Revised & Approved

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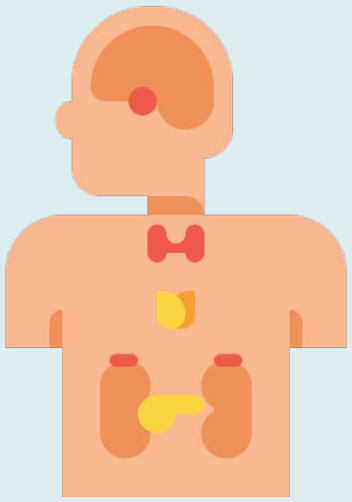
Pharmacology 439

MED439



Endocrine Block

Pharmacology Team 439

Color index:

Main Text

Important

Dr's Notes

Female Slides

Male Slides

Extra

Oral hypoglycemic drugs (T2DM)

Objectives:

1. Classify different categories of oral hypoglycemic drugs (antidiabetic drugs).
2. Identify mechanism of action, pharmacokinetics and pharmacodynamics of each class of oral hypoglycemic drugs.
3. Identify the clinical uses of oral hypoglycemic drugs
4. Know the side effects, contraindications of each class of oral hypoglycemic drugs.

Editing file | Summary

Diabetes Mellitus

Types

Type 1 Diabetes Mellitus

VS

Type 2 Diabetes Mellitus

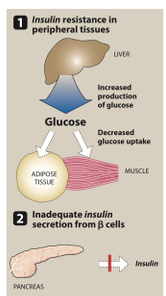
Due to autoimmune or viral diseases (the only treatment for insulin dependent diabetes is insulin injections, but also the patient must make lifestyle changes)

Due to **obesity (imp factor)** (accumulation of fat causes insulin resistance in tissues) & genetic factors.

- 80-90% occurrence
- Over age 35, but still can happen in children

Patients with type 2 diabetes have 2 physiological defects

1. Resistance to insulin action in target tissues associated with decreased number of insulin receptors.
2. Abnormal insulin secretion "Beta cell dysfunction". (partial production of insulin)



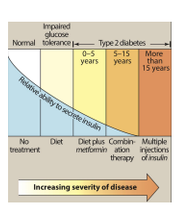
Treatment of Type 2 Diabetes (NIDDM)

NIDDM = Non-Insulin-Dependent diabetes Mellitus

Treatment plan:
1st Diet and lifestyle, if not effective.
2nd first-line therapy metformin, if not effective.
3rd combination with GLP or DPP (incretin mimetics)
4th insulin injections

- Proper dietary management.
- Caloric restriction and weight loss are IMP in obese diabetic patients.
- Increase physical activity. (To reduce accumulation of fat)
- Antidiabetic drugs. only start the patient on antidiabetic drugs after trying lifestyle changes with no decrease in blood glucose.

Anti-Diabetic drugs (Oral Hypoglycemic & others)



- Is insulin used in the treatment of diabetes type 2?
  Of course **not** (initially), but at the very end (~15 years) they may need to shift to insulin, but with the price of risk of hypoglycemia.

01 Insulin secretagogues:

1. **Sulfonylureas.** (-amide/ride/zide)
2. **Meglitinides.** (-glinide)
3. **Incretin mimetics.** (-glutide/gliptin)

02 Insulin sensitizers:

1. **Biguanides** (Metformin)
2. **Thiazolidinediones** (-glitazone)

03 Agents that reduce carbohydrate absorption:

α-glucosidase inhibitors
(Acarbose, Miglitol)

04 Agents that reduce glucose renal reabsorption :

(SGLT-2, Sodium/Glucose cotransporter-2 inhibitors):

(Canagliflozin, **Dapa**gliflozin, **Empa**gliflozin)

1) Insulin Secretagogues

- Drugs which increase the amount of insulin secreted by the pancreas
- ★ Their action depends upon **functioning** pancreatic β-cells (Not for T1DM)
- It includes: 1. Sulfonylureas 2. Meglitinides 3. Incretin mimetics

- Because they release insulin, they have risk of inducing hypoglycemia. (risk from highest to lowest):
1.sulfonylurea. 2.meglitinides. 3.incretin mimetic. (lowest risk of hypoglycemia because they stop releasing insulin once blood glucose is normal since their action depends on hyperglycemia being present).

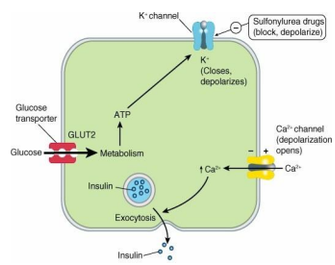
1. Sulfonylureas

Class	**First generation (-amide)**			
Drugs	**Acetohex**amide	**Tolaz**amide	**Chlorprop**amide	**Tolbut**amide
	Long acting			Short acting (shortest of all sulfonylurea)
Class	**Second generation (-ride/zide)**			
Drugs	**Glybu**ride (glibenclamide)	**Glimepi**ride	**Gliclа**zide	**Glipi**zide
	Long acting (-ride)		Short acting (-zide) (used after meal)	

M.O.A

seen in all insulin secretagogues.

- Physiology inside pancreatic β cells: ↑ Hyperglycemia → stimulate glycolysis by hexokinase enzyme → induction of ATP → Blockade of ATP dependent K^+channels → depolarization → Opening of voltage-dependent Ca^+ channels → ↑ intracellular calcium in the β cells → ↑ Insulin release (exocytosis).
- Sulfonylureas stimulate insulin release from functioning β cells by **blocking of ATP-sensitive K channels** which causes depolarization and **opening of voltage- dependent calcium channels,** which causes an increase in intracellular calcium in the β cells, which stimulates insulin release.



P.K

- **Orally**, well absorbed.
- Reach peak concentration after 2-4 hr. (not important).
- ★ All are highly bound to plasma proteins. Especially 1st generation: more drug interactions (High drug distribution).
- Duration of action is variable.
- Metabolized in liver (contraindicated in liver and kidney diseases).
- Excreted in urine (caution: elderly and renal disease).
- ★ Cross placenta, stimulate fetal β-cells to release insulin → **fetal hypoglycemia at birth** (this effect is present with all oral hypoglycemics so it is not advisable to give them to a diabetes type 2 pregnant patient. **Shifting her to insulin is advisable**).
(in addition to causing fetal hypoglycemia, sulfonylurea is possibly **teratogenic**).

Second generation Sulfonylureas:

- More potent than first generation.
- Longer duration of action. (Tolbutamide = 8h, while short acting of 2nd generation > 8h).
- Less frequency of administration.
- Fewer adverse effects & drug interactions.

1. Sulfonylureas, Cont.

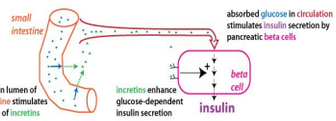
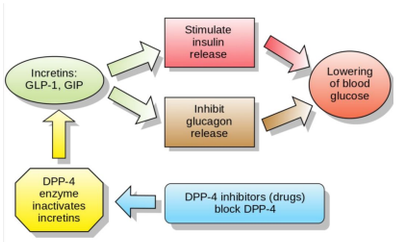
Uses	Treatment of Type 2 diabetes monotherapy or in combination with other antidiabetic drugs
ADRs	1. **Hyperinsulinemia & Hypoglycemia:** ○ More common in long acting *sulfonylureas*; particularly (*glyburide, glimepiride*) ○ More in old age, hepatic or renal diseases. (so it is better to avoid long acting and give short acting instead in these patients) 2. **Weight gain due to increase in appetite** unless the diabetic diet and exercise program are followed. (insulin has anabolic effect) 3. **Allergy manifestation as they contain Sulfa.**

	Glyburide **(Glibenclamide)**	**Glimepi**ride	**Glipi**zide
Absorption	Well		Well, reduced by food
Metabolism	Yes		
Duration of action	12 – 24 hrs (long)		10 – 16 hrs (short)
Doses	Single dose		Divided doses 30 min before meals
Excretion	Urine		

2. Meglitinides

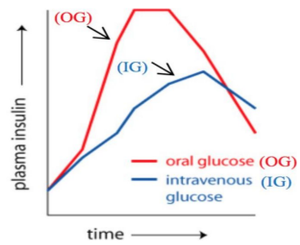
Drug	**Repa**glinide **(-glinide)**
M.O.A	• Rapidly acting insulin secretagogues. • Mechanism of action is identical to sulfonylureas (stimulate insulin release by blocking ATP-sensitive K^+ channels)
P.K	• Orally, well absorbed. • Very fast onset of action (30 min to give an effect), peak 1 h. • Short duration of action (4 h). Less risk of hypoglycemia • Metabolized in liver and excreted in bile. • Taken just before each meal (3 times/day). The dose should be skipped if the meal is missed. Differentiate with sulfonylurea: 1. Onset of action 2. Duration of action 3. Excretion 4. Allergenic.
Uses	• Type 2 diabetes as a monotherapy or in combination with other oral hypoglycemic drugs. ★ As alternative to sulfonylureas in patients allergic to them (SU). (can't be combined with sulfonylureas)
ADRs	• Less incidence than *sulfonylureas*: (due to their shorter DOA) ◦ Hypoglycemia. ◦ Weight gain.

3. Incretin mimetics

Group	Incretins
General info	• They are GI hormones secreted from L cells (enteroendocrine cells) in the small intestine in response to food (not secreted as long as we are not eating) even before blood glucose level becomes elevated. • Carried through circulation to pancreatic β cells.
M.O.A	Regulate blood glucose by: - Increase insulin secretion. - Decrease glucagon secretion.  
includes	1) **GLP-1** (Glucagon-Like Peptide-1) 2) **GIP** (Gastric Inhibitory Peptide) also called glucose-dependent insulinotropic peptide. Both are inactivated by dipeptidyl peptidase-4 **(DPP-4).** Their duration of action is only 2 min. Therefore we developed: - Exogenous drugs that give the same effect as GLP-1. - Drugs that increase the action of GLP-1 indirectly by inhibiting DPP-4.

An experiment shows the comparison between the amount of insulin secretion in response to Oral and I.V glucose

- They noticed that oral glucose (OG) induce larger amount insulin secretion when it compared to I.V glucose (IG).
- Further researches proved that the reason why insulin levels are high in oral glucose (OG) is due stimulation of incretin hormone (GI hormone).



® = Brand names, not required

Types of Incretin mimetics

Both ↓ weight and risk of hypoglycemia

GLP-1 agonists (-glutide)

GLP-1 drugs are non-insulin treatments for T2DM;

- **Dula**glutide (Trulicity®)
- **Lira**glutide
  - Victoza®: the **lower** dose for diabetes (can't be given for obesity because it will not give the same effect as the higher dose)
  - Saxenda®: the **higher** dose for obesity
    - Causes ↓ in appetite and ↑ satiation.
    - C.I for diabetes due to risk of hypoglycemia due to its high dose.
- Exenatide
  - Byetta®: immediate-release given S.C. twice daily (for extended release)
  - Bydureon®: extended-release given once weekly
- **Sema**glutide (Rybelsus®) 1st **oral** GLP-1, New FDA approved. **Only oral drug in this class**

DPP-4 inhibitors (-gliptin)

- **Sita**gliptin (Januvia®)
- **Vilda**gliptin
- **Lina**gliptin

Types of Incretin mimetics, Cont.

Class	**GLP-1 agonists** (-glutide)	**DPP-4 inhibitors** (-gliptin)
Drug	**Lira**glutide (Victoza®, Saxenda®)	**Sita**gliptin (Januvia®)
M.O.A	• Binds to GLP-1 receptors and **stimulates** insulin secretion from β cells (Agonist). • **Reduces** glucagon secretion, by inhibiting α cells of the pancreas. • Decreases appetite (centrally acting) and **inhibits** body weight gain.	• **Inhibit** DPP-4 enzyme and leads to an increase in incretin hormones (GLP-1) level. This results in an **increase** in insulin secretion & **decrease** in glucagon secretion. (mechanism of all Gliptins)
P.K	★ Given S.C. once/day (single-dose prefilled disposable pens) (half-life=13h, because it's combined with FA so it deposits at the site of the injection and is slowly released). • The maximum dose of Victoza is 1.8 mg.	Given orally/once daily.
Uses	• ***Saxenda***®: treatment of obesity in adults who are overweight with at least one weight-related **comorbid condition** (e.g. HTN, T2DM, or dyslipidemia). (Not indicated in patients with no comorbidities because it hasn't been studied on them) • Together with diet and exercise to treat: - Type 2 diabetes. - Patients who are not controlled with other oral antidiabetics. (because it is expensive)	Type 2 DM as an adjunct to diet & exercise as a **monotherapy** or In **combination** with other antidiabetic drugs.
ADRs	• Nausea, vomiting and diarrhea (**most common**) • **Hypo**glycemia when combined with *Sulfonylureas* or *insulin* (as an additive in T1DM) (not alone). • Pancreatitis (rare).	• Nausea, abdominal pain, diarrhea. ★ Nasopharyngitis. • Headache. • ↑ Upper respiratory tract infections.
C.I	• Not used in type 1 diabetes.	-

2) Insulin sensitizers

Drugs that **increase** the sensitivity of peripheral target organs to insulin

"first line therapy after life style modifications"

- Biguanides
  E.g. Metformin
- Thiazolidinediones
  E.g **Pio**glitazone

2) Insulin sensitizers, Cont.

Class	Biguanides
Drug	**Metformin** (Glucophage®)
M.O.A	• **Reduces** insulin resistance. (↑ uptake of glucose by peripheral tissues) • **Increases** sensitivity of liver, muscle & adipose tissues to insulin. • **Increase** peripheral glucose utilization (tissue glycolysis). • **Inhibits** hepatic glucose production (gluconeogenesis). • **Impairs** glucose absorption from GIT. ★ Improve lipid profile: ↓ LDL, ↓ VLDL , ↑HDL (diabetic patients have abnormality in lipid profile)
P.k	• Given orally. • Not bound to serum protein (doesn't have a long duration of action). • t ½: 3 hours (taken 3 times a day). • Not metabolized, excreted unchanged in urine.
Uses	• In patients with type 2 diabetes who are obese, because it promotes modest weight reduction **(first-line therapy)** (obese + blood glucose not that high). • Type 2 diabetes as **monotherapy** or in **combination** with other antidiabetics (insulin secretagogue).
Advantages	• **No** risk of **hypo**glycemia. (advantage) only happens with *insulin secretagogues*, because they ONLY increase the sensitivity and won't increase insulin secretion. • **No** weight gain. • Prominent lipid-lowering activity. very beneficial as most diabetic patients have abnormal lipid profile #438 • Inexpensive.
ADRs	• **GIT disturbances**: (most patients complain of this at first but after a while of taking the drug it becomes tolerable). - Metallic taste in the mouth, nausea, vomiting, diarrhea. - *Metformin* should be taken with meals and should be started at a low dose (e.g. giving one tablet instead of the required three tablets) to avoid intestinal side effects then increase gradually. ★ **Lactic acidosis** due to their glycolytic action (very rare and very serious): Serious lactic acid accumulation (pH around 7.2) usually occurs only in the presence of **predisposing conditions:** - Renal insufficiency. - Severe liver disease. - Alcohol abuse. because alcohol itself increases glycolysis #438 - Heart failure, Pulmonary insufficiency, Cardiogenic or septic shock. Due to low oxygen delivery to tissues. Tissues start depending more on glycolysis and patient already has ↑ glycolysis. #438 - Heart problems also lead to ↓ renal blood flow → ↓ clearance. • **In long term use:** Interference with vitamin B12 absorption (check up and if low give supplements).
C.I	• Renal disease • Liver disease • Alcoholism • Cardiopulmonary dysfunction — Lactic acidosis • Pregnancy

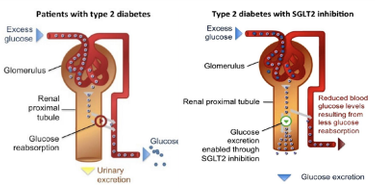
Class	Thiazolidinediones
Drug	**Pio**glitazone, **Rosi**glitazone **(-glitazone)**
M.O.A	• Activate peroxisome proliferator-activated receptor-γ (**PPAR-γ**) (a nuclear receptor) → Increase sensitivity of target tissues to insulin → Increase glucose uptake and utilization in muscle and adipose tissue.
P.K	• **Orally** (once daily dose). • Highly bound to plasma albumins (99%) this explains why it has a short half life but a long duration of action. • Slow onset of activity • Half life 3-4 h. • Metabolized in the liver. • Excreted in bile and urine.
Uses	• Type 2 diabetes with insulin resistance (with obesity). • Used either alone or in combination with *sulfonylurea*, *biguanides* or *insulin*. ★ No risk of hypoglycemia when used alone.
ADRs THiazoLidinedione: Toxic to Heart and Liver	• Hepatotoxicity (monitor liver function tests especially for 1st year of therapy) (it could subside. if persistent stop the medication). ★ Congestive heart failure (CHF). ★ Fluid retention (Edema) Due to its effect on the heart (low cardiotoxicity → CHF → fluid congestion). **Note**: medications in this group were withdrawn from the market because of their cardiotoxicity leaving only Pioglitazone & Rosiglitazone since cardiotoxicity wasn't reported with their use. However the risk is still present. • Mild weight gain due to fluid retention. • Failure of estrogen-containing oral contraceptives due to drug-drug interaction.

3) α-Glucosidase inhibitors

Drug	Acarbose Acarbose = no carbs	Miglitol
M.O.A	• Reversible inhibitors of intestinal α-glucosidases in intestinal brush border cells **that are responsible for carbohydrate digestion.** • Decrease carbohydrate digestion and glucose absorption (because no carbs are in absorbable form) in small intestine (lower postprandial (after a meal) glucose level).	
P.K	• No hypoglycemia if used alone • Given orally, not absorbed and taken just before meals. Excreted in feces	-
Uses	• Effective alone in the earliest stages of **impaired glucose tolerance** (used in pre-diabetes). • Not recommended alone as therapy for moderate to severe hyperglycemia (not effective alone in well proven diabetes type 2). • Most useful in combination with other *oral hypoglycemic drugs* or with *insulin*.	
ADRs	• GIT: **Flatulence, bloating,** diarrhea, abdominal pain. Due to bacteria in the colon (because of increased glucose in intestine).	
C.I	Because they can't tolerate the GIT disturbances: • Irritable bowel syndrome (IBS). • Inflammatory bowel disorders (IBD). • Intestinal obstruction.	

4) Sodium-glucose transporter 2 inhibitors

*Female slides only (except picture)

Drug	**Cana**gliflozin, **Dapa**gliflozin, **Empa**gliflozin **(-gliflozin)**
M.O.A*	• Inhibits **SGLT2** (responsible for the reabsorption of 80-90% of glucose) (mainly located in the proximal tubule) in the kidneys → inhibits glucose and Na reabsorption → allows excess glucose to be excreted in the urine → reduce blood sugar levels. 
Uses*	• With diet and exercise to control high blood sugar in patients with type 2 diabetes. • To **reduce risk of major adverse cardiovascular events** in adults with T2DM and established cardiovascular disease.
ADRs*	★ Urinary tract infections (candida infection) due to glycosuria making medium favorable. • Increased urination and dry mouth. • Thirst. ★ Yeast infections (vagina or penis). • Itching (vagina or penis). • Fatigue. • Risk of hypoglycemia.

Summary (Slides)

Prof Hanan: This table is more than enough just add to it the rest of the drugs mentioned in slides.

Class / drug	Mechanism	Site of action	Main Advantages	Main ADRs
Sulfonylureas E.g Gliclazide	Stimulates insulin secretion (Insulin secretagogues)	Pancreatic β-cells	- Effective - Inexpensive	- Hypoglycemia - Weight gain
Meglitinides E.g Repaglinide			- Sulfa free	
Biguanides E.g Metformin	Decrease insulin resistance	Liver	- Mild weight loss - No hypoglycemia	- GIT symptoms - Lactic Acidosis - Metallic taste
Thiazolidinediones E.g Pioglitazone		Fat, muscle	- No hypoglycemia	- Hepatotoxicity - Edema - Mild weight gain
Incretins mimetics E.g Dulaglutide, Liraglutide, Exenatide	Increase incretin (GLP-1 agonists)	GI tract	- S.C once a day	-N&V
DPP-4 inhibitors E.g Sitagliptin, Vildagliptin	Inhibit incretin breakdown (indirect action)		- Orally	- N & abdominal pain - Nasopharyngitis
a-Glucosidase E.g Acarbose, Miglitol	Decrease glucose absorption in small intestine		- Low risk	- GI symptoms, flatulence
SGLT-2 inhibitors E.g Dapagliflozin, Canagliflozin	Inhibit renal SGLT-2 Increase renal glucose excretion	Kidney	- Orally - Reduced Na (CV benefits)	- Genital yeast infection - UTI - Increased Urination and dry mouth - Itching (vagina or penis)

Only used as additives

Extra Summary

Treatment guidelines in a patient with ↑ BMI (move to the next step if blood glucose still elevated):
Step1: metformin.
Step2: either stop metformin and shift to insulin secretagogue or give a formulation present in the market of metformin combined with one of the sulfonylurea.
Step3: additive medications, we can also we add incretins
Step4: insulin

Class	Drug	M.O.A	Uses	ADRs
Sulfonylureas: 1st generation	**Tolbut**amide (Short acting)	Blockade of ATP dependent K+channels→ Opening of voltage-dependent Ca+ channels → ↑intracellular calcium in the β cells → ↑Insulin release	Treatment of Type 2 diabetes as monotherapy or in combination with other antidiabetic drugs	1. **Hyperinsulinemia & Hypoglycemia:** More common in long acting sulfonylureas; **particularly (glyburide, and glimepiride)** 2. Weight gain due to increase in appetite 3. Allergy
	Acetohexamide (Long acting)			
Sulfonylureas: 2nd generation	**Glybu**ride (Long acting)			
	Glimepiride (Long acting)			
	Gliclazide (Short acting)			
	Glipizide (Short acting)			
Meglitinides	**Repa**glinide		• As alternative to sulfonylureas (SU) in patients allergic to SU.	• Less incidence than sulfonylureas
Incretin mimetics: GLP-1 agonists	**Lira**glutide (Victoza®, Saxenda®)	• Binds to GLP-1 receptors and **stimulates** insulin secretion from β cells • **Reduces** glucagon secretion by inhibiting a cells of the pancreas • It decreases appetite and **inhibits** body weight gain	• ***Saxenda***: As a treatment for adults who are obese or overweight with at least one weight-related comorbid condition • Used together with diet and exercise to treat: - Type 2 diabetes - Patients who are not controlled with other oral antidiabetics.	• Nausea, vomiting and diarrhea (**most common**) • **Hypo**glycemia when combined with *sulfonylureas* or *insulin* (not alone) • Pancreatitis (rare)
Incretin mimetics: Incretin mimetics	**Sita**gliptin (Januvia®)	• **Inhibit** DPP-4 enzyme and leads to an increase in incretin hormones (GLP-1) level.	• Type 2 DM as an adjunct to diet & exercise as a **monotherapy** or In **combination** with other antidiabetic drugs	• Nausea, abdominal pain, diarrhea • Nasopharyngitis • Headache

Extra Summary, cont.

Insulin sensitizers: Biguanides	**Metformin**	• **Reduces** insulin resistance. • **Increases** sensitivity of liver, muscle & adipose tissues to insulin. • **Increase** peripheral glucose utilization (tissue glycolysis). • **Inhibits** hepatic glucose production (gluconeogenesis) • **Impairs** glucose absorption from GIT. • **Improve lipid profile:** ↓ LDL, ↓ VLDL , ↑HDL	• In patients with type 2 diabetes who are obese, because it promotes modest weight reduction **(first-line therapy)**. • Type 2 diabetes as **monotherapy** or in **combination** with other antidiabetics.	• GIT disturbances: Metallic taste in the mouth, nausea, vomiting, diarrhea (should be **taken with meals** and **should be started at a low dose)** • Lactic acidosis • **In long term use:** Interference with vitamin B12 absorption
Insulin sensitizers: Thiazolidinediones	**Pio**glitazone **Rosi**glitazone	• **Activate** peroxisome proliferator-activated receptor-Gamma (PPAR-Gamma) • **Increase** sensitivity of target tissues to insulin. • **Increase** glucose uptake and utilization in muscle and adipose tissue	• Type 2 diabetes with insulin resistance. • Used either alone or in combination with sulfonylurea, biguanides or insulin. • **No risk of hypoglycemia when used alone**	• Hepatotoxicity (monitor liver function test) • **Fluid retention (Edema)** • **Congestive heart failure** • Failure of estrogen-containing oral contraceptives. •Mild weight gain
α-Glucosidase inhibitors	**Acarbose** **Miglitol**	• **Reversible inhibitors** of intestinal α-glucosidases in intestinal brush border cells **that are responsible for carbohydrate digestion** • **Decrease** carbohydrate digestion and glucose absorption in small intestine (lower postprandial glucose level)	• Are effective alone in the earliest stages of **impaired glucose tolerance** (pre-diabetes)	• GIT: **Flatulence, bloating,** diarrhea, abdominal pain.
Sodium-glucose transporter 2 inhibitors	**Cana**gliflozin **Dapa**gliflozin **Empa**gliflozin	Inhibits SGLT2 in the kidneys →inhibits glucose and Na reabsorption→ excess glucose excretion→ reduce blood sugar levels.	• To reduce risk of **major adverse cardiovascular events in adults with type 2** diabetes and established cardiovascular disease.	• **Urinary tract infections** • **Yeast infections (vagina or penis)** • Increased urination and dry mouth • thirst • itching • fatigue

MCQs

★Q1: Liver cirrohitic type 2 diabetes patient presented with Lactic acidosis and low PH, what drug caused his symptoms?			
A- Canagliflozin	B- Pioglitazone	C- Metformin	D- Repaglinide
Q2: A 59-year-old man suffering from type 2 diabetes had been receiving an oral antidiabetic therapy that included a drug that closes adenosine triphosphate (ATP)–sensitive K + channels on pancreatic β-cell membranes. Which of the following drugs most likely uses this mechanism of action?			
A- Glyburide	B- Metformin	C- Exenatide	D- Pioglitazone
Q3: A 78-year-old man was brought to the emergency room e hibiting bizarre behavior and paranoid ideation. He complained of headache, mental confusion, weakness, dizziness, and blurred vision. The man was suffering from type 2 diabetes, which was being treated with an oral antidiabetic drug. Pertinent serum values on admission were creatinine 1.8 mg/dL (normal 0.6–1.2 mg/dL), glucose 50 mg/dL (normal 70–110 mg/dL). Which of the following drugs most likely caused the patient's signs and symptoms?			
A- Metformin	B- Pioglitazone	C- Canagliflozin	D- Glyburide
Q4: A 54-year-old man complained to his physician of dry cough over the past few days and an unexpected weight gain over the past few weeks. The patient had been suffering from type 2 diabetes for 3 years, presently controlled with a combination of oral antidiabetic agents. Physical examination showed evident peripheral edema, mild jugular venous distention, and rales on both lungs. Which of the following drugs most likely caused the patient's signs and symptoms?			
A- Liraglutide	B- Rosiglitazone	C- Glimepiride	D- Miglitol
Q5: A 63-year-old obese man complained to his physician of flatulence, belching, diarrhea, and abdominal pain soon after starting an appropriate oral therapy for type 2 diabetes. The disease was diagnosed after the man was found to have a fasting blood glucose level of 170 mg/dL, and subsequent lab exams revealed decreased glucose tolerance and fasting hyperglycemia. Which of the following drugs most likely caused the patient's symptoms?			
A- Glipizide	B- Dapagliflozin	C- Miglitol	D- Pioglitazone
Q6: Sulphonylureas act by:			
A- Reducing the absorption of carbohydrate from the gut	B- Increasing the uptake of glucose in peripheral tissues	C- Reducing the hepatic gluconeogenesis	D- Stimulating the beta islet cells of pancreas to produce insulin
Q7: Which of the following can be used as monotherapy with NO risk of hypoglycemia?			
A- Glimepiride	B- Rosiglitazone	C- Repaglinide	D- Empagliflozin

1	2	3	4	5	6	7
C	A	D	B	C	D	B

SAQ

Q1) What are the predisposing factors that increase the risk for lactic acidosis while taking metformin?

Q2) What is the mechanism of action of Pioglitazone?

Q3) What are some precautions when taking Sulfonylureas?

Q4) Name GLP-1 agonists and specify their route of administration.

Q5) Mention 3 ADRs for Sitagliptin

Q6) Mention 4 ADRs for Pioglitazone

Answers

A1) Renal insufficiency, Severe liver disease, Alcohol abuse, Heart failure, Pulmonary insufficiency, Cardiogenic or septic shock

A2) Activate peroxisome proliferator-activated receptor-γ (PPAR-γ) → Increase sensitivity of target tissues to insulin → Increase glucose uptake and utilization in muscle and adipose tissue.

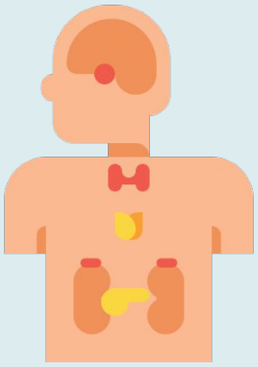
A3) Pregnancy, Allergies, eldery, liver and kidney disease.

A4) Liraglutide (S.C), Dulaglutide (S.C), Exenatide (S.C), Semaglutide (Oral)

A5) Nausea, abdominal pain, diarrhea, Nasopharyngitis, Headache, ↑ Upper respiratory tract infections.

A6) Hepatotoxicity, Fluid retention (Edema), Congestive heart failure, Mild weight gain, Failure of estrogen-containing oral contraceptives

Feedback Form



Endocrine Block

Pharmacology Team 439

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