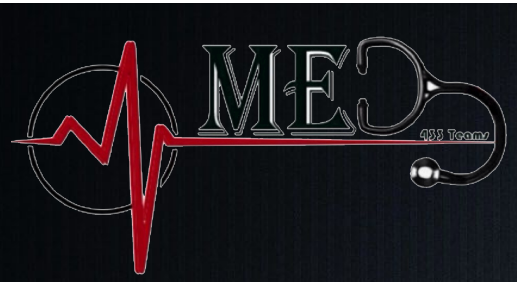
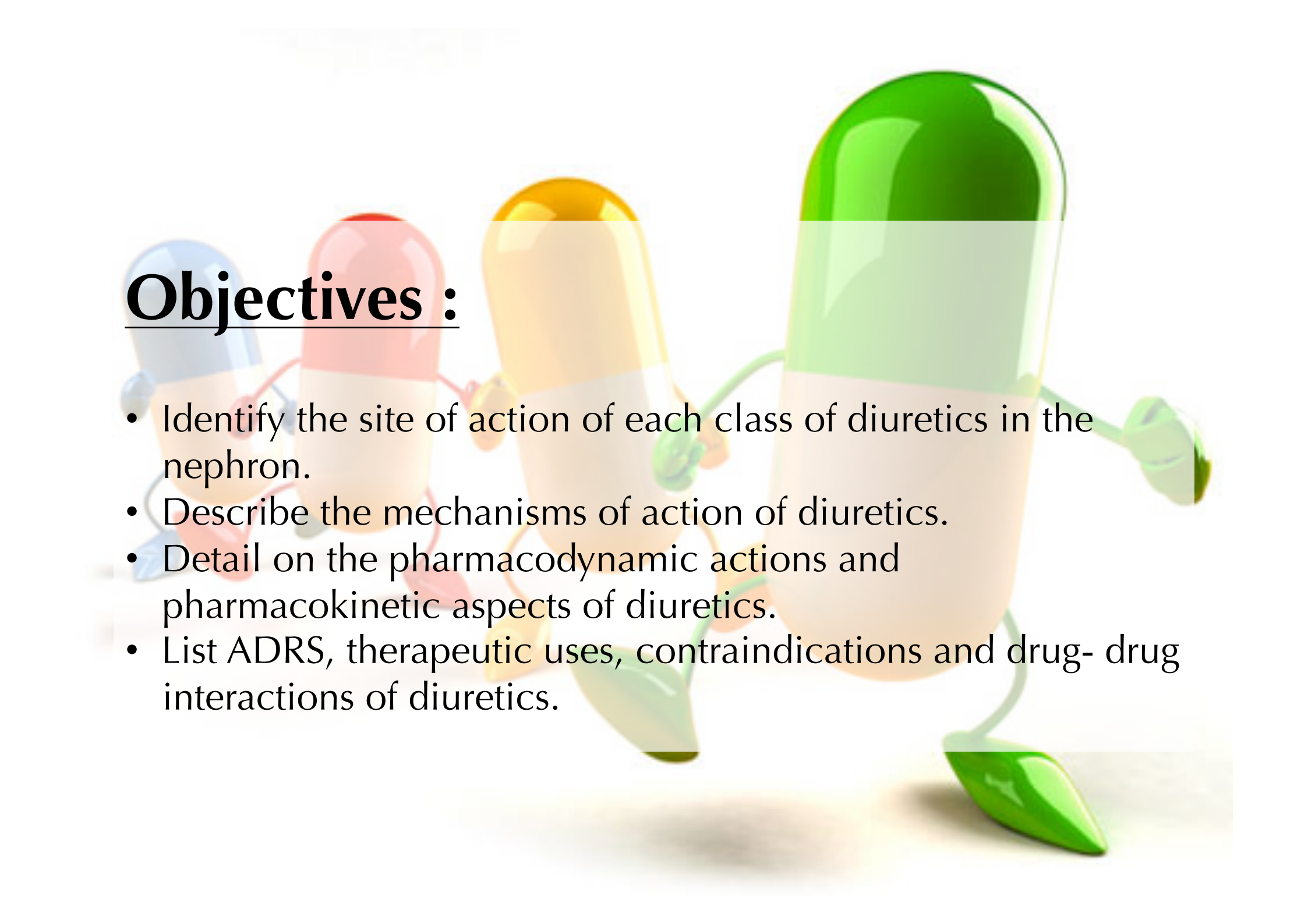


KING SAUD UNIVERSITY
COLLEGE OF MEDICINE
1ST YEAR, 5TH BLOCK

Loop and Thiazide Diuretics 6

RENAL BLOCK



Objectives :

- Identify the site of action of each class of diuretics in the nephron.
- Describe the mechanisms of action of diuretics.
- Detail on the pharmacodynamic actions and pharmacokinetic aspects of diuretics.
- List ADRS, therapeutic uses, contraindications and drug- drug interactions of diuretics.

Na-Cl SYMPORT INHIBITORS

Also Called: Thiazide Diuretics , Thiazide-Like Diuretics

-Hydrochlorothiazide "Potency 1 , t½ 3h"
- Chlorothiazide "Potency 0.1, t½ 2h"
- Indapamide 'Potency 20, t½ 16h"
- Chlorthalidone " Potency 10, t½ 26h"
- Metolazone "Potency 5, t½ 5h"

Thiazides

-Act on early distal tubule[5-10%of filtered load of sodium is reabsorbed].
-Weak inhibitors of carbonic anhydrase , but this does not contribute to their action

Kinetics	- are **lipid soluble** **- Given orally,** efficiently absorbed from the G.I.T. **- Long duration of action** - Eliminated by glomerular filtration & tubular secretion , some is reabsorbed **- May interfere with uric acid secretion and cause hyperuricemia**
Actions	1- considerable K+ loss (**hypoKalemia**) **2-↓uric acid , ↓Ca++ excretion ,↑Mg++ excretion** **3-May give rise to hypochloraemic alkalosis** 4- Causes vaso**d**ilatation , diazoxide , non diuretic thiazide is a potent vasodilator 5-↓of urine volume in case of **diabetes insipidus (decrese blood volume & GFR)**
Mechanism of antidiuretic effect of thiazide in diabetes insipidus	Thiazide → ↑Distal tubular Na+ reabsorption→ ↑Urinary excretion → ↓Extracellula volume →↑Proximal Na+ & Water reabsorption in →↓Distal delivery of Na+ & water →↓Urinary output
Change of urine induced by thiazides	Increase execration of **Na** , **K** and **urinary volume** Decrease execration of **Ca**

INTERACTIONS:

Thiazides diminish affect of :
uricosurics, sulphonylurea.
Thiazides increase affect of :
digitalis, diazoxide.
NSAIDs reduce effect of Thiazide.

ADVERSE EFFECTS:

Extracellular fluid volume depletion, metabolic alkalosis, increased LDL, impotence.
Hypokalemia, hypomagnesmia, hyponatremia.
Hypercalcemia, hyperglycemia, hyperuricemia(gout), hyperlipidemia.

THERAPEUTIC USES:

(Increase Na Excretion to 5% of Filtered Load)
1- Mild edema (ineffective when GFR less than 30-40 ml/min)
2- Hypertension. 3- Nephrogenic Diabetes Insipidus.
4- Ca Nephrolithiasis (kidney stones), Osteoporosis (due to decrease Ca excretion).
5- Mild heart failure (to reduce extracellular volume)

Loop Diuretics:

Na-K-2Cl SYMPORT INHIBITORS **(The most potent diuretic)**

Also called: High Ceiling Diuretics. **(↓Renal vascular resistance &↑renal blood flow)**

1-Bumetanide (the most potent) Potency40 ,t½ 0.8	2-Furosemide Potency **1**, t½ 1.5h	3-Torsemide Potency **3**, t½ 3.5h	4-Ethacrynic Acid Potency **0.7**, t½ 1

Acts on the **thick segment of the ascending loop of Henle[25% of glomerular** filtrate of Na+ is reabsorbed]

M.O.A: Simply they inhibit the coupled NA/K/2Cl transport in the loop of Henle. Also, they have potent pulmonary vasodilation effects.

(↑urinary excretion by ecxcrete Na, cl, ca → ↑urine volume)

Pharmacokinetics: Given orally or I. V. & Have fast onset of action (suitable for emergency) & Have short duration of action.

-Excreted by active tubular secretion of weak acids into urine (avidly bound to plasma proteins).

-Interfere with uric acid secretion(**hyperuricemia**) .

THERAPEUTIC EFFECTS AND USES

1-**Increase Na Excretion to 25% of Filtered Load** → Treatment for Severe Edema

2-**Increase Urine Volume** → Treatment for Oliguric ARF

3-**Increase Ca Excretion** → Treatment for Hypercalcemia

4-**Increase Venous Capacitance** → Treatment for Pulmonary Edema

5-**Increase K+ Excretion** → Acute Treatment for Hyperkalemia

6- increase excretion of Mg

ADVERSE EFFECTS

- Metabolic Alkalosis
- Hyperglycemia
- Hyperuricemia
- Ototoxicity
- Profound Extracellular fluid volume Depletion
- Hypokalemia
- Hypocalcemia
- Hypomagnesemia
- Postural hypotension
- Hyponatremia

DRUG INTERACTIONS

1-NSAIDS Probenecid → **Diminished Diuretic Response**
2- Digitalis → **Arrhythmias**
3- Aminoglycosides → **Enhanced Ototoxicity of Loop Diuretic**

Contraindications:

1- Severe Na^+ and volume depletion
2-Hypersensitivity to sulfonamides
3- Anuria unresponsive to a trial dose of loop diuretic.

S U M M A R Y

Group	Thiazides (Na-Cl SYMPORT INHIBITORS)	Loop diuretics (high Ceiling diuretics) Na-K-2Cl SYMPORT INHIBITORS
Examples	Chlorothiazide, Hydrochlorothiazide, chlorthalidone, Indapamide*, metolazone	Furosemide, Ethacrynic Acid Bumetanide*, Torsemide
Act on	early distal tubule	Thick segment of the ascending loop of Henle
P.K	Lipid soluble – Given orally – Long duration of action – Some is reabsorbed from filtrate.	Fast onset of action (emergency), short duration of action
Action (Effect)	1- K+ Loss 2- Na loss 3- ↓Ca excretion 4-↑Mg excretion 5- ↓Uric acid	Inhibit Na\K\2Cl co-transport system in thick ascending segment off Henle loop
Therapeutic use	Nephrogenic Diabetes Insipidus – Hypertension Mild edema - Calcium Nephrolithiasis – Osteoporosis – HF	Severe edema- Oliguric ARF - Hypercalcemia-Pulmonary edema-Hyperkalemia
Adverse effect	1- Hypokalemia 2- Hyponatremia 3- Hyperglycemia 4- Hyperuricemia 5- Hypercalcemia 6-↑ LDL 7- Metabolic alkalosis 8- Impotence	1-Hypocalcemia 2-Hypokalemia 3- Ototoxicity 4- Hyperuricemia 5-Hyperglycemia 6-Metabolic Alkalosis
Drug interaction	↑ effect of Uricosurics Sulphonylurea ↓ effect of digitalis & Diazoxide NSAIDs reduce thiazide efficacy	1- NSAIDs and probenecid ↓diuretics response 2- Digitalis => arrhythmia 3- Aminoglycosides enhance ototoxicity of loop diuretics

* : Most potent

MCQs

Q1) Which one of the following is true about Thazide ?
A- Acr on PCT + weak inhibetor of carbonic anhydrase .
B- Act on Loop of Henle + strong inhibitor of carbonic anhydrase .
C- Act on early DCT + strong inhibitor of carbonic anhydrase .
D- Act on late DCT + weak inhibitor of carbonic anhydrase .
E- act on early DCT + weak inhibitor of carbonic anhydrase .

Q3) two pateints came to KKUH , first with mild edema , second with severe edema , what choice of diuretic drugs respectively ?
A- chlorothizide – torsomide .
B- Chlorthalidone - Metolazone
C- Bumetanide – Torsemide
D- Furosemide - Metolazone

Q4) patient came to KKUH with shortness of breathing , cough bloody sputum , doctor diagnosed him with pulmonary edema ,
which one of the following a true choice to him ?
A- Metolazone .
B- Chlorthalidone .
C- Bumetanide .
D- Indapamide .

Q5) The most effective diuretics is "high ceiling diuretic":
A. Loop diuretics
B. Thiazide diuretics
C. Potassium sparing diuretics
D. Osmotic diuretics

Q6) Which is the most appropriate diuretic for treating acute pulmonary oedema?
A. Loop diuretics
B. Thiazide diuretics
C. Potassium sparing diuretics
D. Osmotic diuretics

Q7) loop diuretics will have a beneficial effect in all these conditions, except:
A. Edema associated with nephrotic syndrome
B. Gout
C. Acute hyperkalaemia.
D. Acute hypercalcemia

Q8) Combination of loop diuretics and Aminoglycoside will increase the risk of unique side effect of loop diuretics which is:
A. Allergic reaction
B. postural hypertension
C. shock .
D. ototoxicity.

Q9) Which one of the following is example of loop diuretics:
A. Acetazolamide .
B. Torsemide .
C. Metolazone
D. Dorzolamide

Q10) Bumetanide is most efficacious diuretic because?
A) It inhibits 25-30% Na secretion at thin ascending limb
B) It inhibits 25-30% Na reabsorption at thin ascending limb
C) It inhibits 25-30% Na secretion at thick ascending limb
D) It inhibits 25-30% Na reabsorption at thick ascending
Limb

Q11) A patient was diagnosed to have Ototoxicity because he was taking?
A) Gentamycin + Hydrochlorothiazide
B) Tetracycline + Bumetanide
C) Gentamycin + Furosemide
D) Ciprofloxacin + Acetazolamide

1-E, 3-A, 4-C, 5-A, 6-A,
7-B, 8-D, 9-B, 10-D, 11-C

We hope we made this lecture easier for you
Contact us for any questions or comments
Good Luck !

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Jumanah Albeeybe
Hanan Al-Dossari
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