PHARM.D • YEAR 3

Medicinal Chemistry

CHAPTER 10

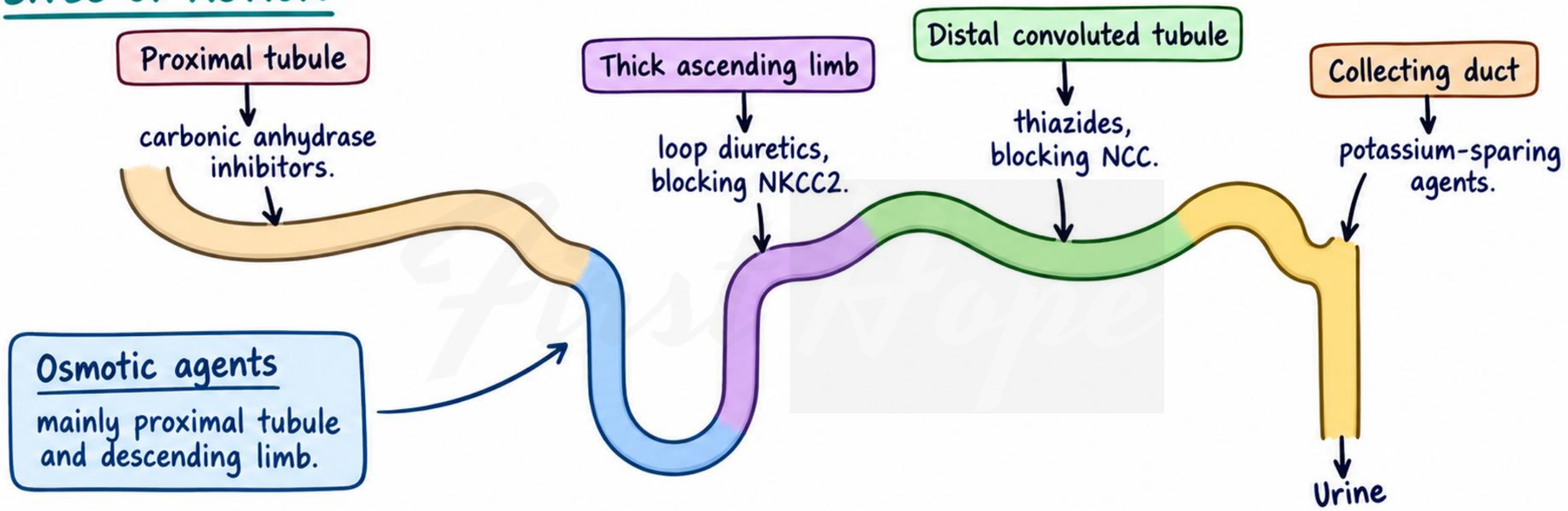
Diuretics

PPT CHAPTER COVER



DIURETICS & THE NEPHRON

SITES OF ACTION



WHAT IS A DIURETIC?

A drug that increases urinary salt or water excretion.
Natriuresis reduces extracellular fluid volume.

MAIN USES

Hypertension and oedema, including heart-failure congestion. Some classes also treat glaucoma or raised intracranial pressure.

CHECK

Drug class determines electrolyte effects.
Not all diuretics conserve potassium.

CARBONIC ANHYDRASE INHIBITION

ENZYME TARGET

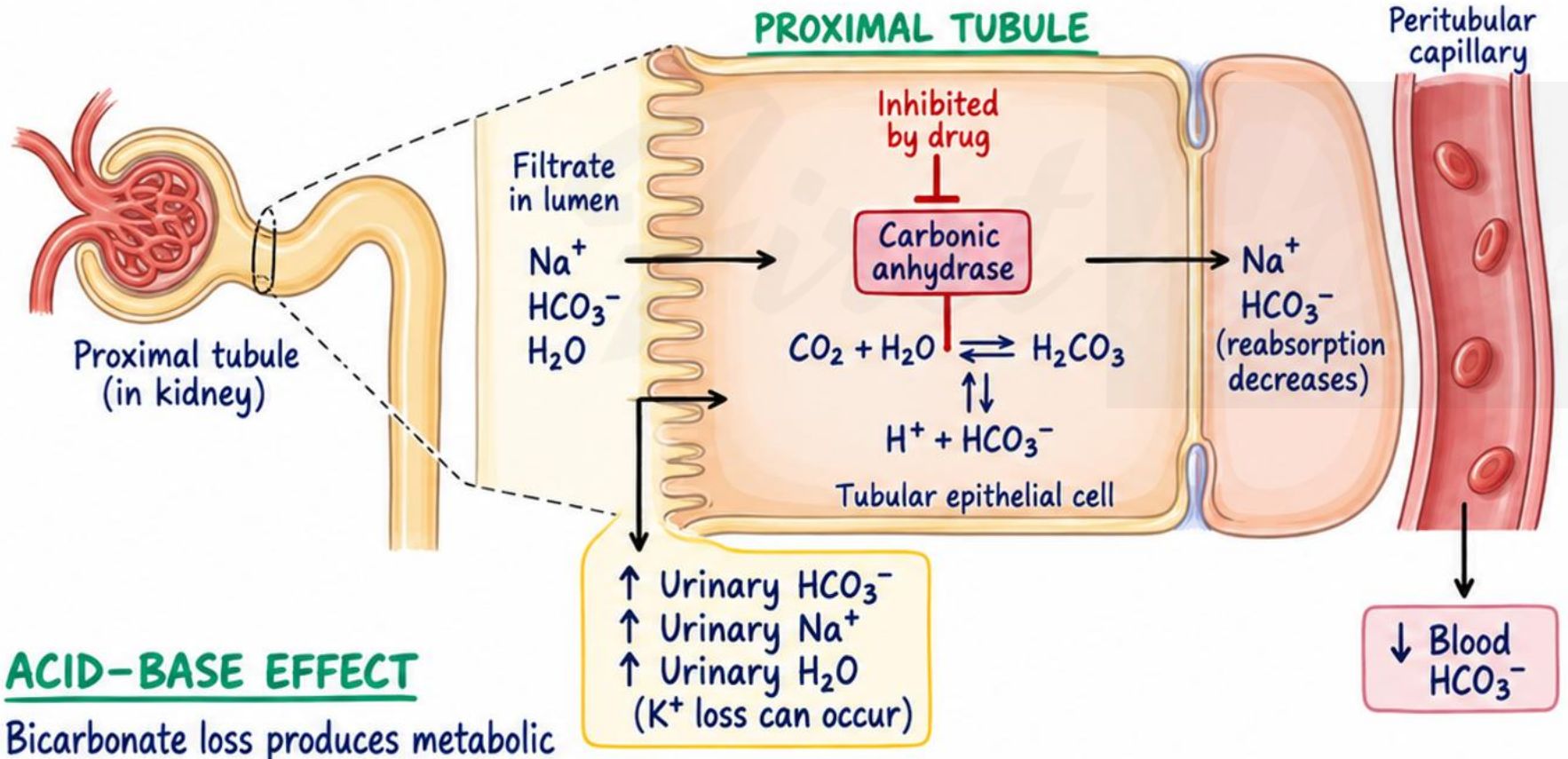
Carbonic anhydrase catalyses $CO_2 + H_2O$ in equilibrium with H_2CO_3, which forms H^+ and HCO_3^-.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

(Carbonic anhydrase)

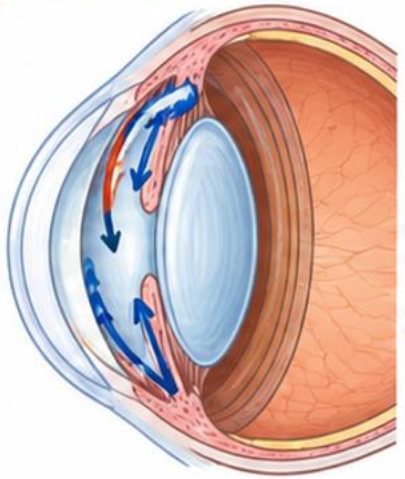
CLASS POINT

Free sulfonamide groups interact with the zinc-containing enzyme active site.



OTHER SITES

Reduced aqueous-humour formation lowers intraocular pressure.



Less aqueous humour formation
↓ Intraocular pressure

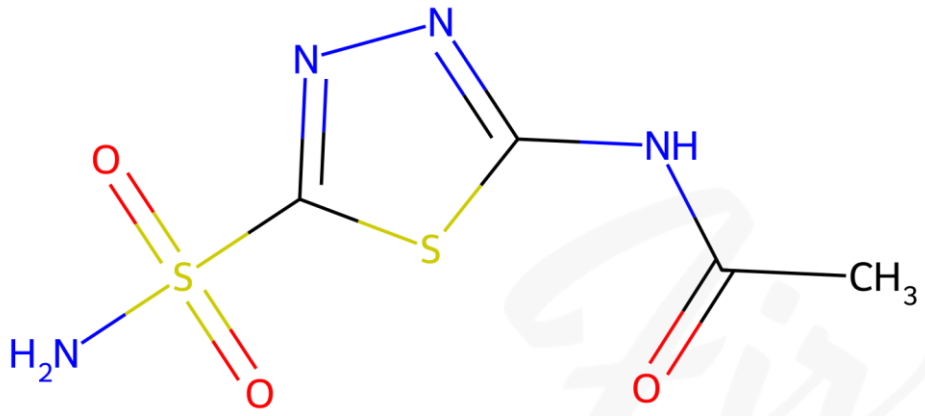
ACID–BASE EFFECT

Bicarbonate loss produces metabolic acidosis. Urine becomes more alkaline initially.

EXAMPLES

Acetazolamide, methazolamide and dichlorphenamide.

ACETAZOLAMIDE: CHEMISTRY & SAR



CHEMISTRY

Formula: $C_4H_6N_4O_3S_2$

IDENTIFY

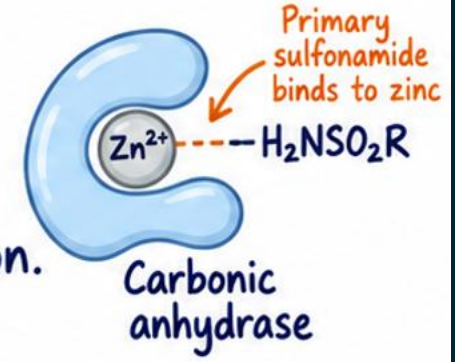
A 1,3,4-thiadiazole bearing an acetamido group and a primary sulfonamide. It has no benzene ring.

SAR

The primary sulfonamide is important for zinc-site binding. The heterocyclic ring and substituents affect affinity and properties.

ACTION

Carbonic anhydrase inhibition causes bicarbonate diuresis and reduces aqueous-humour formation.



USES

Glaucoma, altitude illness and selected metabolic-alkalosis or seizure settings.

CAUTIONS

Metabolic acidosis, electrolyte disturbances and sulfonamide-related reactions. It is not a dithiocarbamate drug.

ACETAZOLAMIDE: SYNTHESIS

1 CONDENSATION

Hydrazine hydrate
+
ammonium thiocyanate
↓
bis-thiocarbamoyl-hydrazine intermediate.

→

2 CYCLISATION

Cyclisation gives 2-amino-5-mercapto-1,3,4-thiadiazole.

→

3 ACETYLATION

Acetylation protects the amino group as an acetamido group.

$NH_2 \rightarrow NHCOCH_3$

→

4 OXIDATIVE CHLORINATION

Oxidative chlorination converts the mercapto group into a sulfonyl chloride.

$SH \rightarrow SO_2Cl$

→

5 AMMONOLYSIS

Ammonia converts the sulfonyl chloride into SO_2NH_2, yielding acetazolamide.

$SO_2Cl \rightarrow SO_2NH_2$

ROUTE OUTLINE IN THE PDF

1. Hydrazine hydrate plus ammonium thiocyanate forms a bis-thiocarbamoylhydrazine intermediate.
2. Cyclisation gives 2-amino-5-mercapto-1,3,4-thiadiazole.
3. Acetylation protects the amino group as an acetamido group.
4. Oxidative chlorination converts the mercapto group into a sulfonyl chloride.
5. Ammonia converts the sulfonyl chloride into SO_2NH_2, yielding acetazolamide.

EXAM FOCUS

- Track ring formation, N-acetylation, oxidation and sulfonamide formation separately.
- The route is a study schematic, not a laboratory protocol; several reagents are hazardous.

First Hope

FREE PREVIEW

Click here to visit our website

PHARMACY PREMIUM NOTES

Complete subject and semesters are available on FirstHope app only.

Scan or click here

Click here to get the app >

Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram >

Scan or click here

@FirstHopeNotes

Instagram

@firsthope.official

Click here to follow >

YouTube channel

FirstHope-Pharmacy / Live streams

Click here to watch >

WhatsApp channel

Follow FirstHope on WhatsApp

Click here to join >

FirstHope website

firsthope.co.in

Click here to visit >

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.