#### CHEM 109, Lecture 14

UV-Visible Spectrum & DNA Mutations Phosphodiester Formation and Cleavage Introduction to Medicinal Chemistry - Reading – Palleros (online) - Drug Design: Pharmaceutical, Pharmacokinetic, and Pharmacodynamic Phases

### **UV-Visible Spectrum**

- UVA (400 320 nm)
- UVB (320 280 nm)

\*UVC (280 - 100 nm)





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**Mutations – Thymine Dimer** 





What's the deal with nitrites?





# **Phosphodiester Formation**



## Phosphodiester Cleavage (Restriction Endonucleases)





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### **Medicinal Chemistry**

<u>Pharmaceuticals</u>  $\rightarrow$  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 itself, 'dose' may also include...

Potential for enzymatic degradation - what happens where?

Saliva

Stomach

Intestines

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

<u>Absorption</u> into bloodstream requires drug to cross cell-membrane(s)

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





Cephalexin (a cephalosporin)

Penicillin G

Blood-brain barrier

Distribution into circulatory system

Metabolism - will it make it to its target receptor intact?



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

**E**xcretion

Half-life

Pharmacodynamic Phase: drug interacts with receptor, elicits effects

## **Specific Drug-Receptor Interactions**

Covalent Binding vs. Intermolecular Forces

## Therapeutic Index, TI = LD<sub>50</sub> / ED<sub>50</sub>

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:



What is the pharmacophore for the collection of compounds above?