



# *Antidiabetics drugs*

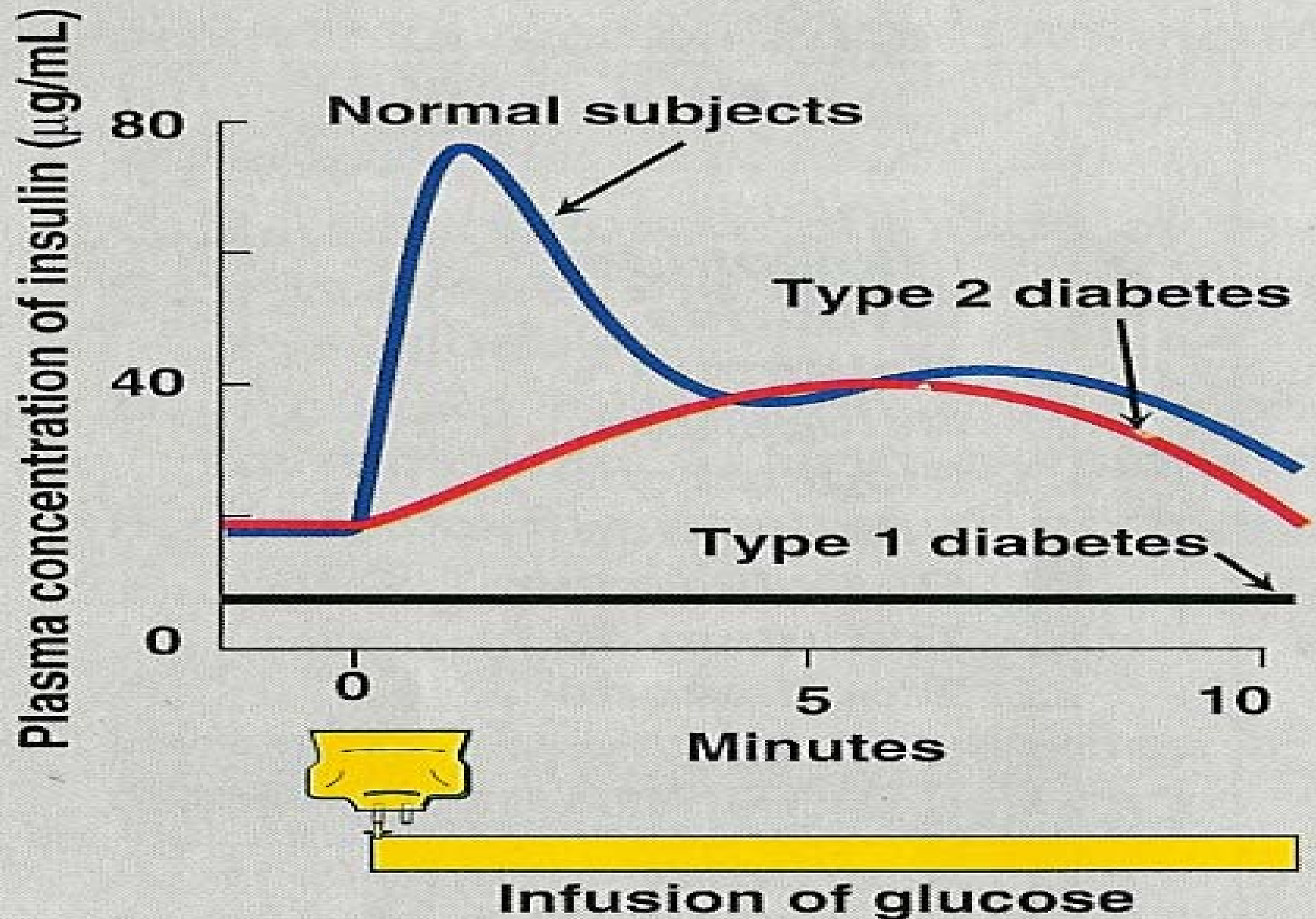
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*What is diabetes?*

*Types of diabetes?*

	<b>Type 1</b> (Insulin-dependent diabetes)	<b>Type 2</b> (Non-insulin-dependent diabetes)
Age of onset	Usually during childhood or puberty	Frequently over age 35
Nutritional status at time of onset	Frequently undernourished	Obesity usually present
Prevalence	10 to 20 percent of diagnosed diabetics	80 to 90 percent of diagnosed diabetics
Genetic predisposition	Moderate	Very strong
Defect or deficiency	$\beta$ Cells are destroyed, eliminating the production of insulin	Inability of $\beta$ cells to produce appropriate quantities of insulin; insulin resistance; other defects

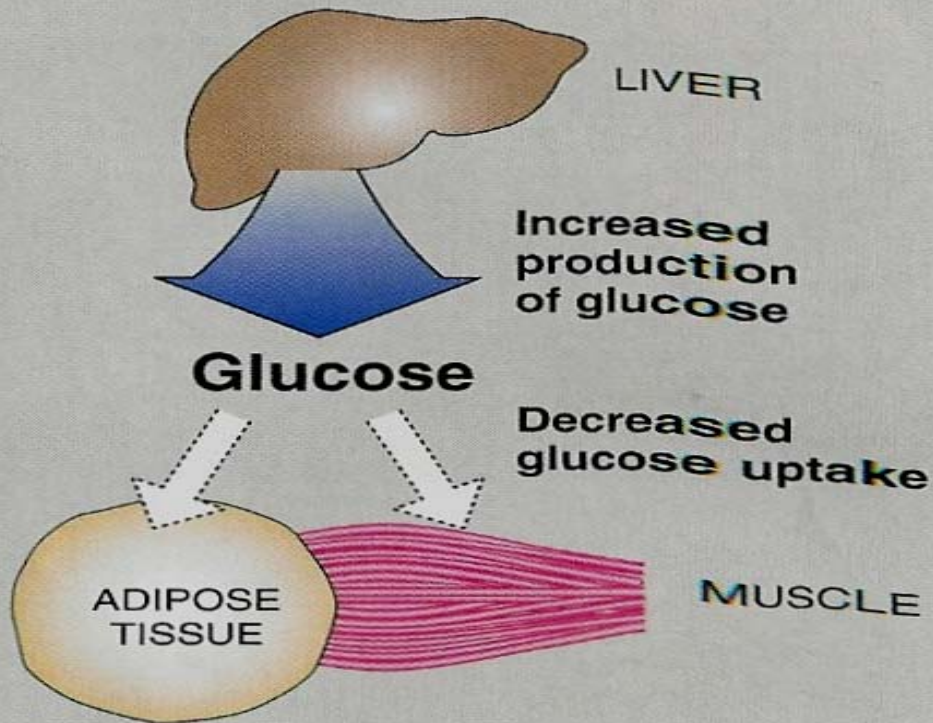
# Types of diabetes



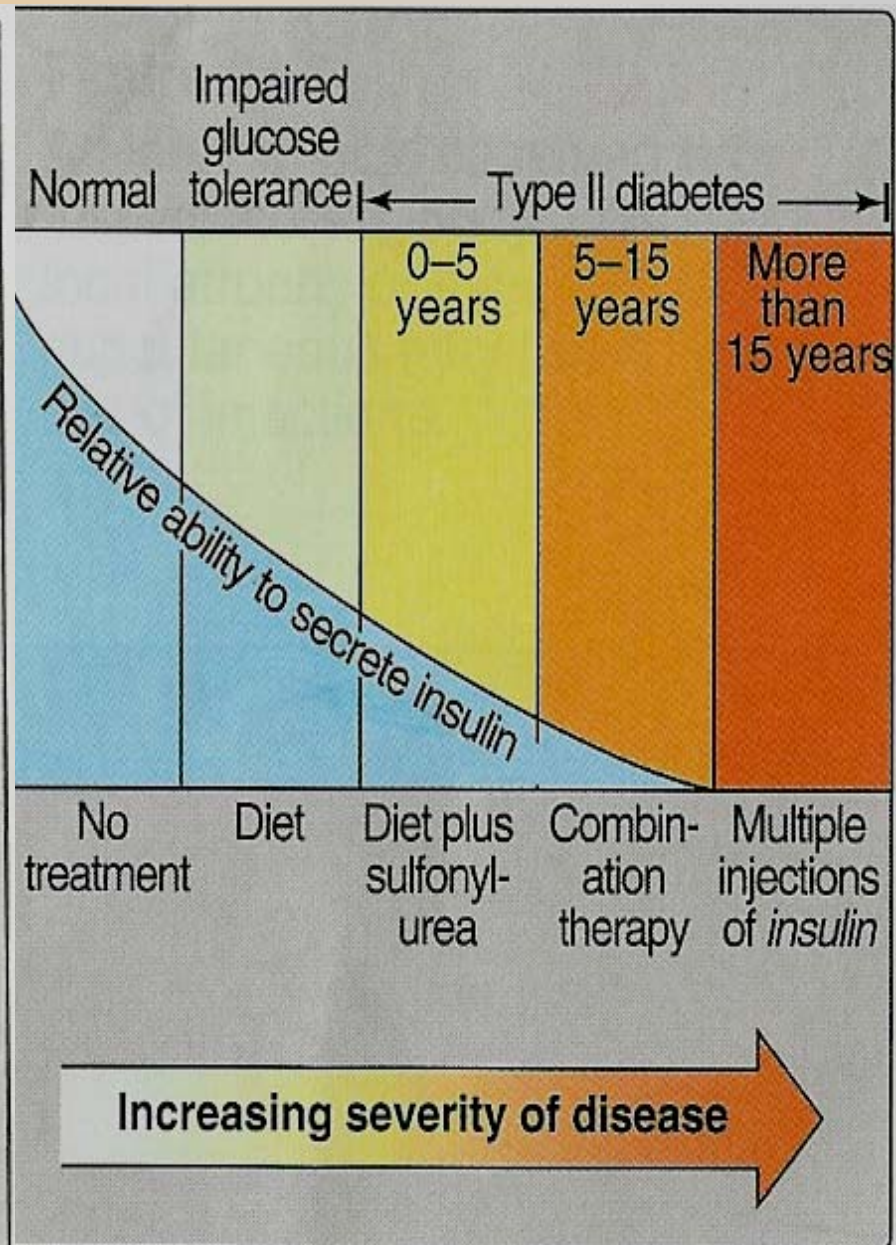


# Types II diabetes

## 1 Insulin resistance in peripheral tissues

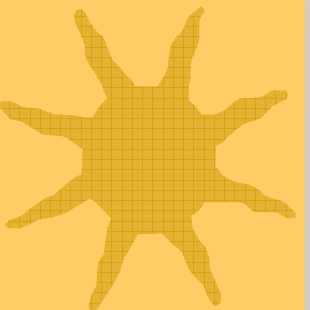
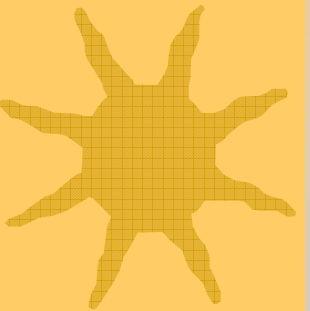
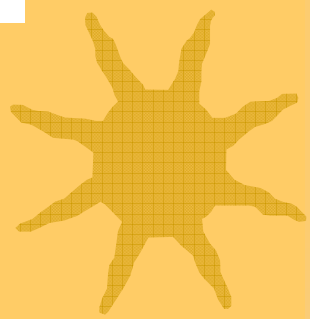


## 2 Inadequate insulin secretion from $\beta$ cells



# Type II Diabetes

- ★ **Inadequate insulin secretion.**
  - ★ **Insulin resistance in target tissues.**
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# Complications of diabetes



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**Renal failure (Nephropathy).**

**Blindness (Retinopathy).**

**Neuropathy.**





# Antidiabetics drugs

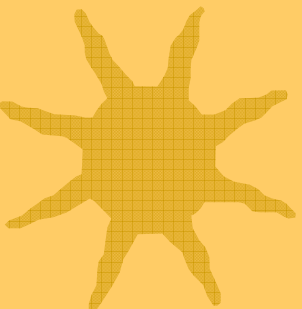
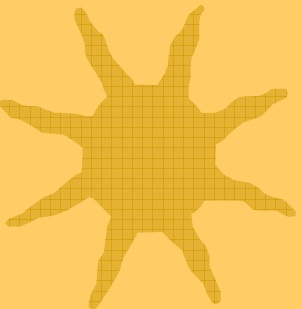


**1. Insulin**

**2. Oral hypoglycemic drugs**

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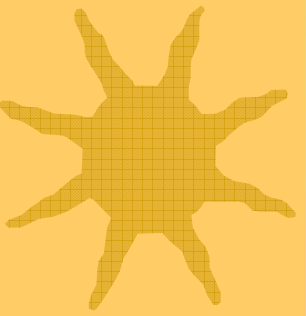
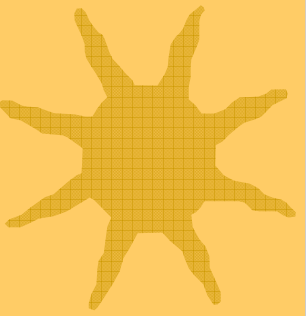
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# *ORAL HYPOGLYCAEMIC DRUGS*

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- ★ **1. Sulfonylurea drugs**
  - ★ **2. Meglitinide analogues**
  - ★ **3. Biguanides**
  - ★ **4. alpha-glucosidase inhibitors.**
  - ★ **5. Thiazolidinediones.**





# ORAL HYPOGLYCAEMIC DRUGS

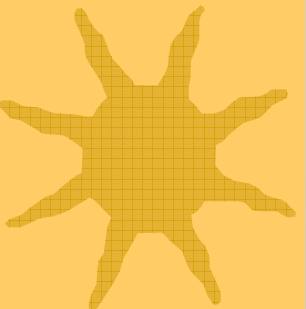
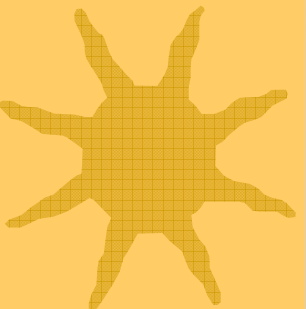
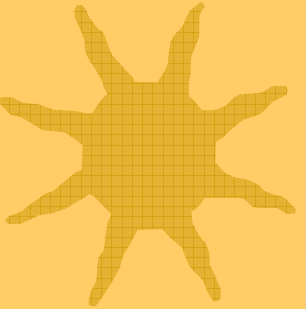
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## Insulin secretagogues

- ★ 1. Sulfonylurea drugs
- ★ 2. Meglitinide analogues
- ★ 3. D-phenylalanine derivatives

## Insulin sensitizers

- ★ 1. Biguanides
- ★ 2. Thiazolidinediones or glitazones



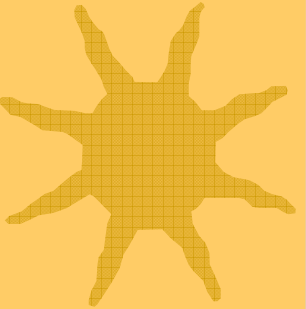
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### **III. Alpha glucosidase inhibitors**

### **IV. Gastrointestinal hormones**



# *Insulin secretagogues*



## **I. SULFONYLUREAS:**

### **First generation**

**Tolbutamide**

**Tolazamide**

**Acetohexamide**

**Chlorpropamide**

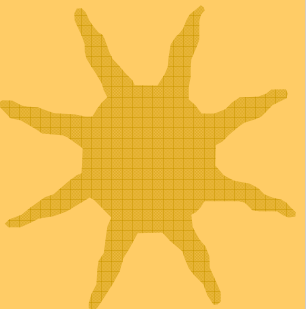
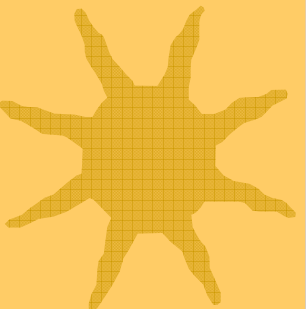
### **Second generation**

**Glipizide**

**Glyburide**

**(Glibenclamide)**

**Glimepiride**





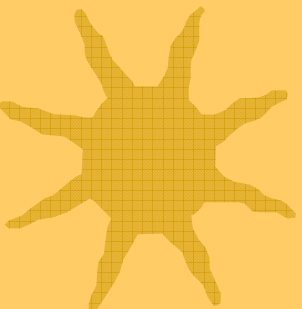
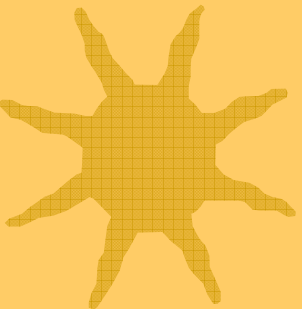
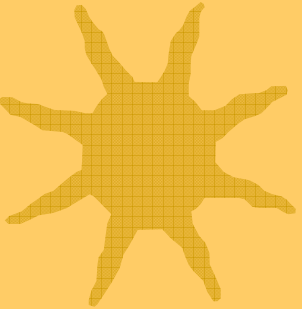
# I. *SULPHONYLUREA*

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## Mechanism of Action:

- ★ Stimulate insulin release from functioning B cells by blocking of ATP-sensitive K channels resulting in depolarization and calcium influx.
- ★ Reduction of serum glucagon concentration
- ★ Increase tissue sensitivity to insulin.







## Pharmacokinetics:

★ Orally, well absorbed.

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★ Reach peak concentration after 2-4 hr.

★ All are highly bound to plasma proteins.

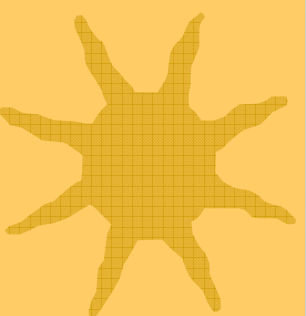
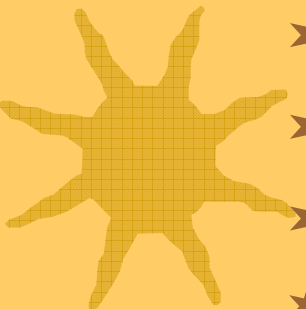
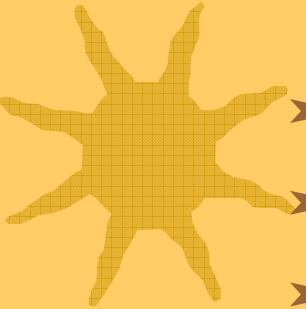
★ Duration of action is variable.

★ Second generation has longer duration.

★ Metabolized in liver

★ excreted in urine (**elderly and renal disease**).

★ Cross placenta, stimulate fetal B cells to release insulin  
—> hypoglycemia at birth.





# *SULFONYLUREAS*

## First generation

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### Short:

**Tolbutamide (8 h)**

### Intermediate:

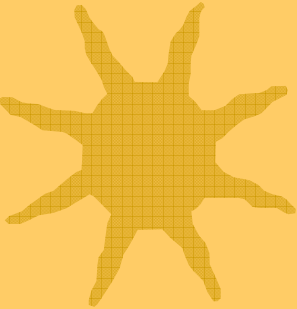
**Tolazamide – Acetohexamide (20 h)**

**Long: Chlorpropamide (60 h)**



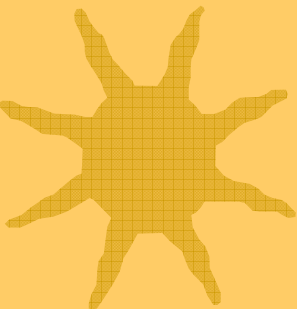
# ***SULFONYLUREAS***

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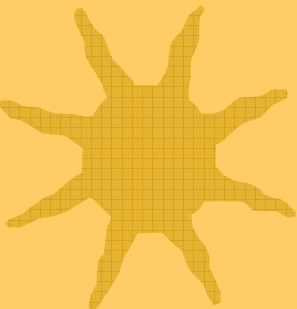
## **Tolbutamide**

- ☞ **Given in divided doses**
- ☞ **no active metabolite**
- ☞ **the Safest sulfonylureas for old patients**



## **Tolazamide**

- ☞ **active metabolites**
- ☞ **slowly absorbed than others**



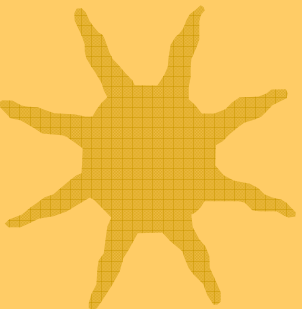
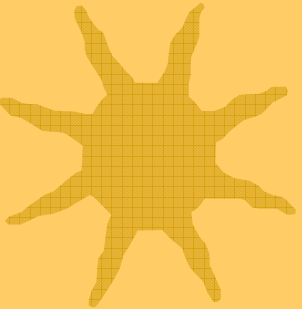
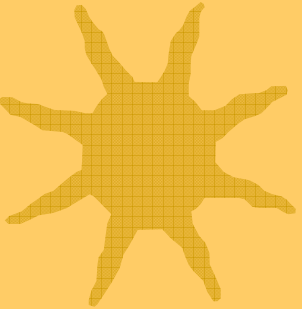


# *SULFONYLUREAS*

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## **Chlorpropamide**

- ☞ Given as single morning dose (60 h)
- ☞ no active metabolite.
- ☞ **XXX** hepatic-renal disease-old patients  
(prolonged hypoglycemia)
- ☞ Dilutional hyponatremia
- ☞ Hyperemic flush after alcohol ingestion.
- ☞ Leukopenia, thrombocytopenia







# *SULFONYLUREAS*

## Second generation

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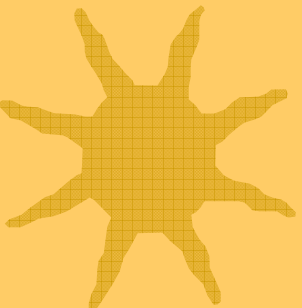
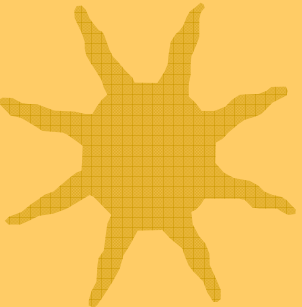
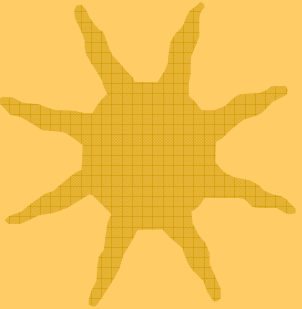
- ★ **More potent**
- ★ **have fewer adverse effects**
- ★ **have fewer drug interactions**
- ★ **has longer duration (24 h)**
- ★ **E.g. Glipizide, glyburide, glimepiride**



## Glipizide,

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- ☞ **Has the shortest half life (2-4)**
- ☞ **duration of action (10-16 h)**
- ☞ **no active metabolites.**
- ☞ **Absorption is retarded with food**
- ☞ **Given in divided doses before meals**
- ☞ **Extended release preparation  
(Glucotrol XL) provides 24 h action  
(a single morning dose).**





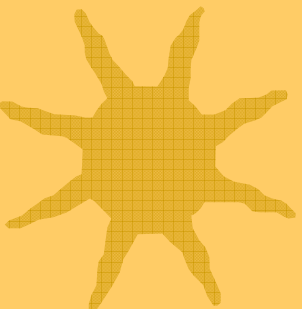
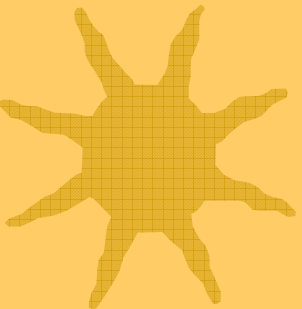
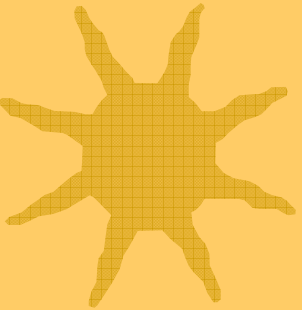
## Glyburide (Glibenclamide)

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- ∞ Long acting (24 h)
- ∞ No active metabolite

## Glimepiride

- ∞ The most potent
- ∞ Single morning dose is used (1 mg)
- ∞ Long acting (24 h)
- ∞ No active metabolite.





## Unwanted Effects:

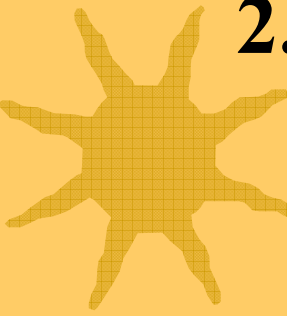
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### 1. Hypoglycemia:

- ★ More in chlorpropamide & glibenclamide
- ★ Less in tolbutamide.
- ★ More in elderly and patients with renal disease.



### 2. Weight gain – increase appetite.





## Unwanted Effects:

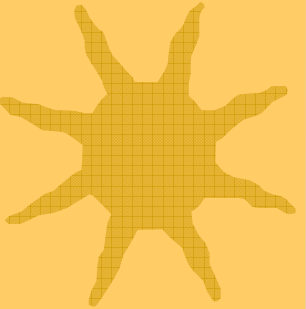
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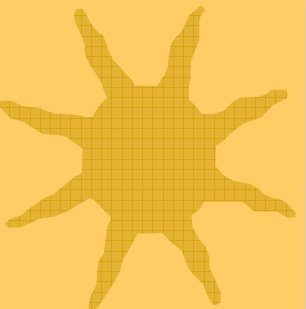
- ★ GIT upset.
- ★ Allergic skin rash.
- ★ Bone marrow damage.
- ★ Dilutional hyponatremia, water intoxication (**Chlorpropamide**) vasopressin effect.
- ★ Disulfiram-like reaction with alcohol (**chlorpropamide**).
- ★ Tachyphylaxis (secondary failure).



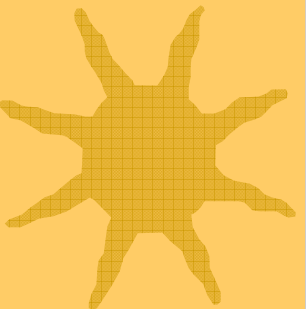
# Drug Interactions



## Drugs Which Augment Hypoglycemic Effect:



- ★ **NSAI: Phenylbutazone and salicylates.**
- ★ **Coumarin anticoagulants.**
- ★ **Alcohol.**
- ★ **Antibiotics: Sulphonamides, chloramphenical.**
- ★ **Antifungal Drugs: Fluconazole.**





## Agents Which Decrease Action of Sulphonylureas:

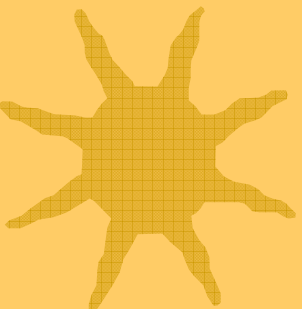
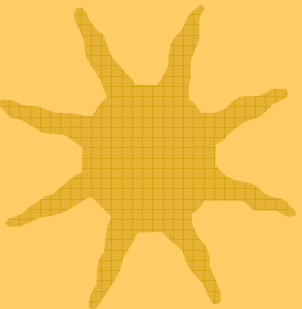
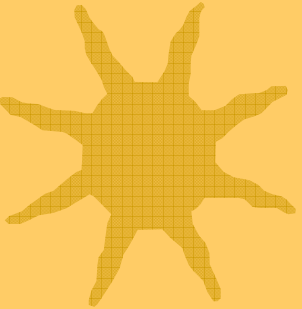
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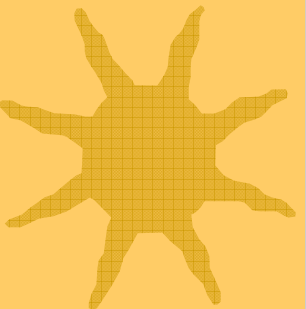
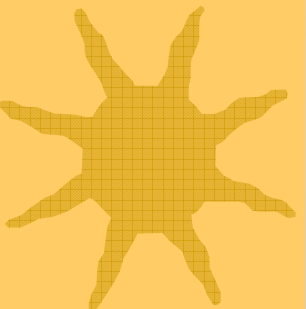
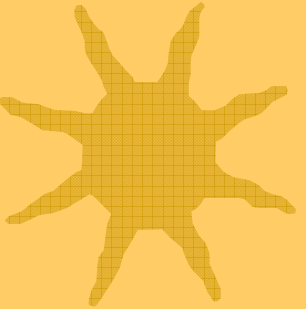
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- ★ **Microsomal inducers.**
- ★ **Diuretics: *Thiazide and Furosemide.***
- ★ **Corticosteroids.**
- ★ **Diazoxide.**

### CONTRAINDICATIONS:

- ★ **Pregnancy (use insulin)**
- ★ **Hepatic or renal insufficiency**





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★ *Insulin secretagogues*

★ **1. Sulphonylurea**

★ **2. Meglitinide analogues**

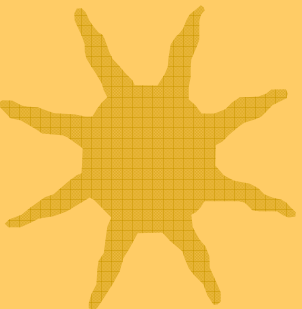
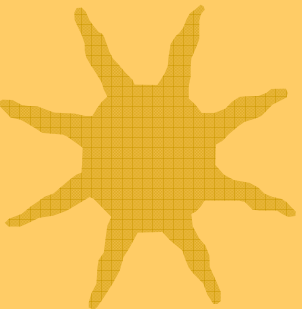
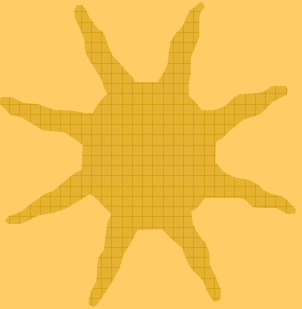




## *Insulin secretagogues*

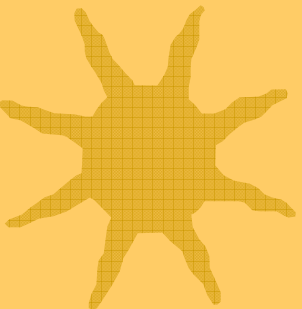
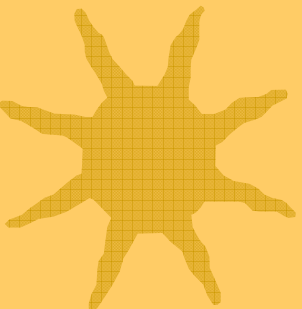
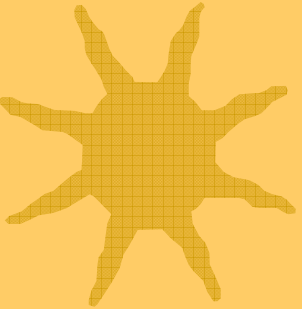
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- ★ **Meglitinide analogues**  
are rapidly acting insulin secretagogues
- ★ **Repaglinide (Prandin)**
- ★ **Nateglinide (Starlix)**





# Repaglinide



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## Mechanism of Action:

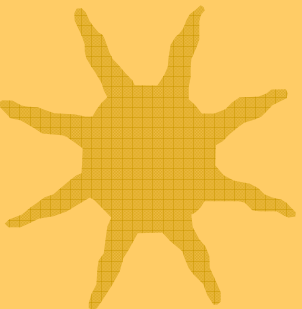
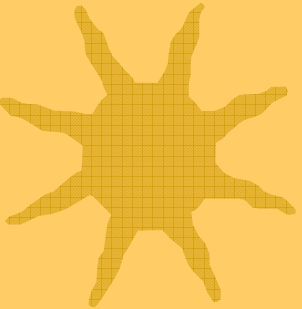
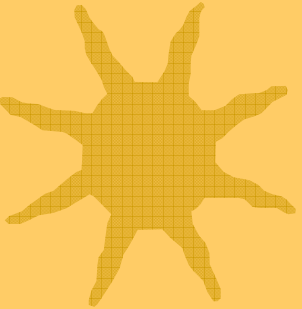
- ★ Stimulate insulin release from functioning B cells by modulating K efflux via blocking ATP-sensitive K channels resulting in depolarization and calcium influx.



# *Pharmacokinetics of repaglinide*

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- ★ Orally, well absorbed.
- ★ Very fast onset of action, peak 1 h.
- ★ short duration of action (4 h).
- ★ Metabolized into inactive products in liver (CYP3A4).
- ★ excreted mainly in the bile.
- ★ Effective in early release of insulin after a meal (**Post prandial glucose regulators**).
- ★ Taken just before meals.





# Uses of repaglinide

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1. Regulation of post prandial glucose excursions.

Monotherapy or combined therapy with metformin (*better than monotherapy*).

2. Patients allergic to sulfonylureas

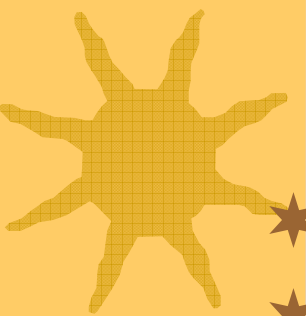
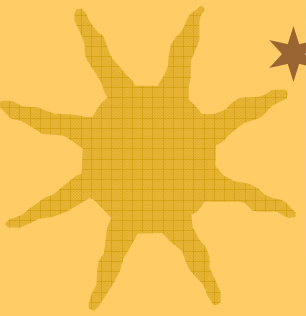
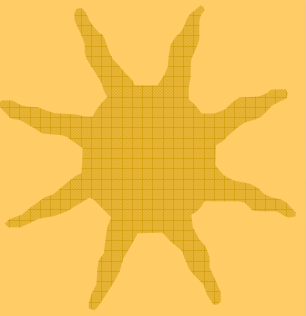


# *Adverse effects of repaglinide*

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**less incidence than sulfonylureas**

- 
- ★ **Hypoglycemia (meal is delayed).**
  - ★ **Weight gain.**
  - ★ **Drug interactions.**
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# Drug Interactions

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1. Enzyme inhibitors as cimetidine, fluconazole, erythromycin.
2. Enzyme inducers barbiturates, rifampicin and phenytoin.
3. Gemfibrozil augment action of repaglinide.

## Contraindications

Hepatic impairment.





# ORAL HYPOGLYCAEMIC DRUGS

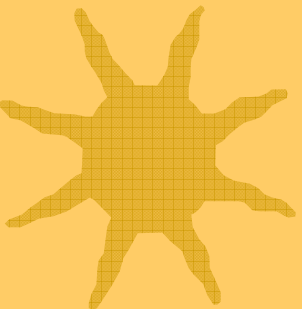
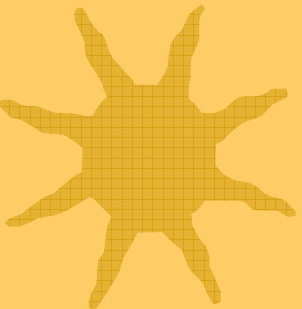
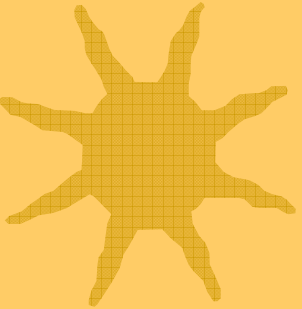
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## ★ Insulin sensitizers

★ 1. Biguanides

★ 2. Thiazolidinediones or glitazones





# *BIGUANIDES*

## *Metformin*

### Mechanism of action:

- ★ Does not require functioning *B* cells.
- ★ Does not stimulate insulin release.
- ★ Increases peripheral glucose utilization (**tissue glycolysis**).
- ★ Inhibits gluconeogenesis.
- ★ Impairs glucose absorption from GIT.
- ★ Increase glucose conversion to lactate.
- ★ Reduces plasma glucagon level.
  - ↓LDL&VLDL.
  - ↑ HDL



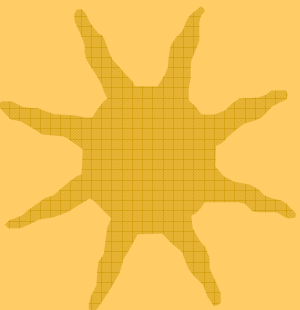
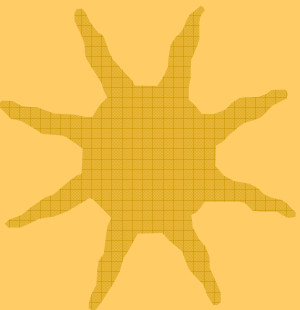
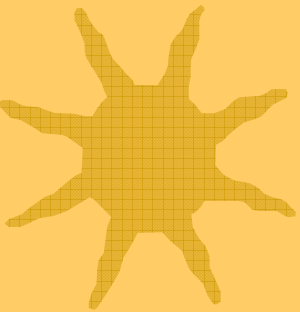
# ***I. BIGUANIDES***

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## **Pharmacokinetics:**

- ★ orally.
- ★ NOT bound to serum protein.
- ★ NOT metabolized.
- ★  $t_{1/2}$  3 hours.
- ★ Excreted unchanged in urine





## Therapeutic Uses:

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- ★ Has insulin sparing effect (insulin sensitizer).
- ★ Obese patients with type II diabetes (with insulin resistance).
- ★ Monotherapy or in combination.

## Advantages:

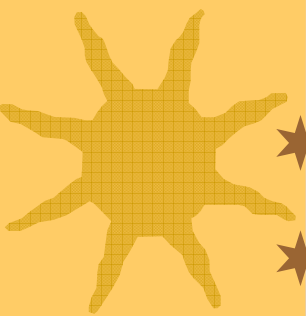
- ★ No hypoglycemia or weight gain (anorexia).



## Adverse Effects:

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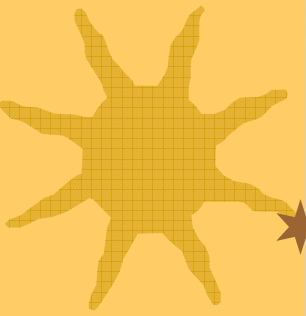
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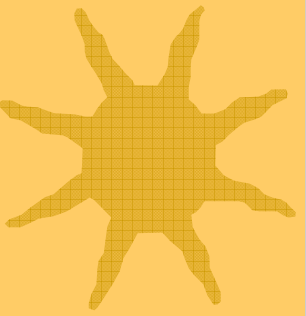
★ **Transient GIT disturbances (NVD).**

★ **Lactic acidosis:**

**Common in patients with Renal disease, Liver, Pulmonary or Cardiac disease.**



★ **Long term use interferes with B<sub>12</sub> absorption.**



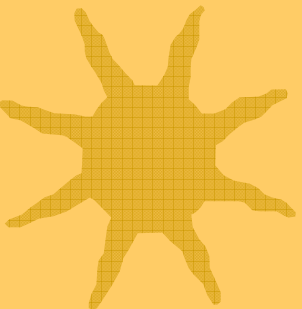
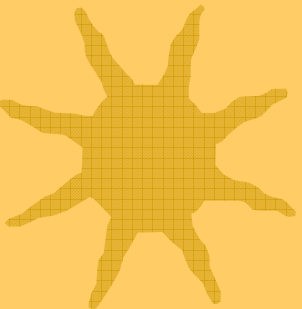
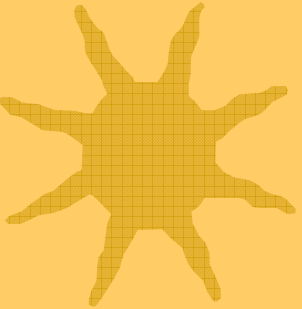


## Contraindications

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- ★ **Pregnancy.**
- ★ **Renal disease.**
- ★ **Liver disease.**
- ★ **Alcoholism.**
- ★ **Conditions predisposing to hypoxia as cardiopulmonary dysfunction.**

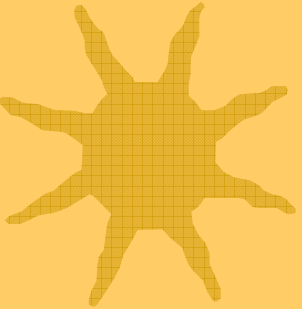




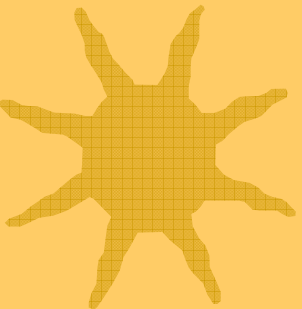
## *Insulin sensitizers*

### *Thiazolidinediones (glitazones)*

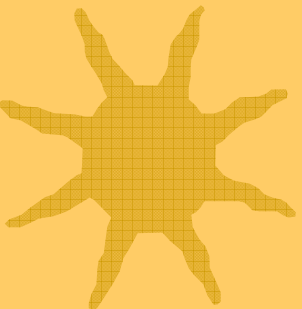
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★ Rosiglitazone (**Avandia**)



★ Pioglitazone (**Actos**)



★ Troglitazone (**withdrawn due to hepatotoxicity**).

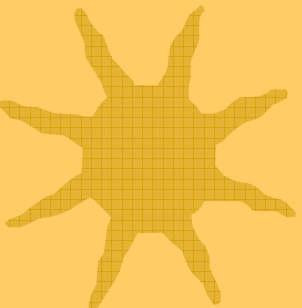
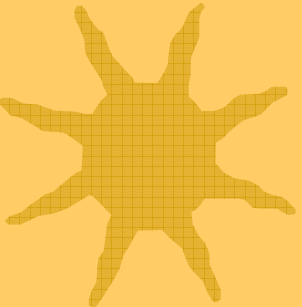
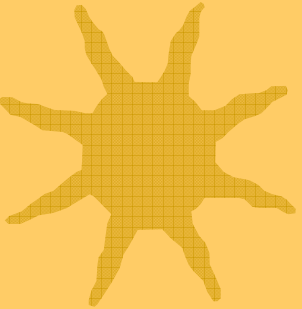




# Thiazolidinediones

## Mechanism of action

- Activate nuclear receptors (peroxisome proliferator-activated receptor - $\gamma$ ) (PPAR- $\gamma$ ).
- Increase sensitivity of target tissues to insulin.
- Increase glucose uptake and utilization in muscle and adipose tissue.
- Increase insulin sensitivity (↓ insulin resistance).





# THIAZOLIDINEDIONES

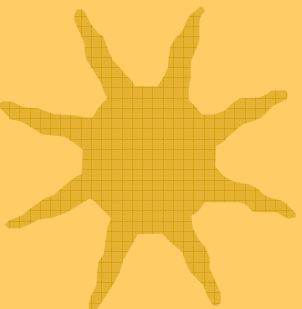
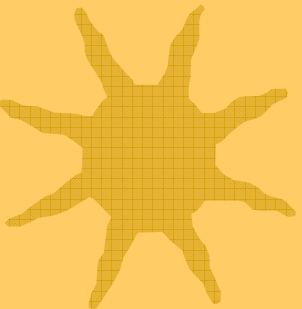
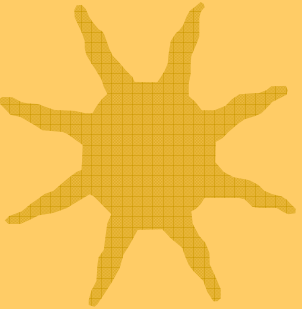
## Mechanism of action

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### PPAR- $\gamma$

- Nuclear receptors.
- Liver, skeletal muscles, Adipose tissue.
- Control genes involved in glucose and lipid metabolism.
- Increase insulin sensitivity in muscle and adipose tissue.
- ↓ triglycerides.
- ↑ HDL

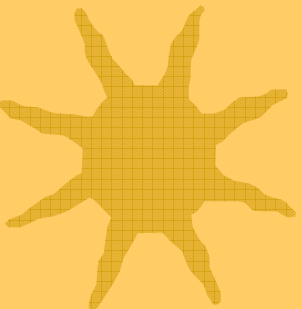
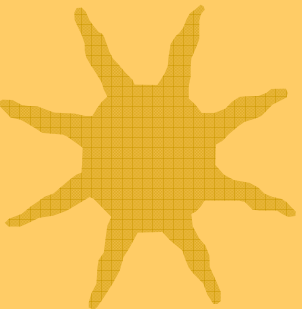
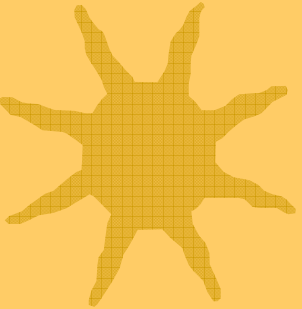




# THIAZOLIDINEDIONES

## Pharmacokinetics

- Orally (once daily dose).
- Highly bound to plasma albumins.
- Slow onset of activity
- Half life 3-4 h
- Metabolized by CYP450.
- Pioglitazone (Active metabolites).
- Excreted in urine & bile.
- Triglyceride lowering effect is more with pioglitazone than rosiglitazone.





# THIAZOLIDINEDIONES

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## Indications:

- ★ Type II diabetes with insulin resistance.
- ★ Used either alone.
- ★ Combined with sulfonylurea, Biguanides or insulin.
- ★ Rosiglitazone should not be combined with insulin (Edema).
- ★ Anovulatory women (polycystic ovarian syndrome).

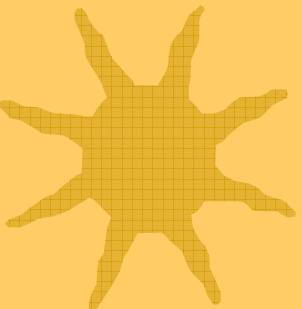
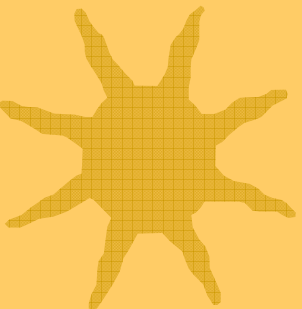
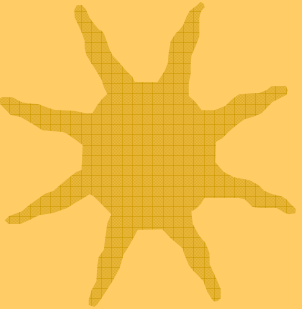


# THIAZOLIDINEDIONES

## Contraindications

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- ★ Heart failure.
- ★ Pregnancy.
- ★ Significant liver disease.



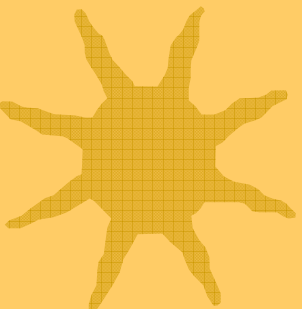
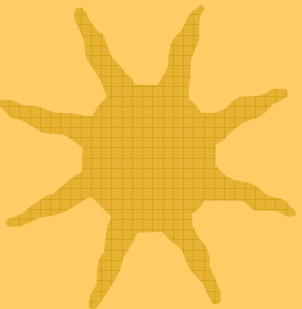
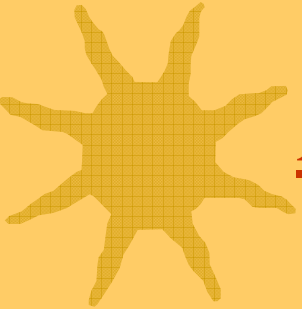


# THIAZOLIDINEDIONES

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## Adverse Effects:

- ★ Fluid retention (Edema).
- ★ Weight gain.
- ★ Headache.
- ★ Liver function tests for 1<sup>st</sup> year of therapy.
- ★ Failure of estrogen-containing oral contraceptives.

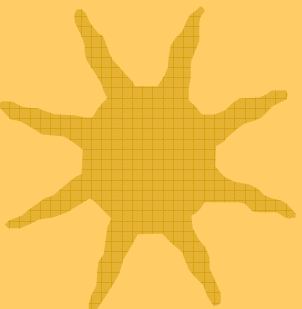
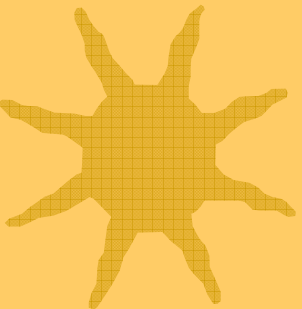
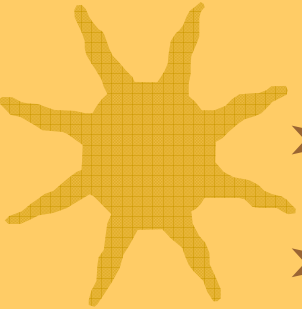




# *$\alpha$ -GLUCOSIDASE INHIBITORS*

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- ★ **Acarbose (Precose).**
- ★ **Miglitol (Glyset).**







# *$\alpha$ -GLUCOSIDASE INHIBITORS*

- ★ Reversible inhibitors of intestinal  $\alpha$ -glucosidases.
- ★  **$\alpha$ -glucosidases:** degradation of oligosaccharides to monosaccharides.
- ★ include sucrase, maltase, dextranase, glycoamylase.



# *$\alpha$ -GLUCOSIDASE INHIBITORS*

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- ★ **Decrease postprandial digestion and absorption.**
- ★ **Decrease postprandial hyperglycemia.**
- ★ **Taken just before meals.**
- ★ **No hypoglycemia if used alone.**



# $\alpha$ -GLUCOSIDASE INHIBITORS

## *Pharmacokinetics*

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### Acarbose

- ★ poorly absorbed.
- ★ Metabolized by bacteria.
- ★ Excreted in urine.

### Miglitol

- ★ Well absorbed, no systemic effects.
- ★ Excreted unchanged in urine.
- ★ 6 times more potent inhibitor for sucrase.



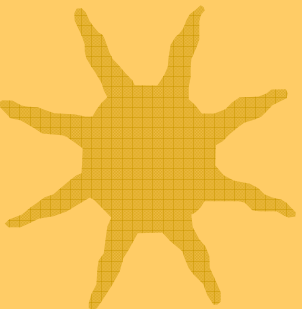
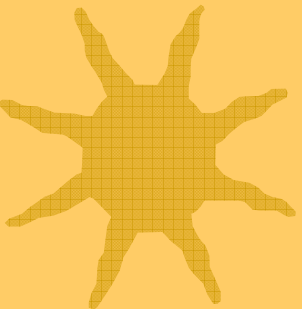
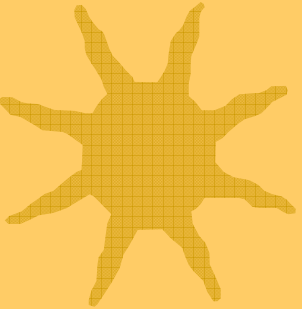
# *$\alpha$ -GLUCOSIDASE INHIBITORS*

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## *Uses*

- ★ **Type II diabetics.**
- ★ **alone or combined with insulin or sulfonylurea.**
- ★ **Hypoglycemia may develop & treated by glucose **Not sucrose**).**



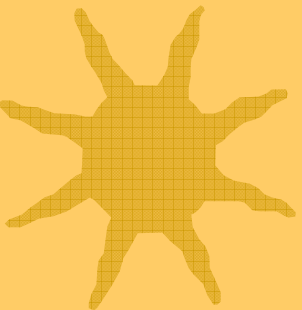
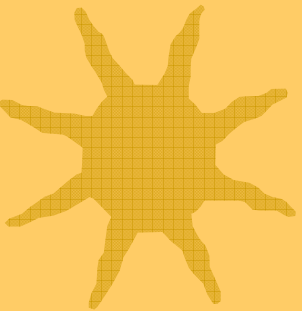
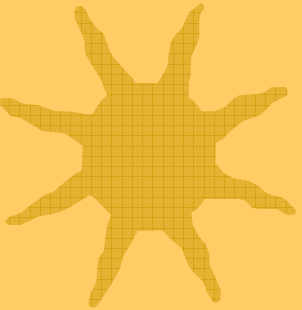


## Adverse Effects:

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- ★ **GIT: Flatulence, diarrhea, abdominal pain, bloating, increase in liver enzymes.**



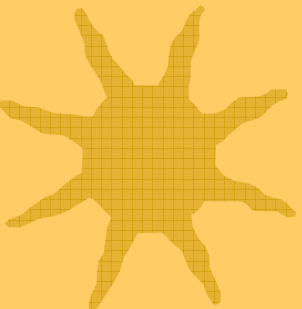
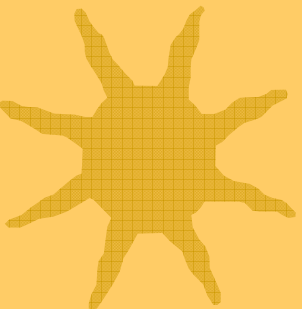
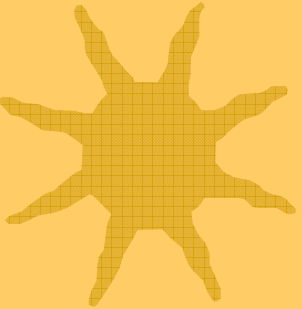


## Contraindications

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- ★ **Inflammatory bowel disorders (IBD).**
- ★ **Renal disease.**
- ★ **Hepatic disease (used with caution).**
- ★ **Intestinal obstruction.**





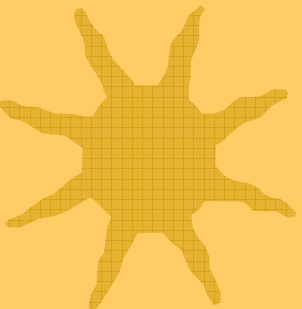
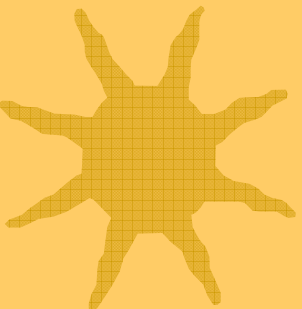
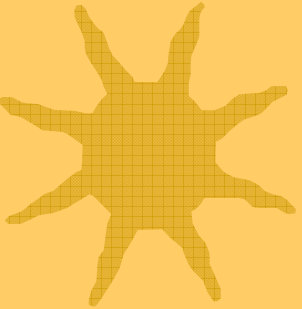
# *INSULIN*

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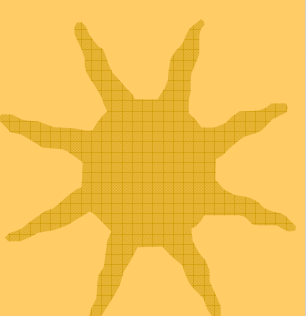
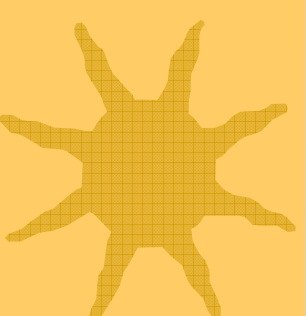
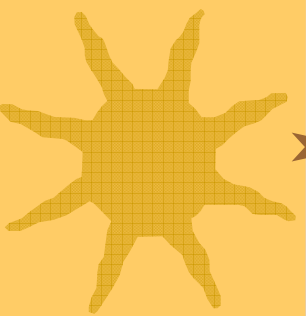
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## HISTORY:

- ★ The hypoglycemic effects of pancreatic extract were first published by Kleiner in 1919.







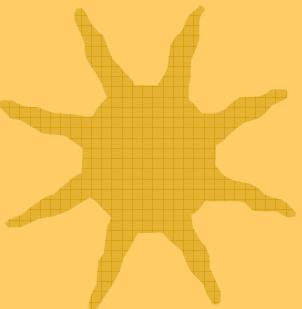
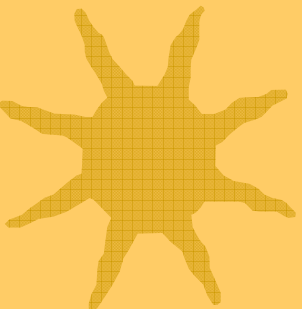
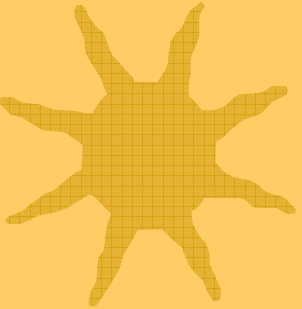
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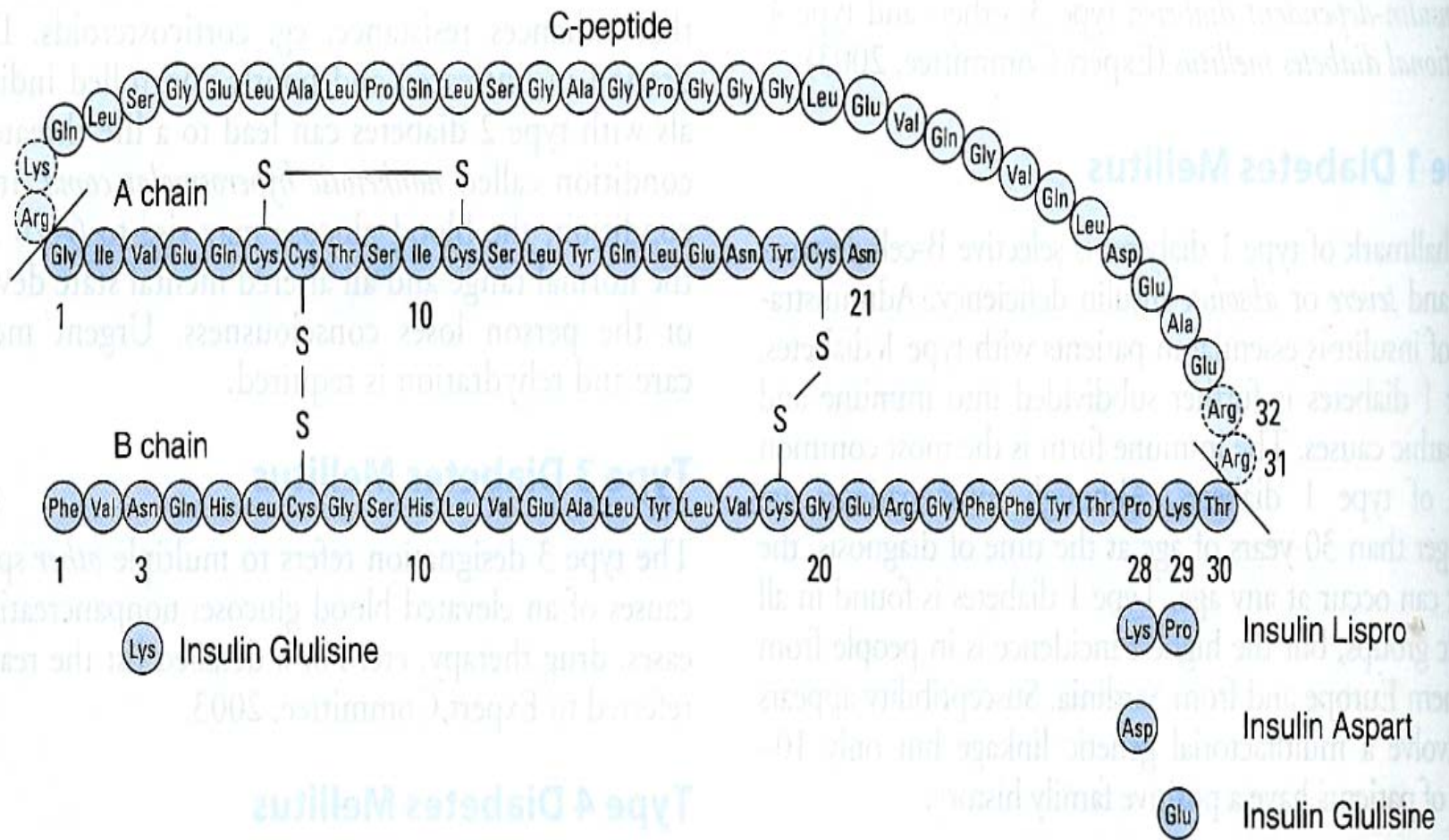
★ **The isolation of insulin in 1921 by Frederick Grant Banting and Charles H. Best ( in collaboration with JJR Macleod and James B. Collip) led to a revolution in the management of diabetes.**



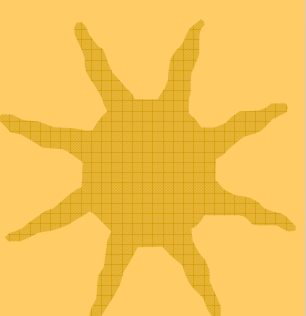
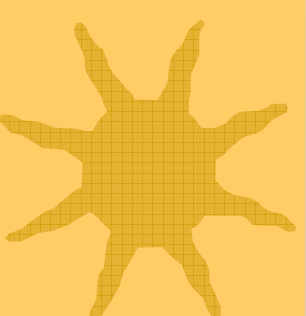
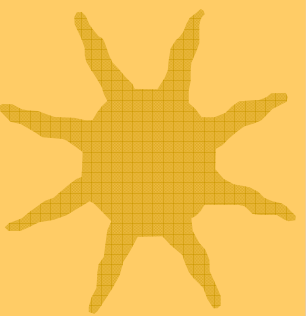
## Chemistry:

- ★ Polypeptide hormone MW 5808.
- ★ Contains 51 amino acids arranged in two chains A (21) & B (30) linked by two disulphide bridges.
- ★ B cells of pancreatic islets synthesize insulin from a single chain precursor called Proinsulin.





**Figure 41-1.** Structure of human proinsulin and some commercially available insulin analogs. Insulin is shown as the shaded (darker color) peptide chains, A and B. Differences in the A and B chains and amino acid modifications for insulin aspart, lispro, and glulisine are noted.



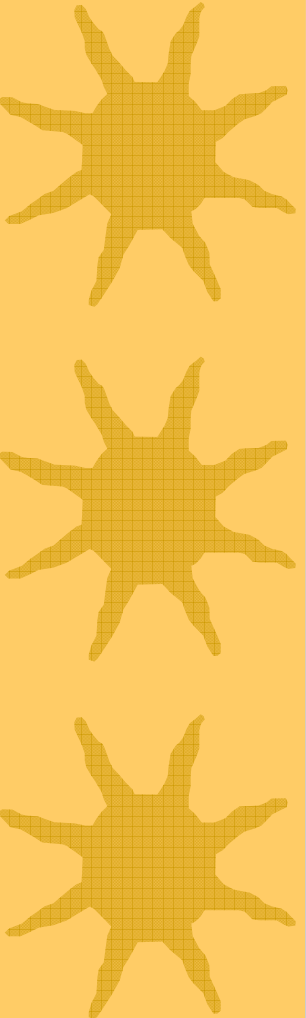
- 
- ★ **Proinsulin is hydrolyzed into insulin & a residual segment C-peptide.**
  - ★ **Insulin and C-peptide are secreted in equimolar amounts in response to all insulin secretagogues.**
  - ★ **Proinsulin might have mild hypoglycaemic action but C-peptide is inactive.**



## Storage

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- ★ Formed insulin is stored within B cell in the form of crystals consisting of **2 atoms of zinc and 6 molecules of insulin** which is equal to 200 biologic units.
- ★ One milligram contains 28 units.





## *Species of Insulin*

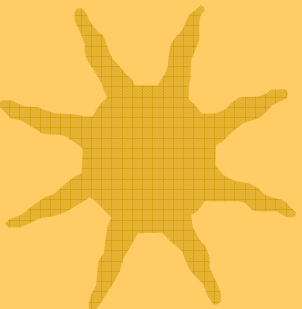
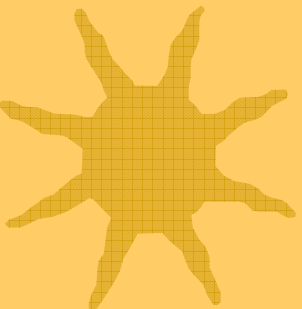
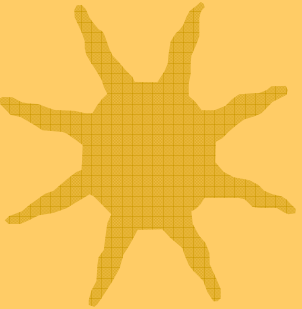
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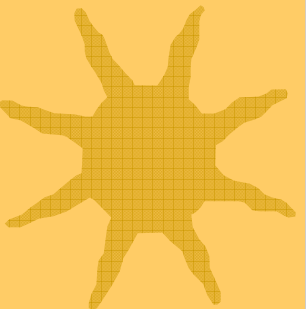
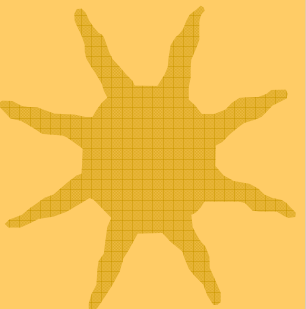
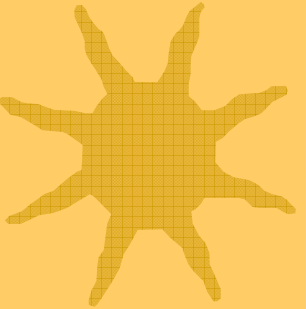
### ★ **Beef Insulin**

- Differs by 3 AA from human insulin (more antigenic). It is isolated and purified from beef insulin.

### ★ **Porcine Insulin**

- Differs by one AA. Now they usually mix 70% beef and 30% pork.





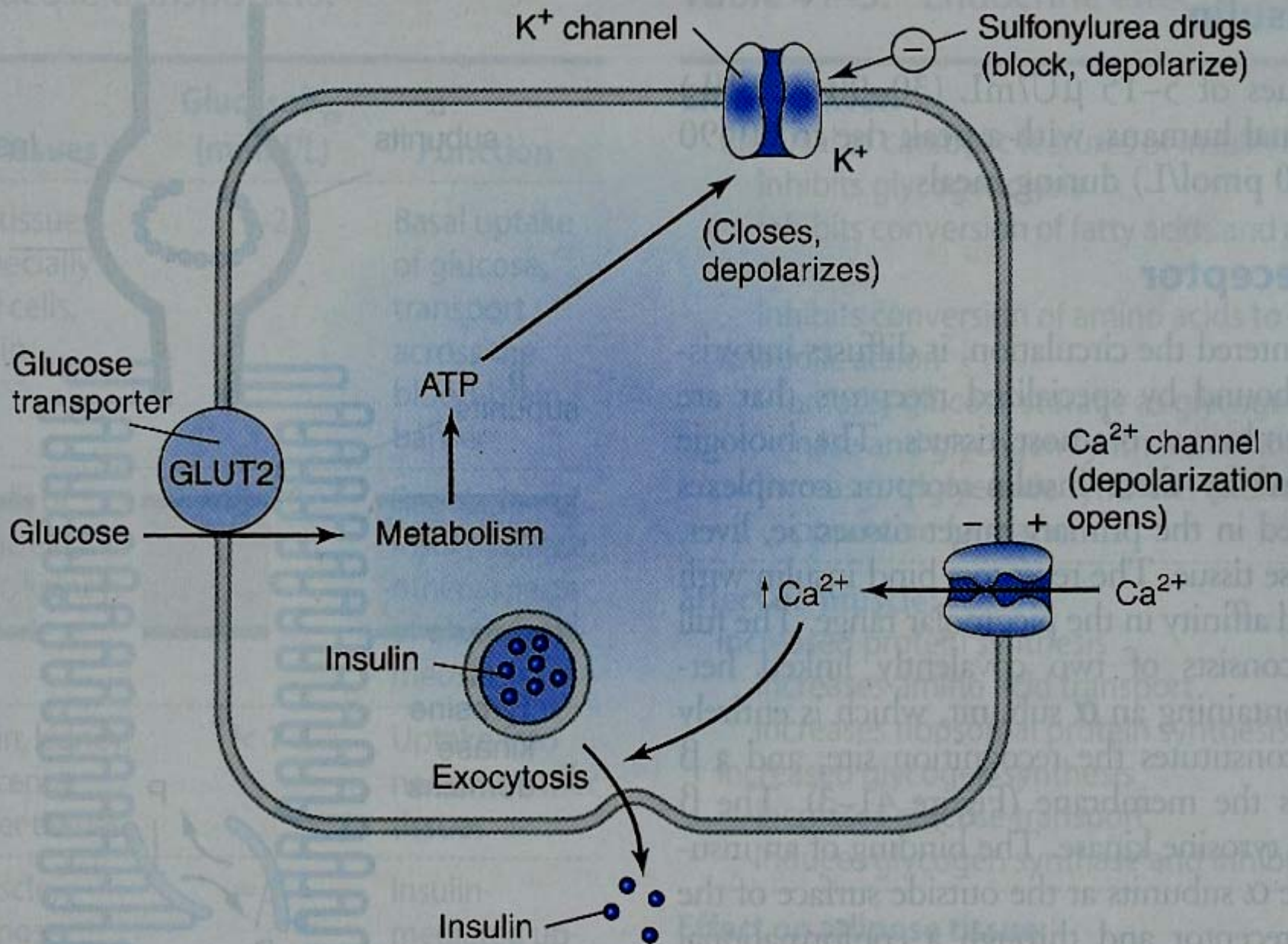
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## ★ **Human Insulin.**

- **Recombinant DNA techniques.**
- **Less immunogenic.**
- **It contains a threonine molecule , allows more rapid absorption and short duration of action.**
- **Mixing with phosphate buffer reduces aggregation of regular insulin in infusion pumps.**



# Mechanisms of Insulin Release:

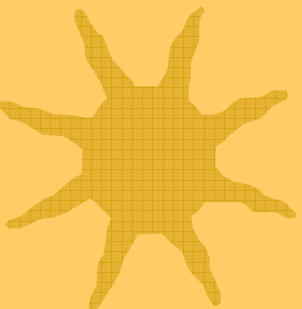
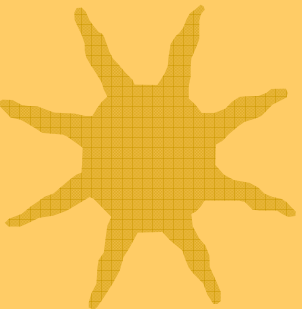
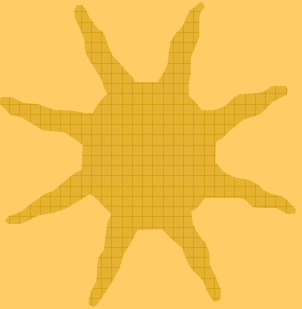






# 1. Stimulants of insulin secretion

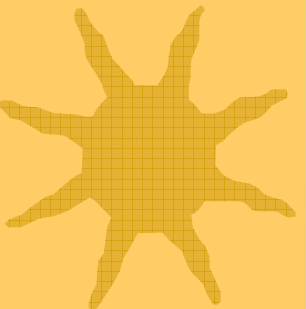
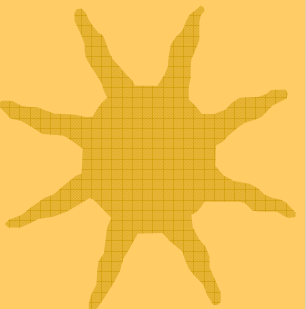
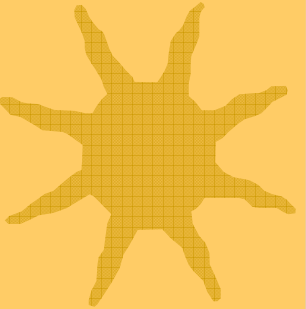
- 
- **Glucose, mannose**
  - **Vagal stimulation.**
  - **Glucose binds to glucoreceptors in  $\beta$  cells  $\rightarrow$   $\uparrow$  cAMP  $\rightarrow$  Ca influx  $\rightarrow$  insulin release by exocytosis.**





## 2. Amplifiers of glucose-induced insulin secretion

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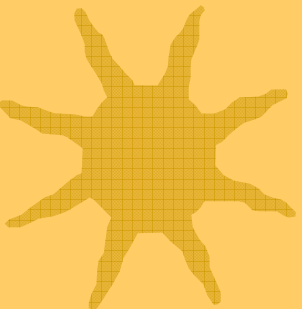
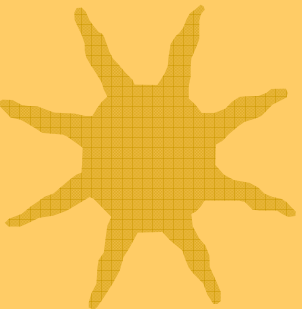
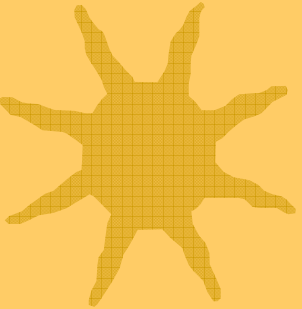


- **Amino acids (arginine)**
- **Gastrointestinal Hormones**
  - **Secretin**
  - **Gastrin**
  - **Cholecystokinin**
- **$\beta$ -adrenergic agonists.**



## ★ 3. inhibitors of insulin secretion

- 
- **$\alpha$ -sympathomimetics**
  - **Somatostatin.**
  - **Drugs: Diazoxide.**

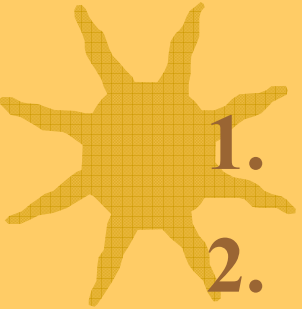




## Insulin degradation

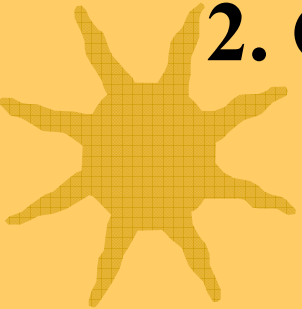
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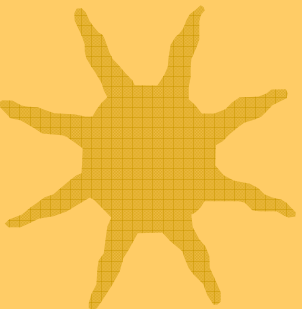


**1. Basal level of insulin is 5-15  $\mu$ U/ml.**

**2. Half life of circulating insulin is 3-5 min.**



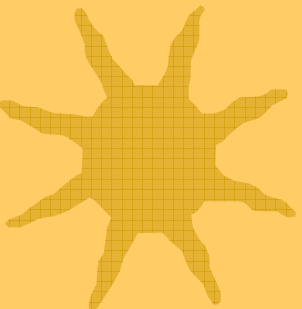
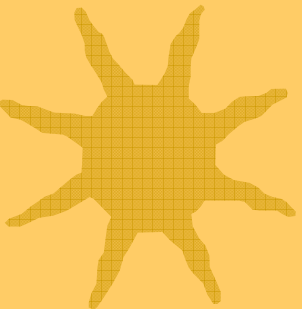
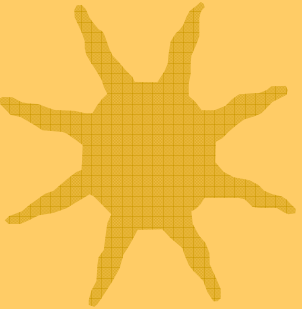
**2. Cleared by kidney & liver.**





## Insulin receptors

- 
- Present on cell membranes of most tissues.
  - Liver, muscle and adipose tissue
  - glycogen in liver and skeletal muscles.





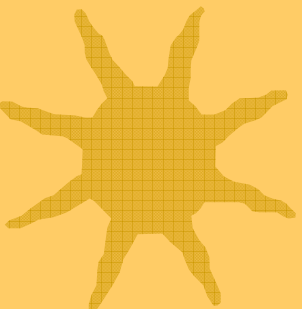
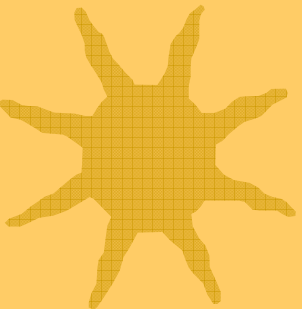
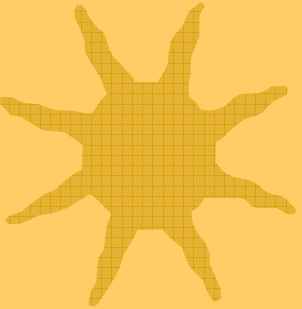
# Pharmacodynamics of insulin:

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## Lowering of blood sugar by:

- Utilization of glucose by peripheral tissues.
- Promoting synthesis and storage of glycogen in liver and skeletal muscles.

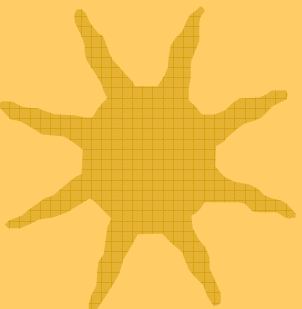
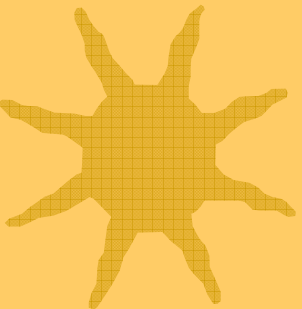
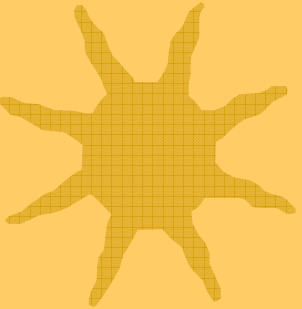




# I. Carbohydrate Metabolism:

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- ↑ glycogen synthesis (**glycogen synthase**)
- ↓ gluconeogenesis.
- ↓ glycogenolysis (liver).
- ↓ Glycolysis (muscle).
- ↑ glucose uptake & utilization.
- ↑ Conversion of carbohydrate to fats.





## II. Fat Metabolism:

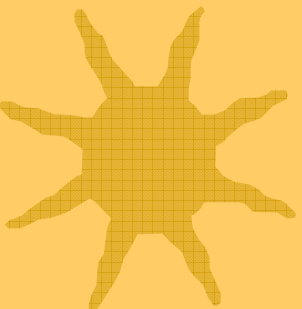
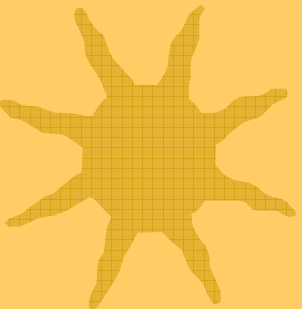
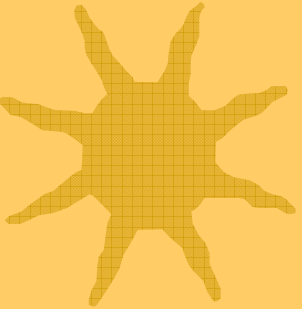
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### ★ **Liver:**

- ↑ triglyceride synthesis.
- Inhibits conversion of fatty acids to keto acids.

### ★ **Adipose Tissue:**

- ↑ Triglycerides storage.
- ↑ Fatty Acids Synthesis.







## III. Protein Metabolism:

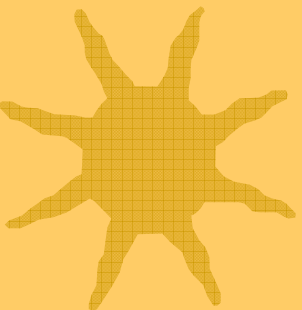
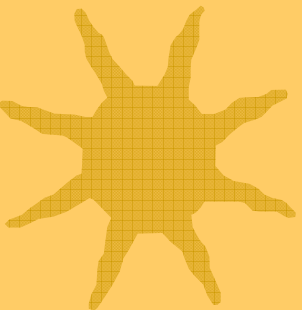
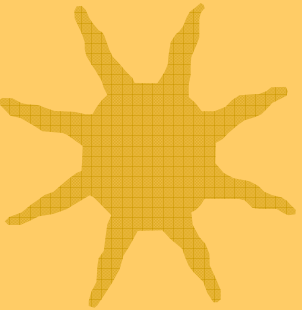
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### Liver:

- ↓ Protein Catabolism.

### Muscle:

- ↑ amino acids Uptake.
- ↑ Protein Synthesis.
- Increased glycogen synthesis





## Types of insulin preparations

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★ Vary in onset and duration of action.

★ **Ultrashort acting**

– *very fast onset and short duration*

★ **Short acting (regular).**

– *fast onset and short duration.*

★ **Intermediate acting.**

★ **Long acting.**

– *Slow onset and long duration.*



# Ultra-short Rapid-acting insulins

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1. Insulin Lispro, insulin aspart, insulin glulisine (**injection**)
2. Inhaled human insulin recombinant (**inhaled**).
3. Do not aggregate or form complexes
4. Fast onset of action (5-15 min)
5. Short duration of action (3-5h)
6. Reach peak level after 1 h.



# **Ultra-short Rapid-acting insulins**

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**Insulin Lispro, insulin aspart, insulin glulisine**

**Clear solutions at neutral pH.**

**Monomeric analogue.**

**S.C. 5 min. before meal.**

**I.V. emergency (Insulin Lispro).**

**2-3 times/day.**

**Mimic the prandial mealtime release of insulin**



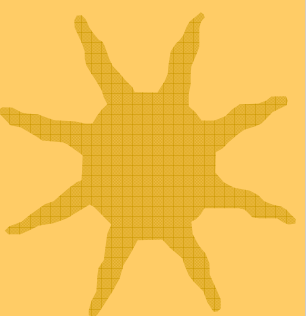
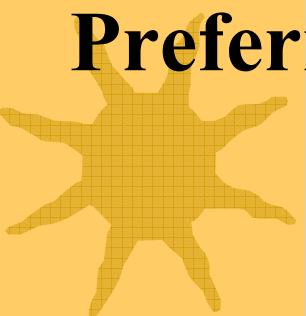
# Ultra-short Rapid-acting insulins

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**Insulin Lispro, insulin aspart, insulin glulisine**

**Have the lowest variability of absorption**

**Preferred insulins for insulin infusion devices.**





# Short acting insulins (Regular insulins)

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## Regular humulin R –regular novolin R

- ★ Soluble crystalline zinc insulin (stability – shelf half life)
- ★ Recombinant DNA technology
- ★ Clear solutions at neutral pH.
- ★ Hexameric analogue.
- ★ Onset of action 30-45 min (s.c.).
- ★ Peak 2-4 h.
- ★ Duration 6-8 h.



# Short acting insulins (Regular insulins)

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## ★ I.V. emergency.

- Management of ketoacidosis
- After surgery
- During acute infection



## ★ 2-3 times/day.



## ★ Control postprandial hyperglycemia & ketoacidosis.



## ★ Pregnancy.



## **Intermediate acting insulins**

### **Isophane (NPH) (Humulin N, Novolin N)**

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★ **NPH, a neutral protamine hagedorn is combination of protamine & crystalline zinc insulin (1: 6 molecules). Proteolysis release insulin.**

★ **Turbid suspension at neutral pH, s.c. only**

★ **Onset of action 1-2 h.**

★ **Peak serum level 5-7 h.**

★ **Duration of action 13-18 h.**

★ **75/25 - 70/30 - 50/50 (NPH/regular).**





# *Intermediate acting insulin*

## **Lente insulin (Humulin L, Novolin L)**

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### **Mixture of**

★ **30% semilente insulin (amorphous precipitate of insulin with zinc in acetate buffer)**

**70% ultralente insulin (poorly soluble crystal of zinc insulin)**

★ **Turbid suspension at neutral pH**

★ **slower onset of action 1-3 h than regular insulin.**

★ **Peak serum level 4-8 h.**

★ **Duration of action 13-20 h.**

★ **Lente and NPH insulins are equivalent in activity.**

★ **Lente and NPH **are Not used** in emergencies.**



# *Long acting insulin*

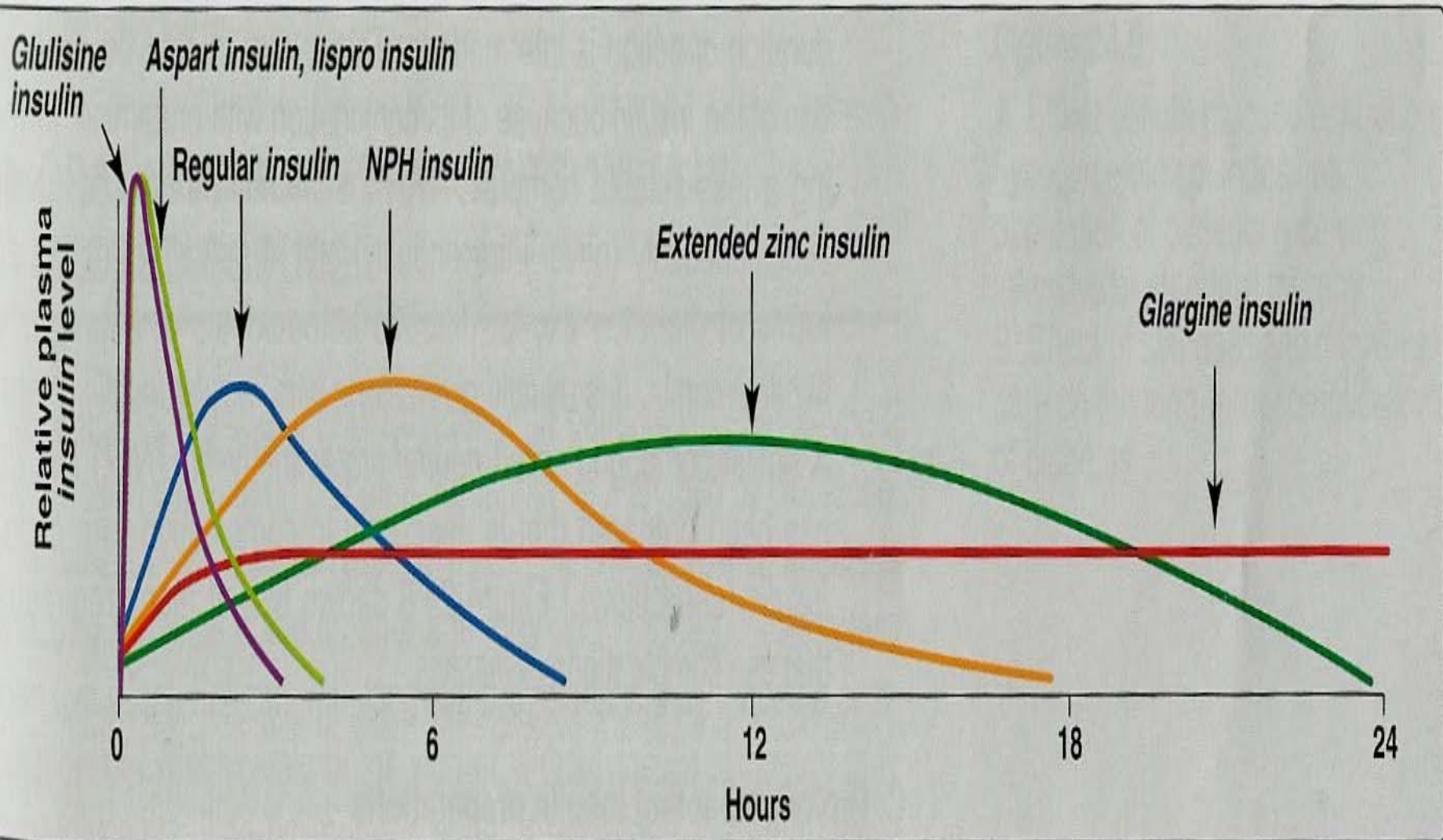
## **Insulin glargine (lantus)**

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- ★ **Slower onset of action 2 h.**
- ★ **Clear solution BUT forms precipitate at injection site.**
- ★ **Given s.c.**
- ★ **Peak 4-5 h.**
- ★ **Absorbed less rapidly than NPH & Lente insulin.**
- ★ **Prolonged duration of action (24 h).**
- ★ **Once daily**



# Insulin preparations





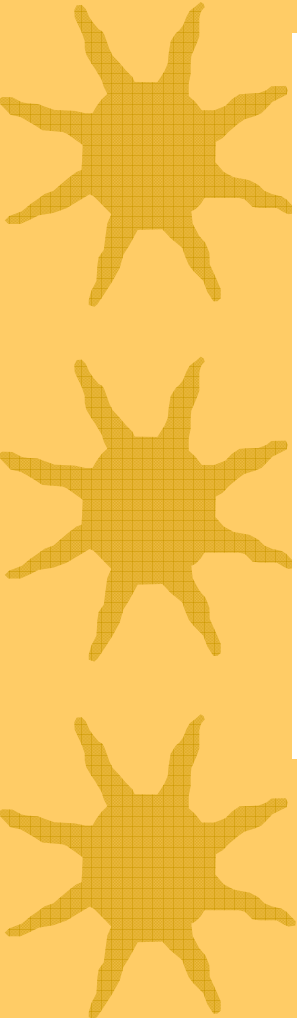
# Routes of administrations of exogenous insulin

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- 1. Given subcutaneously by syringes (arms, abdomen, thighs).**
- 2. Portable pin injector.**
- 3. Continuous S.C. insulin infusion (pump).**
- 4. Inhaled aerosols, transdermal, intranasal.**



# Routes of administrations of exogenous insulin





# Adverse effects of Insulin Therapy:

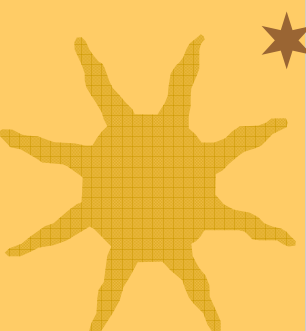
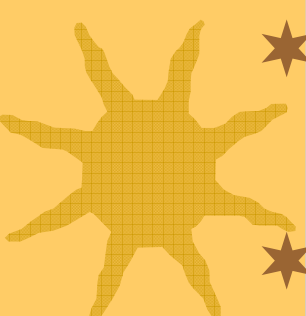
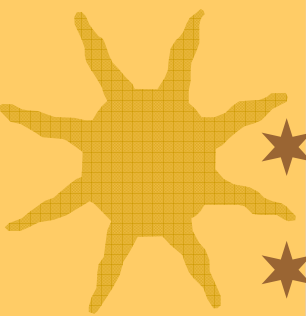
## ★ Hypoglycaemia: Manifested by:-

- Coma due to ↓ blood glucose to the brain.
- ↑ autonomic activity:
- ↑ sympathetic: Tachycardia, Sweating, Anxiety.
- ↑ parasympathetic: Nausea, Vomiting

*Treated by*

*Sugar containing beverage or food.*

*20-50 ml of 50% glucose solution I.V. or glucagon 1 mg S.C. or I.M.*



- 
- ★ **Weight gain**
  - ★ **Hypersensitivity reactions.**
  - ★ **Local reaction at injection site: *Swelling, Erythema, Lipodystrophy.***
  - ★ **Insulin resistance**
  - ★ **Hypokalemia**