)-5-(4-[2-(5-ethylpyridin-2-yl)ethoxy]benzyl)thiazolidine-2,4-dione

### ❖ Physicochemical Properties

- It is white crystalline powder, odourless.
- It is slightly soluble in anhydrous ethanol, very slightly soluble in acetone, acetonitrile and practically insoluble in water.
- It occurs as hydrochloride salt.

### ❖ Pharmaceutical Formulation

- This drug is formulated from of tablet.

### ❖ Stability and storage

- Store it at room temperature (20°C -25°C) and away from light, excess heat, and moisture.

### ❖ Popular Brand Names

- Actos
- Piocare-30
- Nespiz-30

### ❖ Dose

- 15-45 mg once a day.

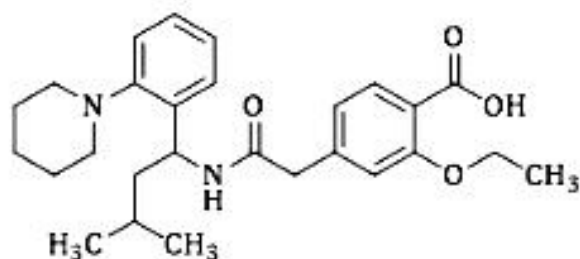
### ❖ Medicinal Uses

- It is used in the treatment of type 2 diabetes.
- It is recommended together with exercise and diet.

### ❑ REPAGLINIDE

- ❖ **Chemical Formula** -  $C_{27}H_{36}N_2O_4$

- ❖ **Structure**



### ❖ IUPAC Nomenclature

- (S)-2-Ethoxy-4-(1-[2-{piperidin-1-yl}phenyl]-3-methylbutylcarbamoylmethyl)benzoic acid



### ❖ **Physiochemical Properties**

- It is poorly water soluble. It is white to off-white crystalline powder with melting point 126-128°C and odourless.

### ❖ **Pharmaceutical Formulation**

- This drug is formulated from of tablet.

### ❖ **Stability and storage**

- Store it at room temperature (20°C -25°C) and away from light, excess heat, and moisture.

### ❖ **Popular Brand Names**

- Prandin
- Novonorm
- Enyglid

### ❖ **Dose**

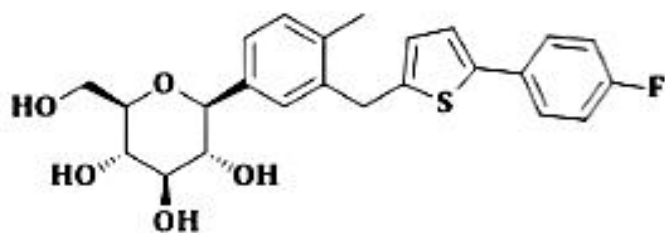
- 1-8 mg/day in 3-4 doses.

### ❖ **Medicinal Uses**

- Repaglinide is an oral medication used in addition to diet and exercise for blood sugar control in type 2 diabetes.

### ❑ **GLIFLOZINS**

- SGLT2 inhibitors, also called gliflozins or flozins are a class of medications that modulate sodium-glucose transport proteins in the nephron.
- The foremost metabolic effect of this is to inhibit reabsorption of glucose in the kidney and therefore lower blood sugar.



Canagliflozin



### ❖ **Physiochemical Properties**

- These are soluble in water.

### ❖ **Pharmaceutical Formulation**

- This drug is formulated from of tablet.

### ❖ Stability and storage

- Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light.

### ❖ Popular Brand Names

- Forxiga (Dapagliflozin)
- Invokana (Canagliflozin)
- Jardiance (Empagliflozin)

### ❖ Dose

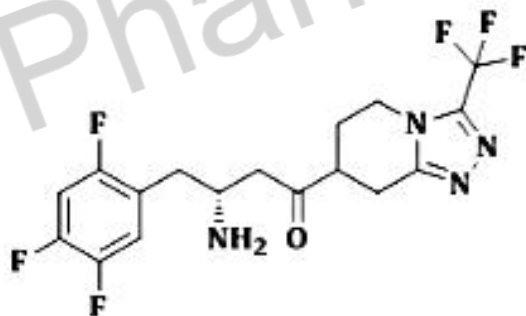
- The recommended starting dose is 5 mg orally once daily and maintenance dose is 10-25 mg once daily.

### ❖ Medicinal Uses

- SGLT2 inhibitors as a first-line pharmacological therapy for type 2 diabetes (usually together with metformin), specifically in patients with chronic kidney disease, cardiovascular disease or heart failure.

### ❑ GLIPTINS

- Dipeptidyl peptidase-4 inhibitors (DPP-4s), also commonly called gliptins, are a relatively new class of drugs for the treatment of type 2 diabetes.
- Glucagon increases blood glucose levels, and DPP-4 inhibitors reduce glucagon and blood glucose levels.



### ❖ Physiochemical Properties

- These drugs are soluble in water and organic solvents such as; ethanol, DMSO, and dimethyl formamide (DMF).
- Sitagliptin is white to off-white crystalline, non-hygroscopic powder.

### ❖ Pharmaceutical Formulation

- This drug is formulated from of tablet.

### ❖ Stability and storage

- Store it at room temperature (20°C -25°C) and away from light, excess heat, and moisture.