

# Pharmacokinetics: Excretion of Drugs

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# Excretion of Drugs

- Drugs are eliminated from the body either **unchanged** or as **metabolites**.
- Excretory organs (except lung) **eliminate polar compounds more efficiently** than substances with high lipid solubility. Thus, lipid-soluble drugs are not readily eliminated until they are metabolized to more polar compounds.
- The **kidney** is the **most important organ** for excreting drugs and their metabolites.

# Excretion of Drugs

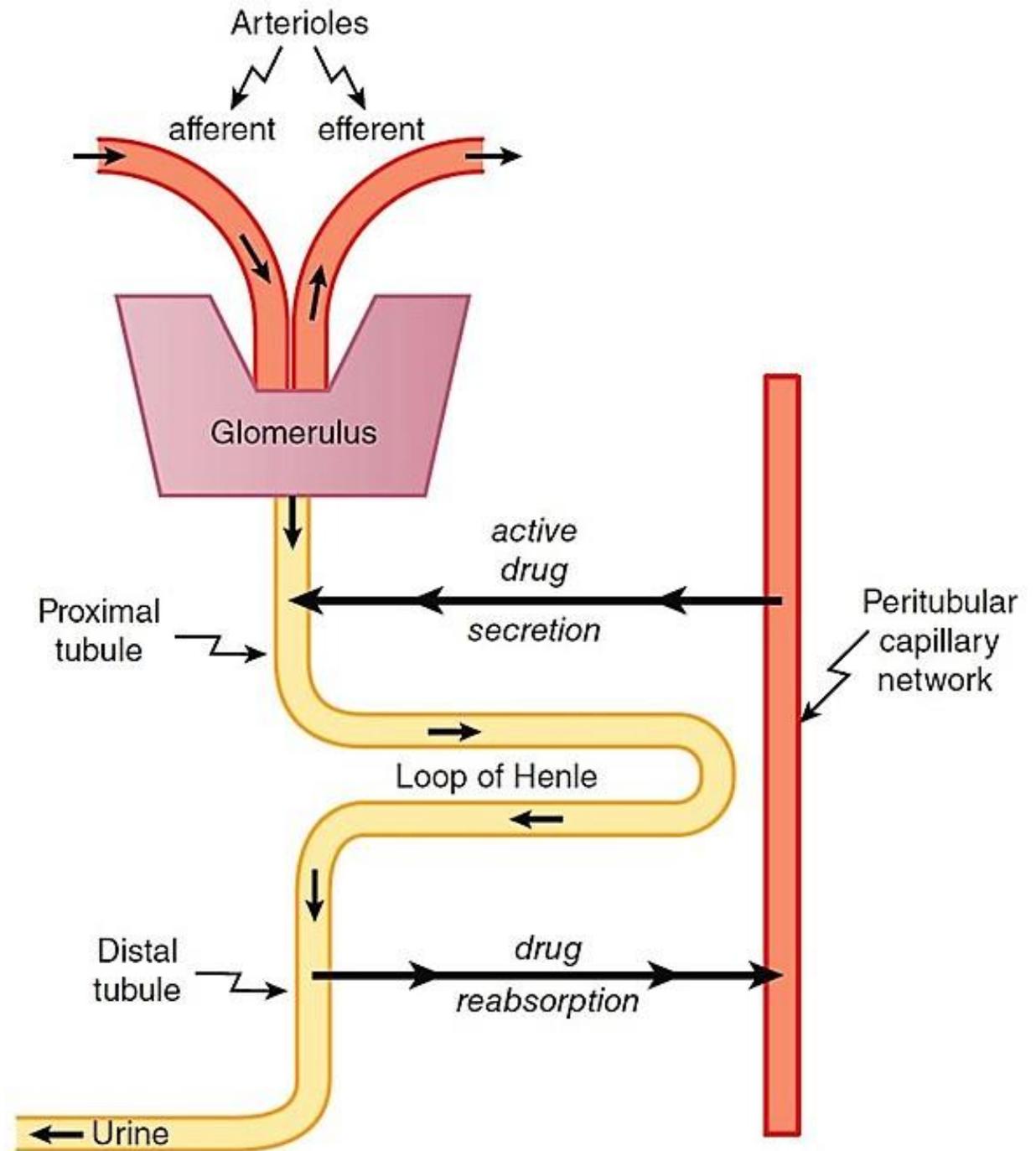
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- **Renal excretion** : Unchanged drug is a major route of elimination for 25%-30% of drugs.
- **Substances excreted in the feces**: Unabsorbed orally ingested drugs or drug metabolites either excreted in the bile or secreted directly into the intestinal tract and not reabsorbed.
- **Excretion of drugs via milk** : Important because the excreted drugs may affect the humans consuming milk.
- **Excretion from the lung**: Important mainly for the elimination of anesthetic gases.

# Renal Excretion

- Excretion of drugs and metabolites in the urine involves **three distinct processes**:
  - **Glomerular filtration,**
  - **Active tubular secretion, and**
  - **Passive tubular reabsorption.**

# Fig.: Renal Drug Handling



Source: Googman & Gilman's The Pharmacological Basis of Therapeutics (13<sup>th</sup> Edn.)

# Renal Excretion

contd...

- **Filtration** : depends on the **GFR** and the extent of **plasma binding of the drug** (only unbound drug is filtered).
- **Tubular secretion** : In the PCT, active, carrier-mediated tubular secretion also may add drug to the tubular fluid.
- Drug from the tubular lumen may be reabsorbed back into the systemic circulation.

# Renal Excretion

contd...

## ➤ Reabsorption :

- In DCT, the non-ionized forms of drugs undergo net passive reabsorption.
- **Alkalinization of urine:** When the tubular urine is made more alkaline, weak acids are largely ionized and are excreted more rapidly and to a greater extent; conversely, acidification of the urine will reduce fractional ionization and excretion of weak acids.

# Biliary & Faecal Excretion

- **Biliary excretion:** Transporters present in the canalicular membrane of the hepatocyte actively secrete drugs and metabolites into bile.
- Biliary excretions and unabsorbed drug are excreted in the feces.

# Biliary & Faecal Excretion contd...

- **Enterohepatic recycling** : Drugs and metabolites present in bile are released into the GIT. Subsequently, they can be reabsorbed into the body from the intestine, which, in the case of conjugated metabolites such as glucuronides, may require enzymatic hydrolysis by the intestinal microflora.
- Such **enterohepatic recycling**, if extensive, may prolong significantly the presence of a drug (or toxin) and its effects within the body prior to elimination by other pathways.
- To interrupt enterohepatic cycling, substances may be given orally to bind metabolites excreted in the bile.

# Excretion by other routes

- Excretion of drugs into **sweat, saliva, and tears** is quantitatively unimportant.
- Because milk is more acidic than plasma, **basic compounds may be slightly concentrated in this fluid**; conversely, the concentration of acidic compounds in the milk is lower than in plasma.
- Nonelectrolytes (e.g., ethanol and urea) readily enter breast milk and reach the same concentration as in plasma, independent of the pH of the milk.

## Excretion by other routes contd...

- Milk can also contain heavy metals from environmental exposures.
- Although excretion into hair and skin is quantitatively unimportant, sensitive methods of detection of drugs in these tissues have forensic significance.

**Thank You**

