جامعة ساوة الاهلية
كلية التقنيات الصحية والطبية
قسم التخدير - اللجنة العلمية

SAWA UNIVERSITY

PHARMACOKINETICS

جامعة ساوة

كلية التقنيات الصحية والطبية

قسم تقنيات التخدير

المرحلة الثانية

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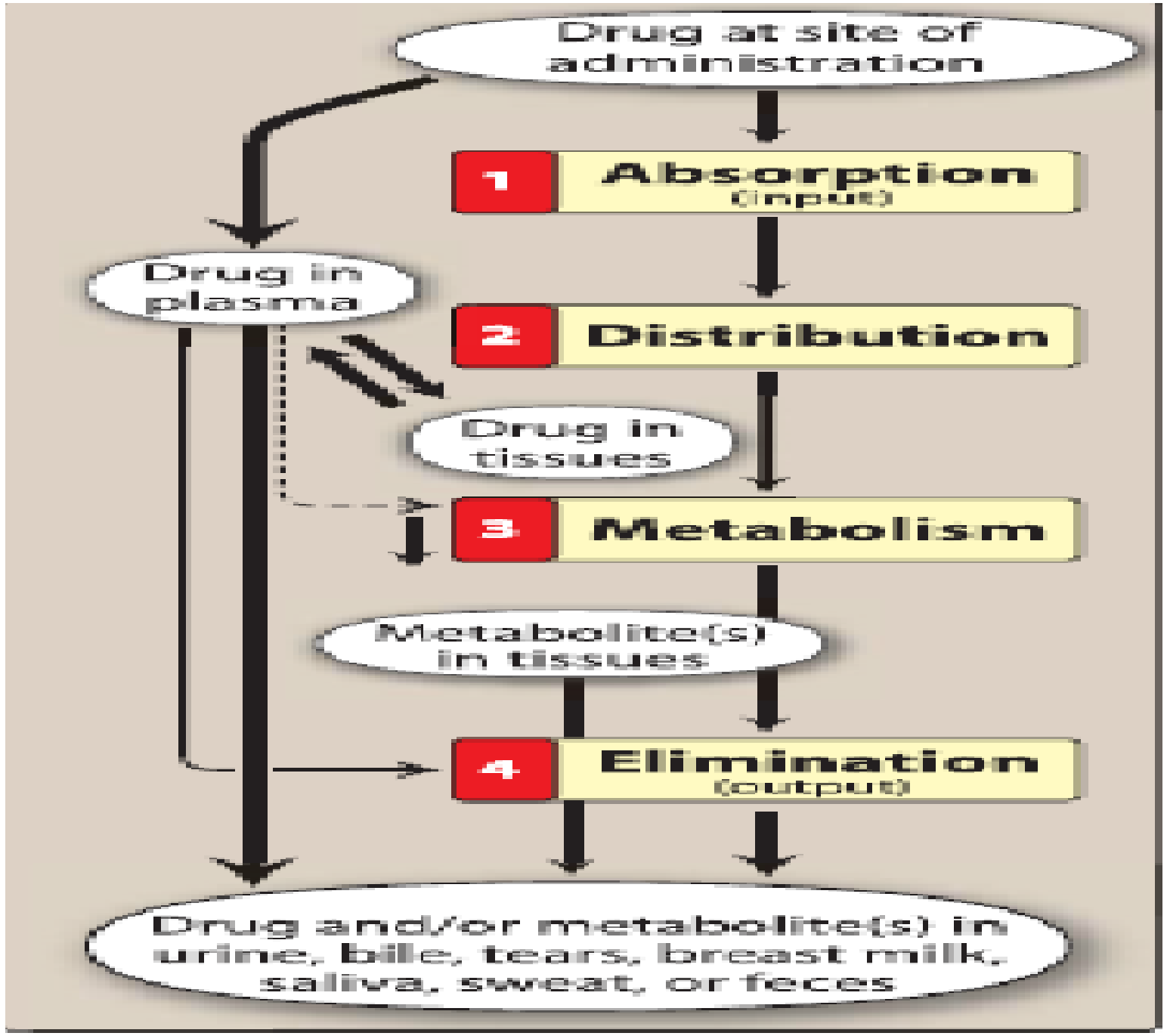
Pharmacokinetics

- Pharmacokinetics refers to what the body does to a drug,

1. **Absorption**: First, absorption from the site of administration permits entry of the drug (either directly or indirectly) into plasma.
2. **Distribution**: Second, the drug may reversibly leave the bloodstream and distribute into the interstitial and intracellular fluids.
3. **Metabolism:** Third, the drug may be biotransformed through metabolism by the liver or other tissues.
4. **Elimination:** Finally, the drug and its metabolites are eliminated from the body in urine, bile, or feces.


Drug at site of administration
1 Absorption (input)
Drug in plasma
2 Distribution
Drug in tissues
3 Metabolism
Metabolite(s) in tissues
4 Elimination (output)
Drug and/or metabolite(s) in urine, bile, tears, breast milk, saliva, sweat, or feces

Absorption

- Absorption is the transfer of a drug from the site of administration to the bloodstream. The rate and extent of absorption depend on the environment where the drug is absorbed, chemical characteristics of the drug, and the route of administration

Mechanisms of absorption of drugs from the Gl tract

- **1. Passive diffusion**: The driving force for passive diffusion of a drug is the concentration gradient across a membrane separating two body compartments. the drug moves from an area of high concentration to one of lower concentration.
- Passive diffusion does not involve a carrier, is not saturable, and shows low structural specificity.
- The vast majority of drugs are absorbed by this mechanism.
- Water-soluble drugs penetrate the cell membrane through aqueous channels or pores
- lipid-soluble drugs readily move across most biologic membranes due to solubility in the membrane lipid bilayers

- **2. Facilitated diffusion**: Other agents can enter the cell through specialized transmembrane carrier proteins that facilitate the passage of large molecules.
- These carrier proteins undergo conformational changes, allowing the passage of drugs or endogenous molecules into the interior of cells.
- This process is known as facilitated diffusion. It does not require energy
- can be saturated

- **3. Active transport**: This mode of drug entry also involves specific carrier proteins that span the membrane.
- active transport is energy dependent, driven by the hydrolysis of adenosine triphosphate (ATP).
- It is capable of moving drugs against a concentration gradient, from a region of low drug concentration to one of higher concentration
- The process is saturable.

- **4. Endocytosis and exocytosis**: This type of absorption is used to
- transport drugs of exceptionally large size across the cell membrane.
- **Endocytosis** involves engulfment of a drug by the cell membrane and transport into the cell by pinching off the drug-filled vesicle Vitamin B12 is transported across the gut wall by endocytosis.
- **Exocytosis** is the reverse of endocytosis. Many cells use exocytosis to secrete substances out of the cell through a similar process of vesicle formation, ex. neurotransmitters norepinephrine are stored in intracellular vesicles in the nerve terminal and released by exocytosis

Factors affecting drug absorption:

1. Effect of pH on drug absorption:
2. Physical factors influencing absorption:

1. **Blood flow to the absorption site:**
   - Decrease in blood flow ⟶ decrease in absorption.
   - Blood flow in the intestine is much greater than the flow of stomach.
2. **Total surface area available for absorption:**
   - Absorption in the intestine is more efficient, because it has a surface rich in microvilli.
3. **Contact time at the absorption surface:**

Distribution

1.Distribution: when the drug leaves the blood and enters the interstitium and/or the cells of the tissue.

1-Blood flow: rate of B.F varies widely

B.F. to the brain, liver and kidney is → greater than B.F. to skeletal muscle.

Adipose tissue has a → low rate of B.F.

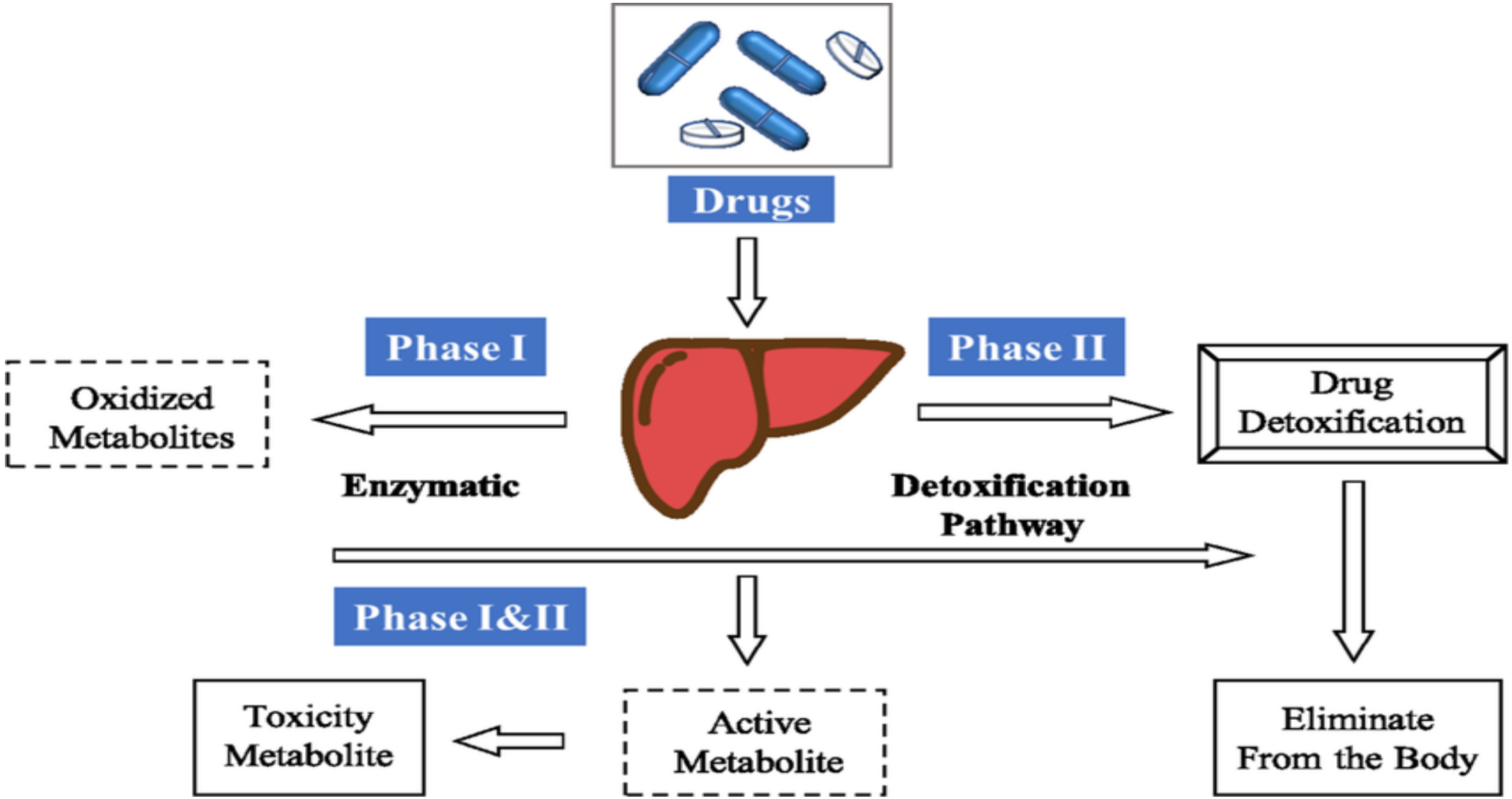
2. Capillary permeability: is determined by:

A- Capillary structure: varies widely, due to → the fraction of the basement membrane that's exposed by → slit (tight) junctions between endothelial cells.

B. Drug structure (chemical nature of the drug):

Drug metabolism:

- Drugs are eliminated by:
  1. Biotransformation.
  2. Excretion into the urine/bile.
- Liver → major site of drug metabolism.
- Specific drugs may undergo → biotransformation in other tissues


Drugs
Phase I
Phase II
Oxidized Metabolites
Drug Detoxification
Enzymatic
Detoxification Pathway
Phase I&II
Toxicity Metabolite
Active Metabolite
Eliminate From the Body

4. Drug elimination

(excretion): removal of drug from the body.

1. **Major organs:**
   - Kidney: into the urine.
   - Liver.
   - GIT and lung.

2. **Minor organs:**
   - Milk: nursing mothers.
   - Salivary glands.
   - Sweat.

Thank you for listening

SCAN TO GET THE LECTURE