

**LECTURE OUTLINE**

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

**Medicinal Chemistry**

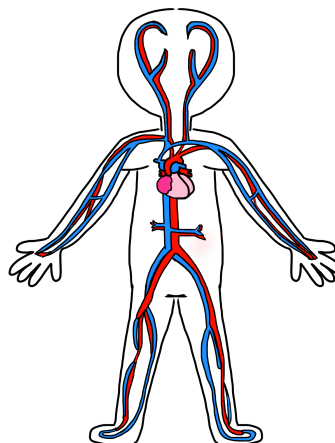
Pharmaceuticals → substance given to alleviate symptoms or treat the cause of a disease

*Potential vs. Effectiveness of a Drug Target***Administration:**

*Enteral*  
(oral/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

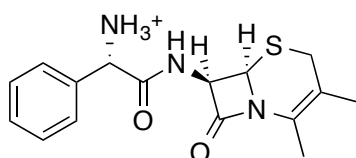
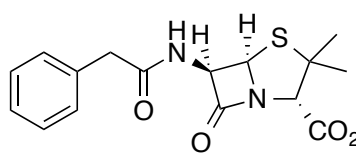
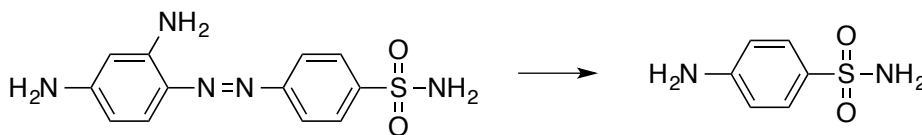
- In addition to the drug, dose may also include...

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?***Cephalexin**  
(a cephalosporin)**Penicillin G***Blood-brain barrier*Distribution into circulatory systemMetabolism – will it make it to its target receptor intact?**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,  $TI = LD_{50} / ED_{50}$**

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:*

