LECTURE OUTLINE
Introduction to Medicinal Chemistry (Lecture 15 & 16 Reading – Palleros – eCommons)
- Drug Design: Pharmaceutical, Pharmacokinetic, and Pharmacodynamic Phases
HW set posted on eCommons

**Medicinal Chemistry**

**Pharmaceuticals** → substance given to alleviate symptoms or treat the cause of a disease

*Potential vs. Effectiveness of a Drug Target*

**Administration:**

*Enteral*  
(or/rectal)

*Parenteral*  
(IV, intramuscular, subcutaneous, sublingual, topical, inhalation)

Barriers to drug effectiveness of a drug are broken down into 3 phases:

1. Pharmaceutical Phase

2. Pharmacokinetic Phase

3. Pharmacodynamic Phase
**Pharmaceutical Phase:** Administration to Absorption

*Dosage form*: tablet, solution, vapor

- In addition to the drug, dose may also include…

Potential for enzymatic degradation – what happens where?

- Saliva
- Stomach
- Intestines

**Pharmacokinetic Phase:** Absorption, Distribution, Metabolism, Elimination (ADME)

*Absorption* into bloodstream requires drug to cross cell-membrane(s)

*Structures of two antibiotics at physiological pH – what conditions would each be absorbed?*

![Structures of two antibiotics](image)

- **Cephalexin** (a cephalosporin)
- **Penicillin G**

*Blood-brain barrier*

*Distribution* into circulatory system

*Metabolism* – will it make it to its target receptor intact?

![Metabolism](image)

- **Prontosil** *inactive prodrug*
- **Sulfanilamide** *active*

**HYDROLYSIS** = easiest metabolic process to predict (look for carboxylic acid derivatives)

*Excretion*

- Half-life
Pharmacodynamic Phase: drug interacts with receptor, elicits effects

Specific Drug-Receptor Interactions

Covalent Binding vs. Intermolecular Forces

Therapeutic Index, $TI = \frac{LD_{50}}{ED_{50}}$

Lethal Dose, $LD_{50}$ - concentration at which 50% of test subject die

Effective Dose, $ED_{50}$ – dose at which 50% of patients get desired effect

Biophores – screening of 10s-1000s of potential targets (“hits”)

Pharmacophore

Toxicophore

Metabophore

Auxophore

Identification of Pharmacophore through “derivatization of a lead”

Opioid alkaloids:

- Morphine
- Codeine
- Levorphanol
- Pentazocine
- Meperidine
- Dextropropoxyphene
- Methodone