

LECTURE OUTLINE

Medicinal Chemistry: Solubility Potential (Palleros – online)

 β -Lactam Antibiotics: Mode of Action

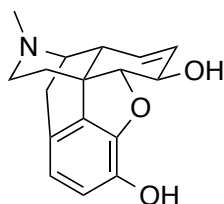
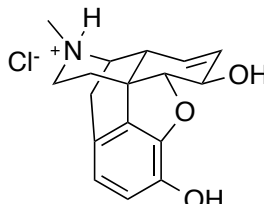
HW online

Solubility Potential

- Hydrocarbons are insoluble in water
- Adding polar functional groups increases water solubility
- The more functional groups, the more carbons the molecule can contain and still be soluble

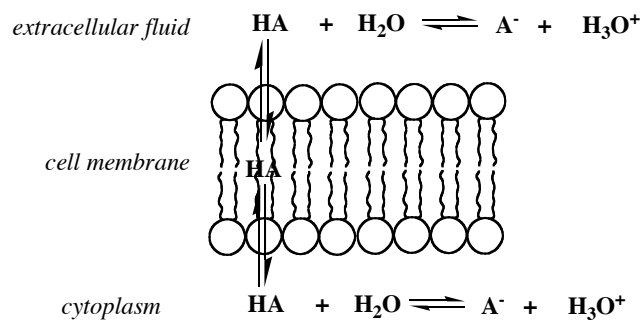
Table 1. Solubility Potential

Functional Group	Solubility Potential (in a polyfunctional molecule)
Alcohol	3-4 carbons
Phenol	3-4 carbons
Amine	3 carbons
Carboxylic acid	3 carbons
Ester	3 carbons
Amide	2-3 carbons
Ether	2 carbons
Aldehyde	2 carbons
Ketone	2 carbons
Urea	2 carbons
Charged groups (N ⁺ : ammonium salts; O ⁻ : carboxylates, phenolates, sulfates; N ⁻ : sulfonamides)	20-30 carbons

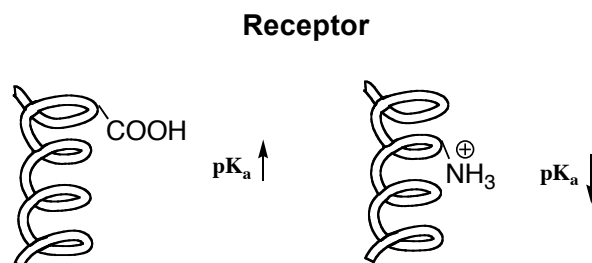
**Morphine****Morphine-HCl**

Effects of pKa on Solubility and Binding

Pharmaceutical & Pharmacokinetic Phases



Pharmacodynamic Phase – binding of drug to receptor



Hydrophobic pocket of peptide backbone effects pKa's
(typically we think of pKa as dissociation in water, this is different!)

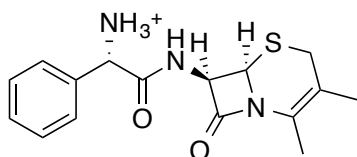
****Ionization states dictate whether drug can bind to receptor****

Natural Products – broad class of naturally occurring substance, typically secondary metabolite (no essential metabolic function for the organism)

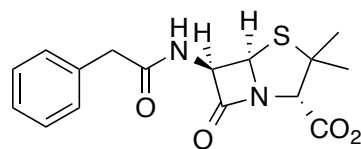
- Terpenoids (Lectures 11/12)
- Nonribosomal Polypeptides (today)
- Alkaloids (Lecture 17)
- Fatty acid-derived substances & Polyketides (Lecture 18)
- Enzyme Cofactors

β -Lactam Antibiotics

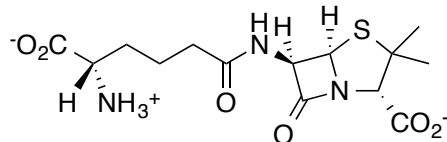
- Non-ribosomal Tripeptides



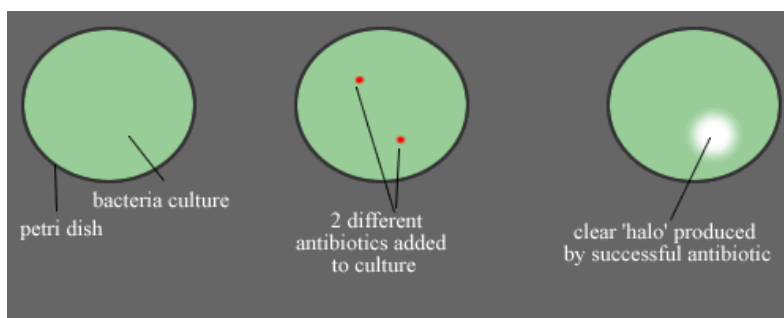
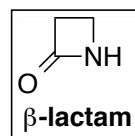
**Cephalexin
(a cephalosporin)**



Penicillin G



Isopenicillin N



Penicillin's Mechanism of Action: Deactivation of Bacterial Transpeptidase

Bacterial cell walls surrounded by *murein*,
synthesized by *Transpeptidase* (aka *penicillin-bind protein*, PBP)

