ANTI-DIABETIC DRUGS

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Diabetes Mellitus:

It is metabolic disorder characterized by

- ✓Hyperglycaemia
- ✓Glucosuria
- ✓Negative Nitrogen Balance
- ✓Sometime Ketonaemia

Types of Diabetes Mellitus

Two major Type

- Type I : Insulin-Dependant Diabetes Mellitus (IDDM)

- Type II : Non Insulin-Dependant Diabetes Mellitus (NIDDM)

Management of DM

- The major components of the treatment of diabetes are:

A	• **Diet and Exercise**
B	• **Oral hypoglycaemic therapy**
C	• **Insulin Therapy**

Diet and Exercise

Insulin

One of a number of hormones that is required for normal growth and development

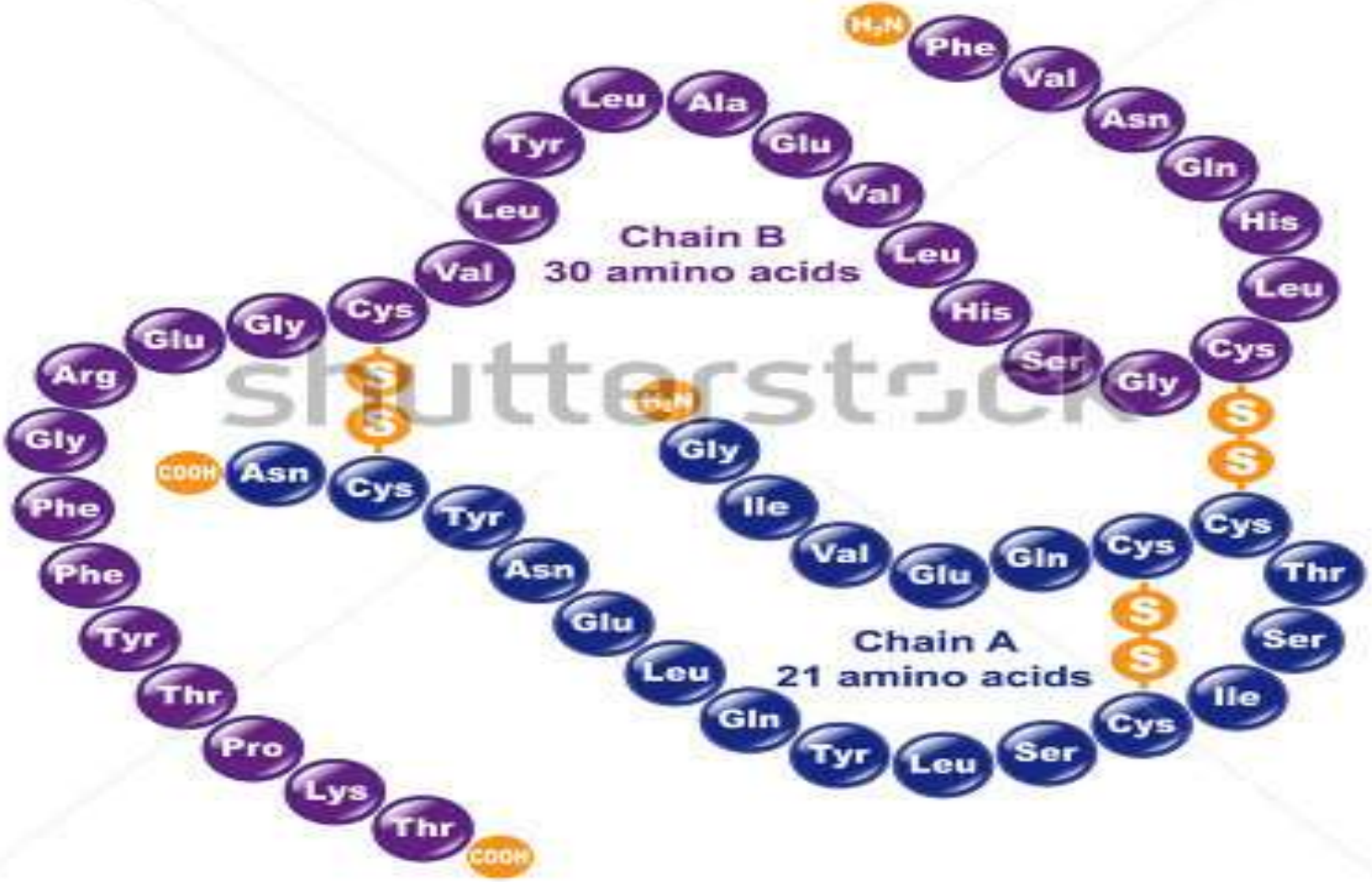
Insulin was discovered in 1921 by Banting and Best.

It is a Peptide Hormone

produced by beta cells in the pancreas

regulating carbohydrate and fat metabolism in the body.

Human Insulin



Types of Insulin

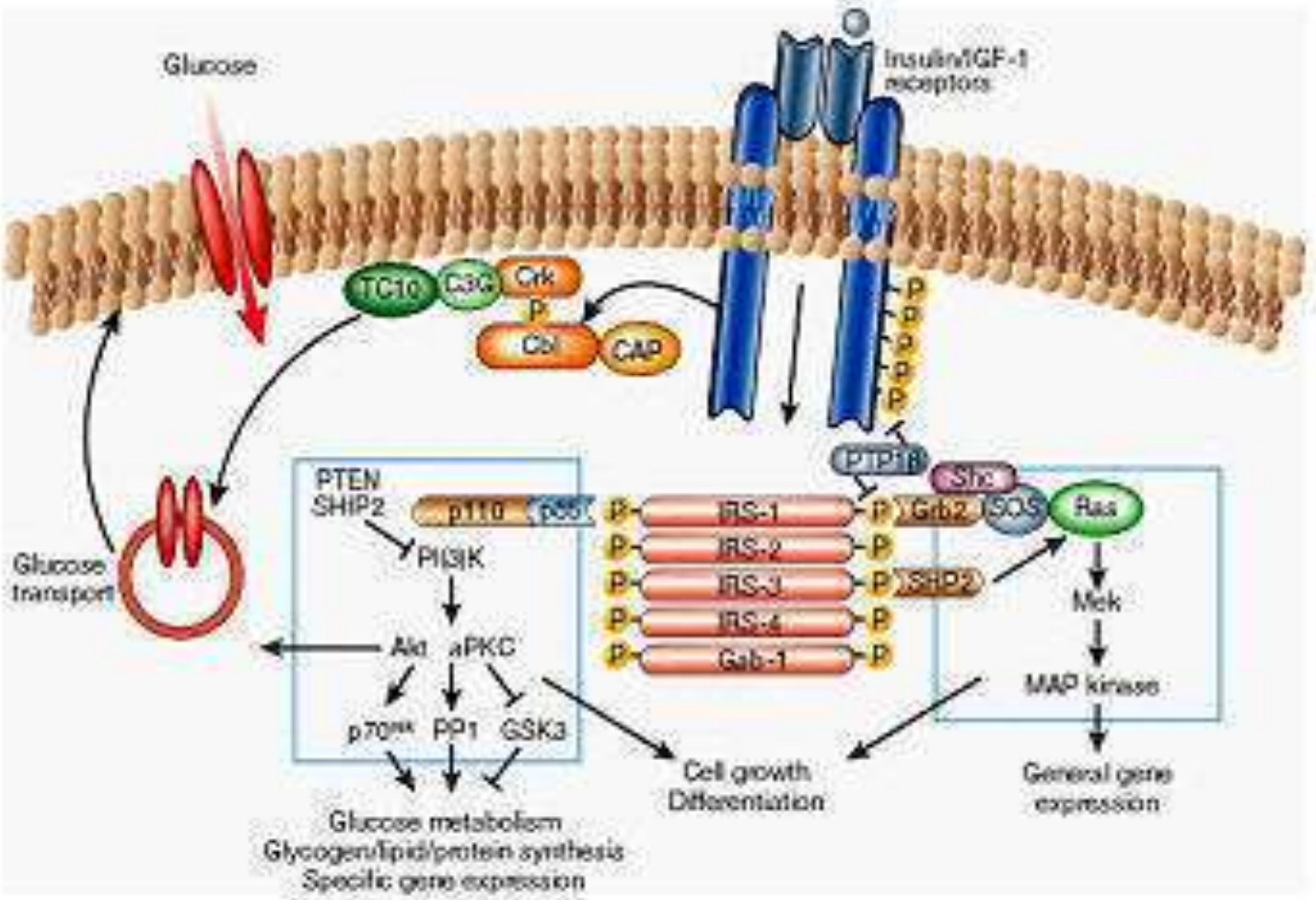
Rapid Acting
- Insulin Lispro
- Insulin Aspart
- Insulin Glulisine

Short Acting
- Regular (Soluble) insulin

Intermediate Acting
- Insulin Zinc Suspension or Lente*
- Neutral Protamine Hagedorn

Long Acting
- Protamine zinc insulin
- Insulin glargine

Mechanisms of Insulin Action



Saltiel and Kahn, Nature 414, 799-806, 2001

Types of insulin

Insulin type/action (appearance)	Brand names (generic name in brackets)	Basal/bolus	Dosing schedule
Rapid-acting analogue (clear) Onset: 10–15 minutes Peak: 60–90 minutes Duration: 4–5 hours	Humalog® (insulin lispro) NovoRapid® (insulin aspart)	Bolus	Usually taken right before eating or to lower high blood glucose
Short-acting (clear) Onset: 0.5–1 hour Peak: 2–4 hours Duration: 5–8 hours	Humulin®-R Novolin®ge Toronto	Bolus	Taken about 30 minutes before eating, or to lower high blood glucose
Intermediate-acting (cloudy) Onset: 1–3 hours Peak: 5–8 hours Duration: up to 18 hours	Humulin®-N Novolin®ge NPH	Basal	Often taken at bedtime, or twice a day (morning and bedtime)
Extended long-acting analogue (Clear and colourless) Onset: 90 minutes Peak: none Duration: 24 hours	Lantus® (insulin glargine) Levemir® (insulin detemir)	Basal	Usually taken once or twice a day
Premixed (cloudy) A single vial contains a fixed ratio of insulins (the numbers refer to the ratio of rapid- or fast-acting to intermediate-acting insulin in the vial)	Humalog® Mix 25™ Humulin® (20/80, 30/70) Novolin®ge (10/90, 20/80, 30/70, 40/60, 50/50)	Combination of basal and bolus insulins	Depends on the combination

Insulin function

Increased glucose uptake

Increased glucose use and storage

Increased protein synthesis

Increased fat storag

Oral hypoglycaemic therapy

Category	Examples
Sulfonylurea's	1st generation Tolbutamide Tolazamide Chlorpropamide Acetohexamide 2nd generation Glipizide Glyburide Glimepride Gliclazide
Biguanides	Metformin
Meglitinides	Repaglinde Nataglinide

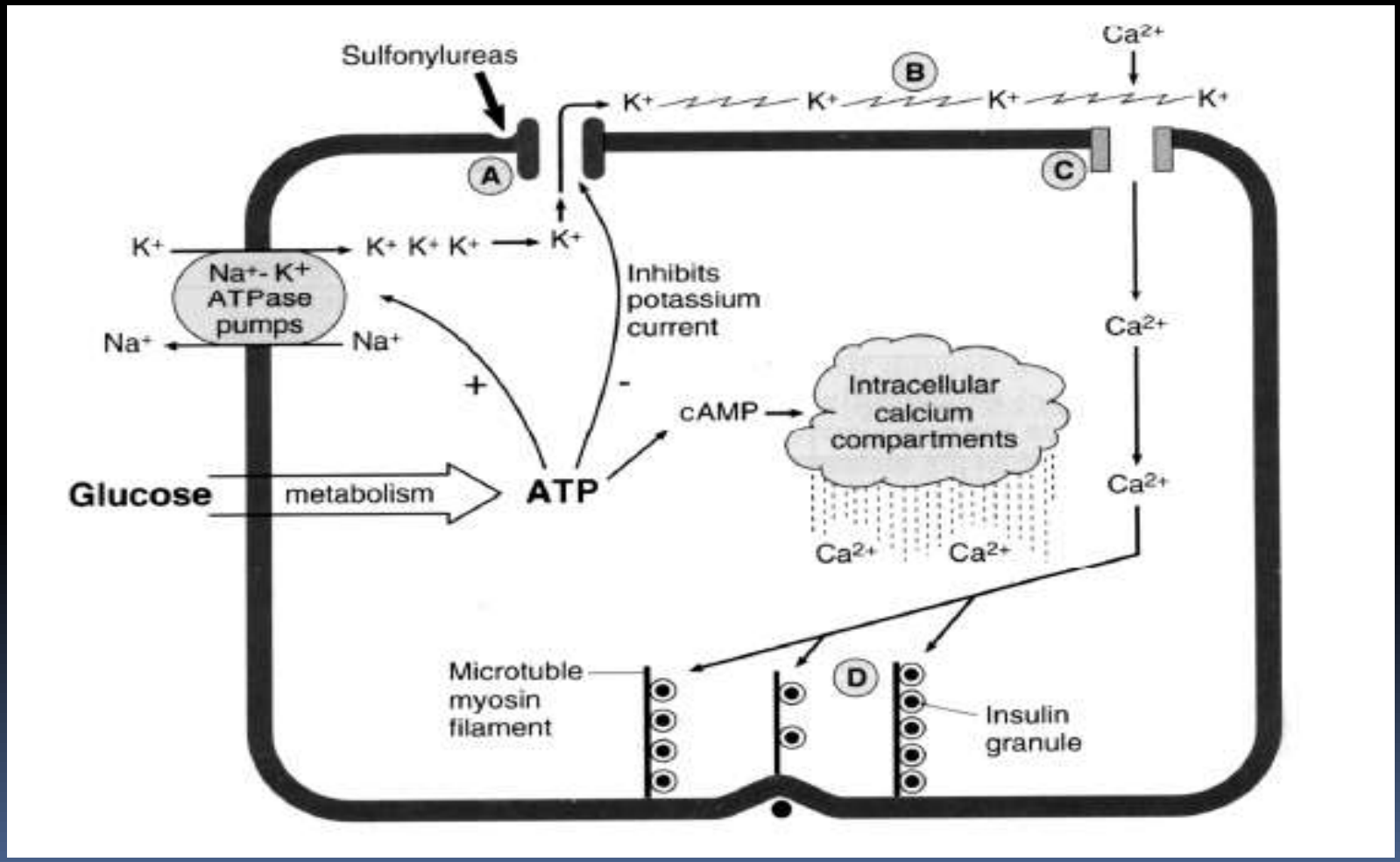
Thiazolidiones or Glitazones	**Pioglitazones** **Troglitazone** **Rosiglitazone**
Alpha-glycosidase inhibitor	**Acarbose** **Miglitazone**
Incretin mimetic	**Glucagon like peptide analogue(GLP)** **Exenatide** **Liraglutide** **Gastric inhibitory peptide analogue(GTP)**
Dipeptide peptidase inhibitor(DPP-G)	**Vidagliptin** **Sitagliptin**
Amylin analogue	**Pramlintide**

Oral Hypoglycaemic Medications

AGENTS & ACTIONS

Drug Class	Drug Name	Brand Name	Mechanism of Action
Biguanides	Metformin	Glucophage®	Inhibit glucose production by the liver
Sulfonylureas (second-generation)	Glimepiride Glipizide Glyburide	Amaryl® Glucotrol® Diabeta®, Glynase PresTab®, Micronase®	Increase insulin secretion by pancreatic beta cells
Meglitinides	Repaglinide Nateglinide	Prandin® Starlix®	Increase insulin secretion by pancreatic beta cells
Thiazolidinediones (TZDs)	Pioglitazone Rosiglitazone	Actos® Avandia®	Increase glucose uptake by skeletal muscle
Alpha-glucosidase inhibitors	Acarbose Miglitol	Precose® Glyset®	Inhibit carbohydrate absorption in the small intestine

Sulfonylurea's Jack,2013



Advantage

- ✓Inexpensive
- ✓Fast onset of action
- ✓No effect on blood pressure
- ✓No effect on low-density lipoprotein
- ✓lower risk ofgastrointestinal problems than with metformin
- ✓more convenient dosing

Disadvantages:

- causes an average of 5–10 pounds weight gain
- Increased risk of hypoglycemia
- Glyburide has increases risk of hypoglycemia slightly more as compared with glimepiride and glipizide

Absorption, Fate, and Excretion Goodman Gilman's

- Orally Absorbed
- 90% bound to plasma protien
- Excreted through urine

Adverse Effect

- Hypoglycemia
- Nonspecific Side Effect
- Hypersensitivity

Drug Interactions Tripathi, 2008

Inhibit metabolism/excretion:Cimetidine, Sulfonamide, Warfarin, Chloramphenicol.

Synergise With Drug: Salicylates, Propanolol, Lithium, Theophylline.

Displace from protein binding: Phenylbutazone, Sulfinpyrazone, Sulfonamide.

Induce Metabolism: Phenobarbitone, Phenytion, Rifampicin.

Opposite action/suppress insulin release: Corticosteroids, Diazoxide, Thaizides, Frusemide,

Biguanides

➢Lowers blood glucose- increases glucose uptake and utilisation in muscle + reduces hepatic glucose production (gluconeogenesis)

➢reduction of intestinal glucose absorption

Adverse effects:

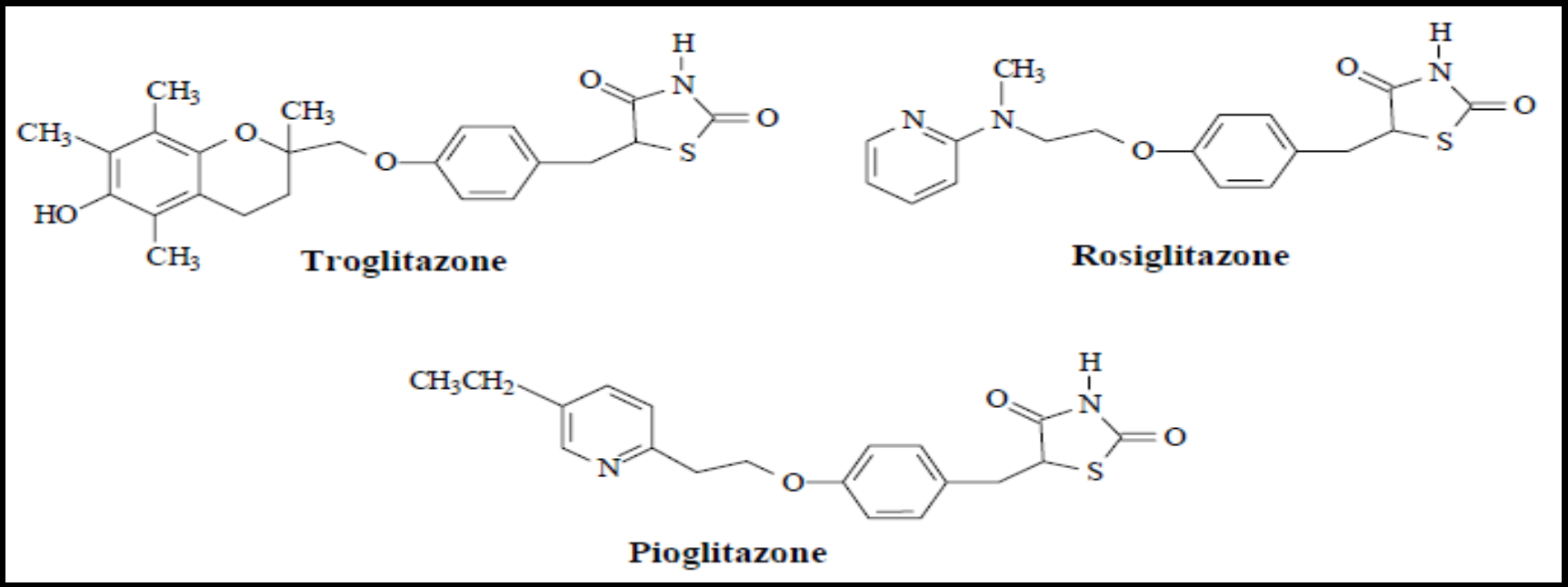
✓- GIT disturbancies (anorexia + weight loss, diarrhea)

✓- lactic acidosis rare but potencially fatal

✓Metformin should be avoided in patients who predispose to lactic acidosis (renal and hepatic disease, heart failure…)

✓Vit.B_{12} Deficiency

Thiazolidinediones



- Three thiazolidinediones have been used in clinical practice (troglitazone, rosiglitazone, and pioglitazone

- troglitazone was withdrawn from use
- Thiazolidinediones act on adipose, muscle, and hepatic tissue
- Selective agonists for nuclear peroxisome proliferator-activated receptor-g (PPARΎ).
- bind to PPARΎ
- Their main action is to diminish insulin resistance by increasing glucose uptake and metabolism in muscle and adipose tissues

Advantages

- ✓Lower risk of hypoglycemia
- ✓Slight increase in high-density lipoprotein
- ✓Actos linked to decreased triglycerides
- ✓Convenient dosing

Alpha-glucosidase inhibitor

- Reduces glucose absorbance by acting on small intestineto cause decrease

in production of enzymes needed to digest carbohydrates

- Slightly decreased risk of hypoglycemia as compared to sulfonylurea
- Not associated with weight gain
- Decreases triglycerides
- No effect on cholesterol

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Thank You