Oral Hypoglycemics

Objectives:

- **Classify** different categories of oral hypoglycemic drugs.
- **Explain** the mechanism of action, pharmacokinetics and pharmacodynamics of each class of oral hypoglycemics.
- **Describe** the clinical uses of oral hypoglycemics
- **Know** the side effects, contraindications of each class of oral hypoglycemics.

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Drug's name | Doctors' notes | Important | Extra

« لو أن الناس كلما استصعبوا أمرًا تركوه؛ ما قام للناس دنيا ولا دين! »
عمر بن عبدالعزيز

❖ Thanks to our super members!

قال رسول الله صلى الله عليه وسلم:

"إذا مات ابن آدم انقطع عمله إلا من ثلاث، صدقة جارية، أو **علم ينتفع به**، أو ولد صالح يدعو له"

كلمات الشكر لا تسعكم؛ فخورون بكم!

اسرار باطرفي
أمل العمران
آية غانم
جواهر الحربي
جوهرة المالكي
حصه المزيني
دلال الحزيمي
رغد النفيسه
رغده القاسم
رناد القحطاني
ساره الخليفه
شادن العمران
شماء السعد
لمى الزامل
لينه الشهري
ملاك الشريف
ملاك اليحيا
منيرة السلولي
منيره السلمان
نورة البصيص

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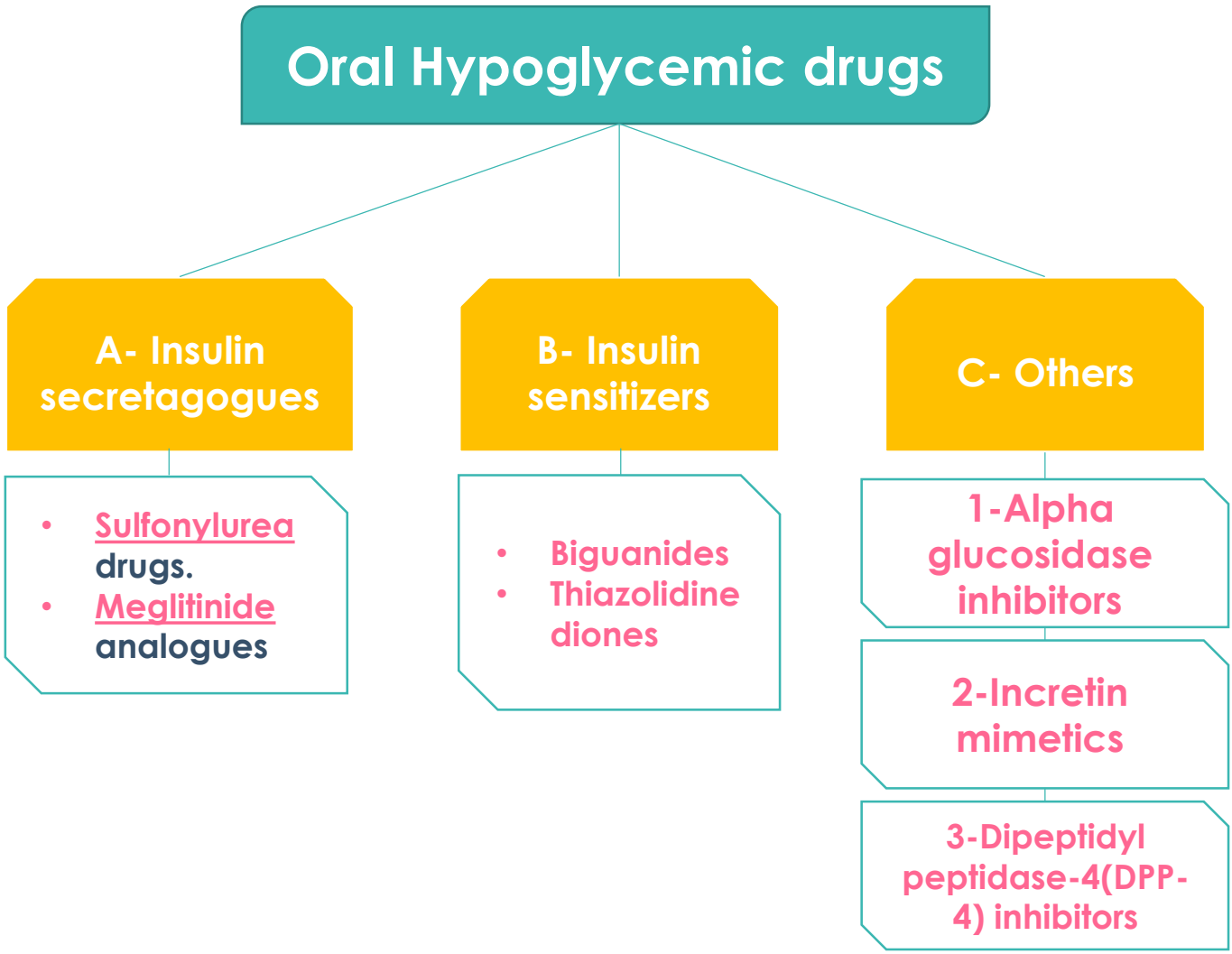
فوزان العتيبي
قصي عجلان
محمد ابونيان
محمد السحيباني
يوسف الصامل

Pharmacology 435

قادة فريق علم الأدوية:

أثير النشوان & خالد أبوراس

Mind Map


Oral Hypoglycemic drugs
A- Insulin secretagogues
B- Insulin sensitizers
C- Others
Sulfonylurea drugs.
Meglitinide analogues
Biguanides
Thiazolidine diones
1-Alpha glucosidase inhibitors
2-Incretin mimetics
3-Dipeptidyl peptidase-4(DPP-4) inhibitors

Types of diabetes mellitus

(Type II) due to obesity, genetic factors
This type has 2 physiological defects:

1. Abnormal insulin secretion.
2. Resistance to insulin action in target tissues associated with decreased number of insulin receptors.

(Type I) due to autoimmune or viral diseases

Treatment of DM type II (non-insulin dependent DM)

1. Proper dietary management.
2. **Caloric restriction** and **weight loss** are important in obese diabetic patients.
3. Increase physical activity.
4. Oral antidiabetic drugs.

أمشي معه خطوة خطوة، مو كل الخطوات مع بعض
لو ما نفع معه أول ٣ خطوات، أحول على الخطوة الرابعة.

Oral hypoglycemic drugs:

A- Insulin <u>secretagogues</u>

- **Sulfonylurea** drugs.
- **Meglitinide** analogues.

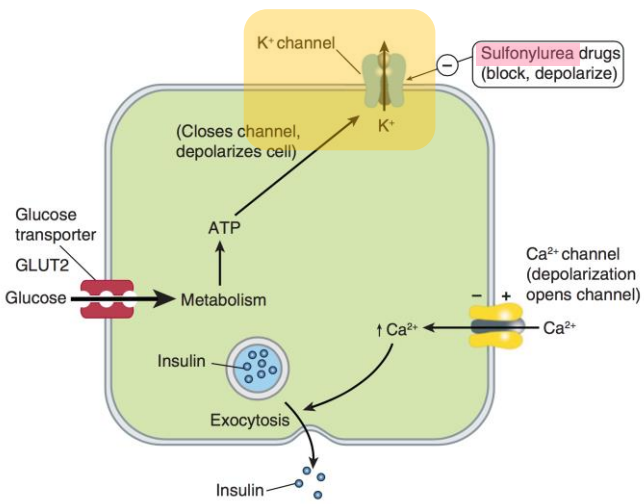
B- Insulin <u>sensitizers</u>

- **Biguanides**.
- **Thiazolidinediones** (**glitazone**)

C- Others

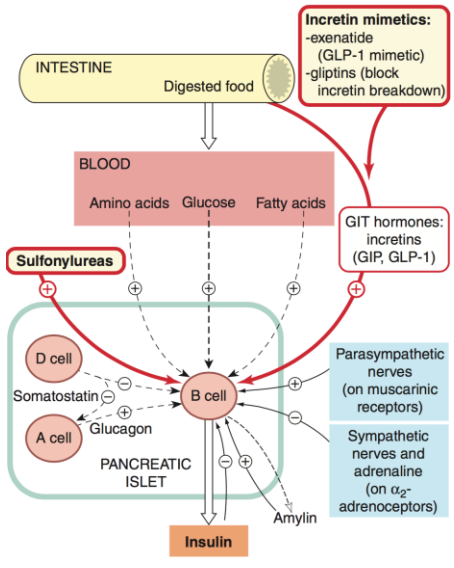
1. **Alpha glucosidase inhibitors** → reduce carbohydrate absorption.
2. **Incretin** mimetics (could be with <u>A</u>)
3. **Dipeptidyl peptidase-4 (DPP-4) inhibitors**.
- 2 & 3 → are new agents (GI hormones)

Mechanisms of Insulin Release:



Factors regulating insulin secretion

Extra



A- Insulin secretagogues

- Are drugs which **increase the amount of insulin secreted** by the pancreas.
- Their action depends upon **functioning pancreatic Beta-cell.**
- Which includes :
  1. **Sulfonylureas**
  2. **Meglitinides**

Classification of sulfonylureas

First generation

Prescribed in other countries other than KSA; they are cheap.

- **Short acting**
  - **Tolbutamide**
    مشهور أوي في البلدان التانية
- **Intermediate acting**
  - Acetohexamide
  - Tolazamide
- **Long acting**
  - Chlorpropamide

second generation

Commonly prescribe in KSA

- **Short acting**
  - Glipizide
- **Long acting**
  - Glibenclamide (Glyburide)
  - Glimepiride

A- Insulin secretagogues (cont.)

Mechanism of action of Sulfonylureas & Meglitinides

- Their action depends upon functioning pancreatic β-cells.
- Stimulate insulin release from functioning* B 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 beta cells, which stimulates insulin release. (see FIGURE 41–2 to understand better)
- **In a simple way**: when↑ hyperglycemia → ⊗ **ATP-sensitive K channels** → opening of voltage-dependent Ca^{2+} channels → ↑ insulin release
  - (Hence, not effective in totally insulin-deficient patients -Type I- bc their beta cells are dysfunctioned)

❖ They are the traditional treatment choice for type 2 diabetes.

1- Sulfonylureas

(Both **First** and **Second** generations)

MOA

- Potentiation of insulin action on target tissues.
- Reduction of serum glucagon concentration.
  - Appears to involve indirect inhibition due to enhanced release of both insulin and somatostatin, which inhibit alpha-cell secretion.
  - Long-term administration to type 2 diabetics reduces serum glucagon levels, which may contribute to the hypo- glycemic effect of the drugs.

P.K

- **Orally**, well absorbed. (almost **all** drugs in this lecture are taken orally except some of the incretin analogues)
- Reach peak (max. effect) concentration after 2-4 hr.
- All are **highly bound to plasma proteins** → drug-drug interaction
- Duration of action is variable. (short, intermediate, long)
- **Second** generation has **longer duration** (and are more potent) than first generation → 2nd gen. has lower frequency of administration (bc of long duration) يعني بدل ما أخليه يأخذ من الفرست جنريشن ٣ مرات في اليوم، أقول له خذ السكند جنريشن مرة وحدة في اليوم.
- Metabolized in liver.
- **Excreted in urine →** (all drugs in this family are excreted by urine. So you should **be careful** with **old patients** and patients with **renal impairment + DM II → the drug is not excreted → risk of accumulation & increase insulin secretion → result in hypoglycemia!!**)
- **Cross placenta**, stimulate **fetal Beta cells to release insulin → hypoglycemia at birth**. → if pregnant women → don't prescribe her an oral hypoglycemic, switch to insulin injection (even if she is DM II). why? Bc it has a teratogenic effect + fetal hypoglycemia.

Use

- Type II diabetes: monotherapy or in combination with other antidiabetic drugs.
- The second-generation sulfonylureas are prescribed more frequently, because they have fewer adverse effects and drug interactions.

ADRs

- **Hypoglycemia** due to hyperinsulinemia: (Sulfonylurea is the No. 1 in causing hypoglycemia.)
  - More common in long acting sulfonylureas. particularly (glyburide, and glimepiride) → bc they are very potent.
  - More in **old age**, **hepatic or renal diseases**.
- **Weight gain** due to increase in appetite unless the diabetic diet and exercise program are followed.

1- Sulfonylurea (cont.)

❖ Second generation Sulfonylurea

- More potent than first generation
- Have longer duration of action.
- Less frequency of administration
- Have fewer adverse effects & drug interactions

	Glipizide	Glibenclamide (Glyburide)	Glimepiride The **most potent**, bc it is taken in 1mg dose, while the others needs more dose.
Absorption	Well	Well	Well
Metabolism	Yes	Yes	Yes
Metabolites	Inactive	Moderate activity	Moderate activity
Half-life	2 – 4 hrs	Less than 3 hrs	5 - 9 hrs
Duration of action	**short** (**10 – 16 hrs**)	long (12 – 24 hrs)	long (12 – 24 hrs)
Doses ما نحفظ الدوز	Divided doses 30 min **before meals** If he responses well, single dose is enough.	Single dose	Single dose
Excretion	Urine	Urine	Urine

2- Meglitinide analogues

Drug: Repaglinide, Nateglinide

MOA

- **Rapidly acting Insulin secretagogue**.
- Mechanism of action is identical to sulfonylureas.

P.K

- **Orally**, well absorbed.
- **Very fast onset of action, peak 1 h.** (the most important thing to remember in this family)
- **Short duration of action (4 h).** وهذا فرق عن الsulfa
- Taken just before each meal → (3 times/day) the dose should be skipped if the meal is missed. (they are taken with meals , if you skip the meal you skip the dose)
- Metabolized in the liver & excreted in bile. → a benefit for meglitinide, when pt has renal failure → can't use sulfonylurea → he can use meglitinide.

Uses

- Type II diabetes (monotherapy or in combination with other oral hypoglycemic drugs).
- Patients **allergic to sulfonylurea** (allergic to anything from any sulfur containing drug)

ADRs

- **Hypoglycemia**. (**less common** because of short duration of action)
- Weight gain.
- Its ADRs are less incidence than sulfonylureas.

B- Insulin sensitizers

Increase the sensitivity of target organs to insulin (no effect on insulin secretion) → no hypoglycemia effect.

Drug: 1- Biguanides, e.g. Metformin (glucophage)

MOA

- Increases peripheral glucose utilization (tissue glycolysis) → Reduce insulin resistance.
- Inhibits hepatic gluconeogenesis & Impairs glucose absorption from GIT.
- ↓ LDL, ↓ VLDL & ↑ HDL.

P.K

- Orally.
- NOT bound to serum protein.
- NOT metabolized.
- T ½ 3 hours. (patient should use it **3 times** a day)
- Excreted unchanged in urine

Uses

- Obese patients with type 2 diabetes (recently diagnosed) → because it promotes modest weight reduction (**first-line therapy**).
- Type II diabetes as monotherapy or in combination.

أول ما يشخص بالسكر، أبدأ معه بال diet & exercise وإذا ما نفع أبدأ أعطي **المتفورمن**، أنتبه إني مب أول شيء أعطي الsulfa!

ADRs

- **GIT disturbances**: Metallic taste in the mouth, nausea, vomiting, diarrhea → **Should be taken with meals** and **started at a low dose** to avoid intestinal side effects then **increase gradually**. هذي المشكلة مهمة أوي لأن ممكن العيان يوقف استخدام الدواء منها
- **Lactic acidosis** (rare)→ (bc it ↑ glycolysis) **Serious** lactic acid accumulation usually occursonly in the presence of a predisposing conditions: Renal insufficiency, sever liver disease, **alcohol abuse**, heart failure & **hypoxic** states (the most imp., bc of increased anaerobic glycolysis), Pulmonary insufficiency, cardiogenic or septic shock.
- **Interference with vit. B12 absorption** (long term use).

When pt is going to do CT → have to take **radiocontrast** → may result in **nephrotoxicity** → **STOP metformin** bc of the lacic acidosis risk!

Advantages

- **No risk of hypoglycemia or weight gain**
- has prominent lipid-lowering activity
- Improvement of lipid profile
- Inexpensive.

C.I

- Renal disease. (excreted in urine)
- Liver disease.
- Pregnancy.
- Alcoholism. (can increase lactic acid)
- Cardiopulmonary dysfunction.

متفقين من الأول إن الحامل ما تُعطى oral hypoglycemic drugs إنما نستخدم لها الإنسولين

Drug: 2- Thiazolidinediones (Glitazone), e.g. Pioglitazone, Rosiglitazone

MOA

- Activate peroxisome proliferator-activated receptor -γ (**PPAR-γ**) [nuclear receptors in muscles, liver and adipose tissue (a major site of action in persons with diabetes)].
- Increase glucose uptake and utilization in muscle and adipose tissue (PPAR-γ receptors modulate the expression of the genes involved in lipid and glucose metabolism)
- Increase sensitivity of target tissues to insulin

P.K

- Orally (once daily dose). Follow up is imp. in determining the daily dose
- **Highly bound to plasma albumins** (99%)
- **Slow onset of activity**
- Half life 3-4 h
- Metabolized in liver.
- Excreted in bile & urine.

Uses

- Type II diabetes with **insulin resistance**.
- Used either alone or combined with sulfonylurea, biguanides or insulin.

الInsulin sensitizersd أقدر أعطيهم للDM I بس لازم أعطيهم إنسولين اللي هو الأساس..
فايدة الInsulin sensitizersd إنهم ممكن يقللون الجرعة اللي يحتاجها المريض ب DM I

ADRs

- **Hepatotoxicity** (liver function tests for 1st year of therapy)
- Congestive heart failure
- **Fluid retention** (Edema) "common" → cause mild **weight gain**
- **Failure of estrogen-containing oral contraceptives**.

ممكن يجيك المريض وتصير الكبد عنده ماشية تمام، بس جاي يشتكي من زيادة الوزن الناتجة من استخدام هذا الدواء.

Advantages

- No risk of hypoglycemia when used alone

C- Others

1- α-Glucosidase inhibitors (reduce carbohydrate absorption)

Drug

Meglitol, Acarbose

Mech. of action

- Reversible **inhibitors of intestinal α-glucosidases** in intestinal brush border responsible for degradation of oligosaccharides to **monosaccharides** (carbohydrate digestion) → reduce postmeal glucose excursions by delaying the digestion and absorption of starch and disaccharides → **Only** monosaccharides, such as glucose and fructose, can be transported out of the intestinal lumen and into the bloodstream.
  *α-glucosidases: sucrase, maltase, glucoamylase, and dextranase.
  → **Decrease carbohydrate digestion and absorption in small intestine.**
  → **Decrease postprandial hyperglycemia.**
  بس خذوا بالكم! الدواء هذا mainly depends on type of eating، بمعنى لو فرضنا إن الشخص ما يأكل كاربوهيدريت فما راح نشوف نتائج للدواء، لأنه يشتغل على الكارب فقط!
- No hypoglycemia if used alone.
- Bind to carbohydrate-splitting enzyme (α-glucosidases) at the receptors site, By blocking these sites Glucobay (acarbose) competitively and reversibly inhibits the digestion of carbohydrate in the small intestine.
- Competitively inhabits the breakdown of non absorbable complex carbohydrates to absorbable monosaccharides.

P.K

- **Acarbose:**
  - Given orally, **poorly absorbed** → Excreted in feces → produce ADRs.
  - Taken just before meals.
  - Metabolized by intestinal bacteria.
- **No hypoglycemia** if used alone. If hypoglycemia occurs should be corrected with **glucose tablets or gel**. Glucose (monosaccharides) بس ال

في حالات نادرة جدًا ينتج عندنا الhypoG ، لكن لو حصلت.. هنا زي ما نعرف لازم to correct hypoG لكن ما أستخدم أي عصير أو حلاوة بجيبي! لازم يكون الشيء اللي باكله **monosaccharides** عشان يصير له امتصاص؛ لأن زي ما نعرف إن هالدواء سوى inhibition of glucosideas اللي يكسر الoligosaccharides to monosaccharides (مهم نعرفها)

Uses

- Effective alone in the **earliest stages** of impaired glucose tolerance → α-glucosidase therapy in prediabetic persons successfully prevented a significant number of new cases of type 2 diabetes and helped restore beta- cell function.
- **Not** recommended alone as therapy for **moderate to severe hyperglycemia**
- Most useful in combination with other oral hypoglycemic drugs or with insulin.

ADRs

- **GIT**: **Flatulence**, **diarrhea**, abdominal pain.
  - Result from the appearance of undigested carbohydrate in the colon that is then fermented into short-chain fatty acids, releasing gas

C.I

- Irritable bowel syndrome .
- Intestinal obstruction.
- Inflammatory bowel disorders

→ Because they could be worsened by gas and distention.

Anything related to GIT

2- Incretin mimetics

- Incretins are GI hormones secreted **in response to food**, carried through circulation to the beta cells, they regulate blood glucose by: **stimulate insulin secretion** & **inhibit alpha cells** → **decrease glucagon** secretion. → This effect is referred to as the "incretin effect" and is markedly reduced in type 2 diabetes.
- Incretin hormones are responsible for 60 to 70 percent of postprandial insulin secretion.

كيف اكتشفوها؟ سووا تجربة وجربوا يعطون oral glucose & I.V. Glucose ، وجدوا إن نسبة الإنسولين الموجودة في الدم لما أعطوا السكر بالفم أعلى من نسبة الإنسولين في الدم لما أعطوا السكر intravenously

- The production of these incretins depends on the existence of food → no risk of hypoG.
- Two main Incretin hormones:
  1. **GLP-1** (glucagon-like peptide*-1)
  2. **GIP** (gastric inhibitory peptide* or glucose-dependent insulinotropic peptide)

✓ Both are inactivated by **dipeptidyl peptidase-4** (DPP-4) → that's why they have very short T1\2 (around min)

* Peptide → not taken orally.

GLP-1 agonists (Incretin mimetics)

Drugs	Dulaglutide, Exenatide
	Dulaglutide
Mnemonic	○ الأقونيست ل GLP-1 السفيكس حقها هو تايد ، وتايد معروف يغسل الملابس (مبيّض) ودايما الشي اللي ينوصف إنه أبيض هو القلب يعني ال GLP-1 (قلبي أبيض).
MOA	○ Is glucagon-like peptide-1 (GLP-1) agonist. ○ Binds to GLP-1 receptors &stimulates insulin secretion from β cells. ○ It also reduces glucagon secretion by inhibiting alpha cells of the pancreas.
ROA	○ Given **S.C**. taken by injection الدوائين الوحيدين في هالمحاضرة , once/week
Indications	○ Used together with diet and exercise to treat type 2 diabetes and in patients who are **not controlled with other oral antidiabetics**. ○ **Not used in type 1 diabetes**.
ADRs	○ **Nausea & vomiting** (most common) ○ Abdominal pain, decreased appetite & fatigue. ○ Hypoglycemia when combined with sulfonylureas or insulin.

3- Dipeptidyl peptidase-4 (DPP- 4) inhibitors

Drug	**Sitagliptin, Vildagliptin**
MOA	○ Inhibit DPP-4 enzyme and leads to an increase in incretin hormones level. This results in an increase in insulin secretion & decrease in glucagon secretion.
P.K	○ Orally, once a day. ○ half life 8-14 h
Use	○ Type 2 DM as an adjunct to diet & exercise as a monotherapy or in combination with other antidiabetic drugs.
ADRs	○ Nausea, abdominal pain, diarrhea ○ Runny nose. Joint & muscle pain. ○ Nasopharyngitis.

Summary from prof.Hanan's slides

Class	Mechanism	Site of action	Main advantages	Main side effects
Sulfonylureas	Stimulates **insulin secretion**	Pancreatic beta cells	• Effective • Inexpensive	• Hypoglycemia • Weight gain
Meglitinides **repaglinide**		Pancreatic beta cells	Sulfa free	• Hypoglycemia • Weight gain
Biguanides **Metformin**	Decreases **insulin resistance**	Liver	• mild weight loss • No hypoglycemia	• GIT symptoms, • Lactic acidosis • Metallic taste
Thiazolidinediones **pioglitazone**		Fat, muscle	No hypoglycemia	Hepatoxicity Edema, mild weight gain
α-Glucosidase inhibitors **Acarbose**	Inhibits **α-glucosidase**	GI tract	Low risk	• GI symptoms, flatulence
Incretins mimetics **Dulaglutide**	Increase incretin	GI tract	Once/week, **s.c.**	Nausea & vomiting
DPP-4 inhibitors **Sitagliptin**	Inhibit incretin breakdown	GI tract	orally	Nausea & abdominal pain

Summary-1

A- Insulin Secretagogues
(increase the amount of insulin secreted by the pancreas)

Class

1- Sulfonylureas

MOA

- This drug Stimulate insulin release from functioning B 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 beta cells, which stimulates insulin release.
- ↑ Hyperglycemia → Blockade of ATP dependent K+ channels → Opening of voltage-dependent Ca++channels → ↑ intracellular calcium in the beta cells → ↑ Insulin release.

P.K.

- Orally, well absorbed.
- Reach peak concentration after 2-4 hr.
- All are highly bound to plasma proteins.
- Duration of action is variable.
- Second generation has longer duration than first generation.
- Metabolized in liver
- Excreted in urine (elderly and renal disease)
- Cross placenta, stimulate fetal β-cells to release insulin → fetal hypoglycemia at birth.

First generation			Second generation	
Tolbutamide (shrt acting)	**Acetohexamide** **Tolazamide** (intermediate acting)	**Chlorpropamide** (long acting)	**Glipizide** (short acting)	**glibenclamide** (**Glyburide**) **Glimepiride** (long acting)

- Tolbutamide:
has **short** duration of action
safe for elderly diabetic patients or patients with renal impairment.

- **More potent** than first generation
- Have **longer** duration of action.
- Less frequency of administration
- Have **fewer adverse effects**
- Have **fewer drug interactions**

ADRs

- **Hyperinsulinemia** & **Hypoglycemia**:
  - More common in long acting sulfonylureas. particularly chlorpropamide, glyburide, and glimepiride)
  - More in **old age, hepatic or renal diseases.**
  - Less in tolbutamide.
- Weight gain due to increase in appetite unless the diabetic diet and exercise program are followed.

Drug

2- Meglitinides Repaglinide, Nateglinide

MOA

- Repaglinide are rapidly acting insulin secretagogues
- Insulin secretagogue.
- Mechanism of action is identical to sulfonylureas.

P.K

- **Orally**, well absorbed.
- Very fast onset of action, peak 1 h.
- **Short duration of action (4 h).**
- 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.

Indications

- Type II diabetes (monotherapy or in combination with other oral hypoglycemic drugs)
- As alternative to sulfonylureas in **patients allergic to sulfur**.

ADRs

- **Less incidence than sulfonylureas**
- Hypoglycemia.
- Weight gain.

Summary-2

B- Insulin sensitizers

Are drugs which increase the sensitivity of target organs to insulin.

Drug	Biguanides e.g: **Metformin**	Thiazolidinediones (glitazones) e.g: **Pioglitazone**
MOA	- Increases glucose utilization by peripheral tissues (tissue glycolysis) - Reduces insulin resistance. - Inhibits hepatic gluconeogenesis. - Reduce LDL and VLDL & Increase HDL.	- Activate peroxisome proliferator-activated receptor - (PPAR-γ). - Increase glucose uptake and utilization in muscle and adipose tissue. - Increase sensitivity of target tissues to insulin.
P.K	- orally. - NOT bound to serum protein. - NOT metabolized. - t ½ 3 hours. - Excreted unchanged in urine	- Orally (once daily dose). - **Highly bound to plasma albumins (99%)** - **Slow onset of activity** - Half life 3-4 h - Metabolized in liver. - Excreted in urine 64% & bile
Indications	- In patients with type 2 diabetes who are obese because it promotes modest weight reduction (first-line therapy). - Type II diabetes as monotherapy or in combination.	- Type II diabetes with insulin resistance. - Used either alone or combined with sulfonylurea, biguanides or insulin. - No risk of hypoglycemia when used alone
ADRs	- No risk of hypoglycemia - **No weight gain** - has prominent lipid-lowering activity - Lactic acidosis - GIT disturbances: **Metallic taste** in the mouth, nausea, vomiting, diarrhea - **Interference with vitamin B12 absorption** (long term use).	- Hepatotoxicity (liver function tests for 1st year of therapy). - Fluid retention (Edema). - Congestive heart failure - Mild weight gain. - Failure of estrogen-containing oral contraceptives
C.I	- Renal disease. - Liver disease. - Alcoholism. - Cardiopulmonary dysfunction. - Pregnancy.	

C- Others

Glucosidase inhibitors

drug	Acarbose	Miglitol
MOA	- Reversible **inhibitors of intestinal-glucosidases** in intestinal brush border that are responsible for carbohydrate digestion. - Decrease carbohydrate digestion and glucose absorption in small intestine (lower postprandial glucose level).	
P.K	**Acarbose**: - Given orally, **poorly absorbed**. - Metabolized by intestinal bacteria. - Excreted in stool and urine.	
ADRs (Both)	- **GIT side effects:** Flatulence, diarrhea, abdominal pain, bloating.	
Uses	- Effective alone in the **earliest stages** of impaired glucose tolerance - **Not** recommended alone as therapy for **moderate to severe hyperglycemia** - Most useful in combination with other oral hypoglycemic drugs or with insulin.	
C.I	- irritable bowel syndrome - Inflammatory bowel disorders - Intestinal obstruction.	

Summary -3

Incretins mimetics

- Incretins are **GI hormones** secreted from intestine in response to food even before blood glucose level becomes elevated. They are carried through circulation to beta cells.
- Increase insulin secretion & decrease in glucagon secretion (regulate blood glucose).

Drug	GLP-1 agonists Dulaglutide
P.K	- Is glucagon-like peptide-1 (GLP-1) agonist. - **Given S.C**. once a week.
Uses	- patients with type 2 diabetes who are **not** controlled with oral medication
ADRs	- **Nausea & vomiting** (most common). - Abdominal pain, decreased appetite & fatigue.

Dipeptidyl peptidase-4 inhibitor (DPP- 4 inhibitors)

Drug	Sitagliptin, Vildagliptin
MOA	- Inhibit DPP-4 enzyme thus increase incretin hormone (GLP-1).
P.K	- Orally - Given once daily
Uses	- Type II DM as an adjunct to diet & exercise as a monotherapy or in combination with other antidiabetic drugs.
ADRs	- Nausea, abdominal pain, diarrhea - **Nasopharngitis**

you can find extra-summaries for this lecture in our folder in the download center.

VERY HELPFUL!!!

Treatment guidelines for type 2 diabetes

Extra, but has been explained by Prof.Hanan

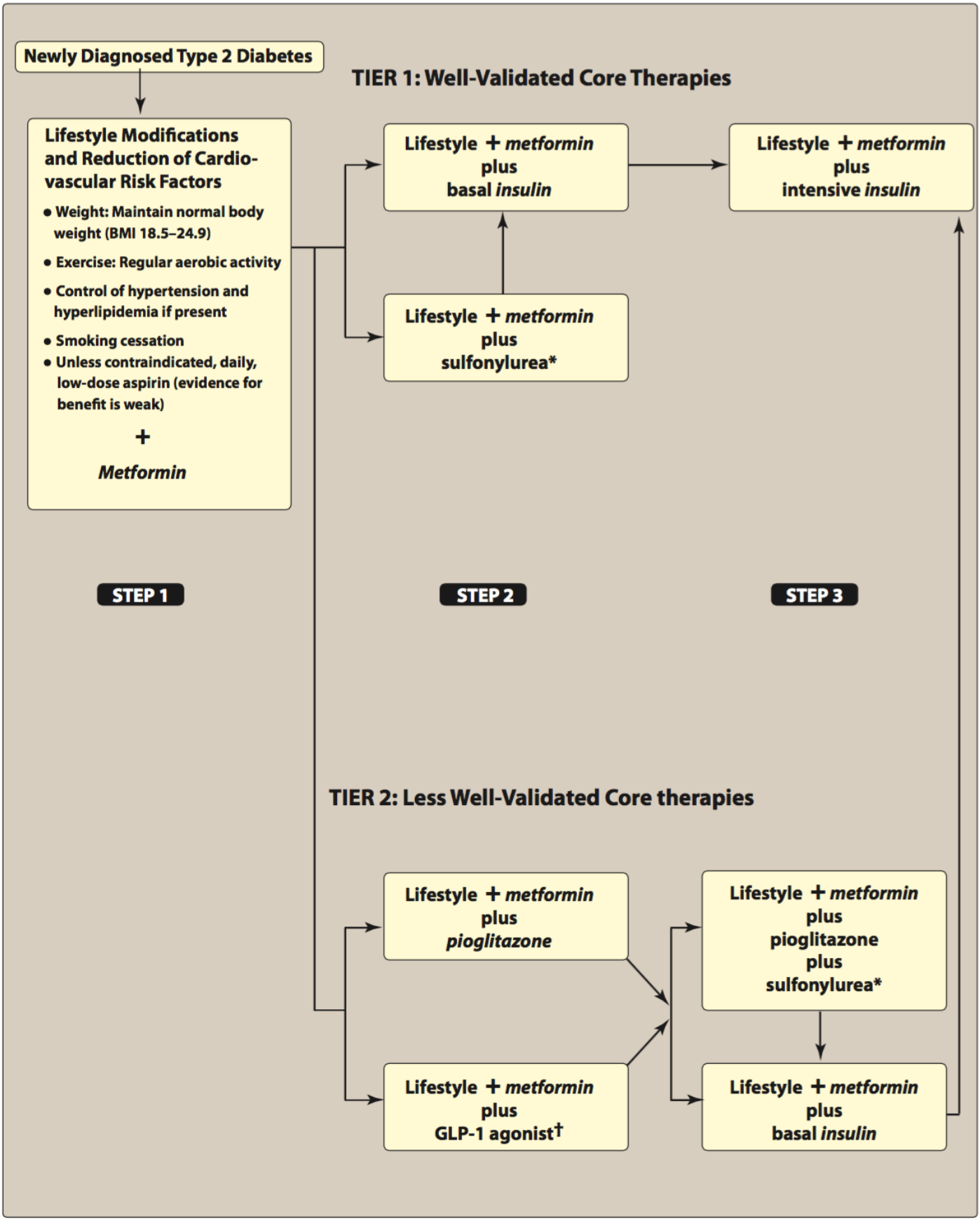


Figure 24.14
Treatment guidelines for type 2 diabetes *Sulfonylureas other than *glyburide* or *chlorpropamide*. †Insufficient clinical use to be confident regarding safety.

MCQs

1- Which of the following drugs is inactivated by dipeptidyl peptidase-4 (DPP-4):
A- Acarbose
B- Meglitol
C- Sitagliptin
D- None of the above

2- Which of the following drugs is not used in type 1 diabetes:
A- Acarbose
B- Meglitol
C- Sitagliptin
D- Dulaglutide

3- Overweight lady with type 2 diabetes she has history of pernicious anemia what is drug contraindicated?
A- Metformin
B- Pioglitazone
C- Insulin
D- Sulfonylurea

4- Overweight man with type 2 diabetes and high blood cholesterol. what is most appropriate drug?
A- Metformin
B- Pioglitazone
C- Insulin
D- Sulfonylurea

5- The following antidiabetic drug inhibits intestinal brush border a-glucosidase enzymes:
A- Acarbose
B- Pioglitazone
C- Metformin
D- Sulfonylurea

6- Meglitinide analogues differ from sulfonylureas in:
A- Metabolized by the liver
B- Absorbed orally
C- Used in type 2 diabetes
D- Fast onset of action

7- Which of the following is true of acarbose:
A- It reduces absorption of glucose from intestines.
B- It produces hypoglycaemia in normal as well as diabetic subjects.
C- It limits postprandial hyperglycaemia in diabetics.
D- It raises circulating insulin levels

8- Select the drug which tends to reverse insulin resistance by increasing cellular glucose transporters:
A- Glibenclamide
B- Rosiglitazone
C- Acarbose
D- Prednisolone

9- Choose the correct statement about nateglinide:
A- It is a long acting oral hypoglycaemic drug
B- Taken just before a meal, it limits postprandial hyperglycaemia in type 2 diabetes mellitus
C- It lowers blood glucose in both type 1 and type 2 diabetes mellitus
D- It acts by opening K+ channels in myocytes and adipocytes

10- Metformin acts by:
A- Releasing insulin from pancreas
B- Suppressing gluconeogenesis and glucose output from liver
C- Up regulating insulin receptors
D- Inhibiting degradation of insulin

11- Choose the correct statement(s) about pioglitazone:
A- It acts as an agonist on nuclear paroxisome proliferator receptor γ
B- It enhances transcription of insulin res ponsive genes
C- It lowers blood sugar in type 2 diabetes mellitus without causing hyperinsulinemia
D- All of the above

Answers: 1-D 2-D 3-A 4-A 5-A 6-D 7-C 8-B 9-B 10-B 11-D

Thank you for checking our team!

Pharmacology 435

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Sources:

1. 435's slides.
2. Pharmacology (Lippincotts Illustrated Reviews Series), chapter 24, 5th edition.
3. Basic & Clinical Pharmacology by Katzung, chapter 41,12th edition.
4. Rang & Dale's pharmacology, chapter 30, 7th edition.