LECTURE OUTLINE
Medicinal Chemistry: Solubility Potential (Palleros – online)
β**-Lactam Antibiotics:** Mode of Action

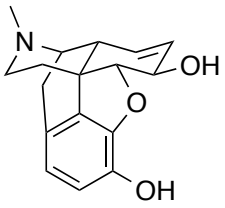
HW online

Solubility Potential

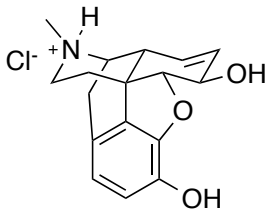
- Hydrocarbons are insoluble in water
- Adding polar functional groups increases water solubility
- The more functional groups, the more carbons the molecule can contain and still be soluble

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



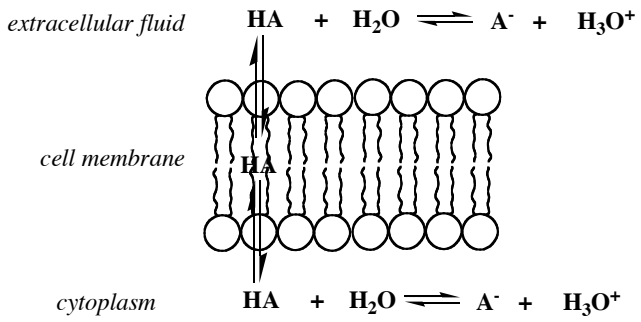
Morphine



Morphine-HCl

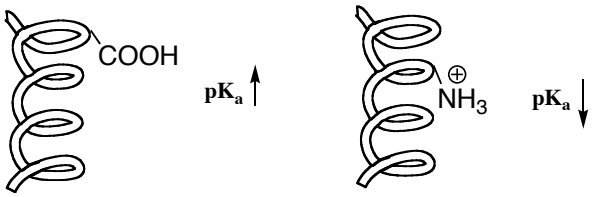
Effects of pKa on Solubility and Binding

Pharmaceutical & Pharmacokinetic Phases



Pharmacodynamic Phase – binding of drug to receptor

Receptor



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

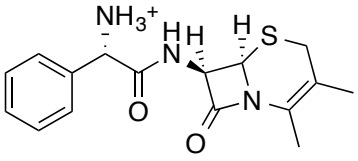
Ionization states dictate whether drug can bind to receptor

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

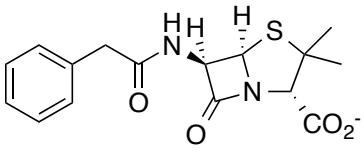
- Terpenoids (Lectures 11/12)
- Nonribosomal Polypeptides (today)
- Alkaloids (Lecture 17)
- Fatty acid-derived substances & Polyketides (Lecture 18)
- Enzyme Cofactors

β-Lactam Antibiotics

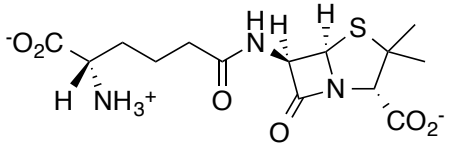
- Non-ribosomal Tripeptides



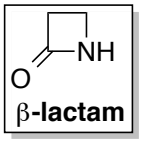
Cephalexin (a cephalosporin)

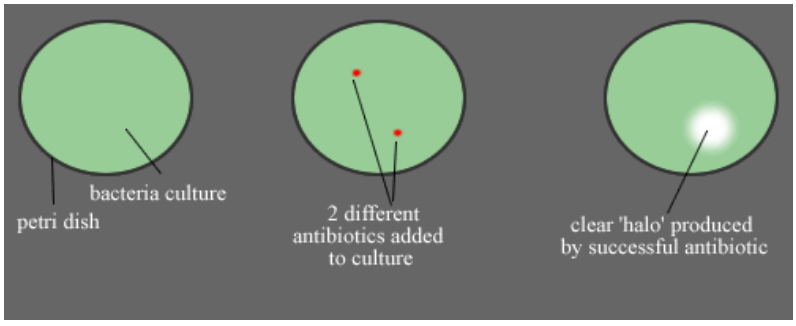


Penicillin G



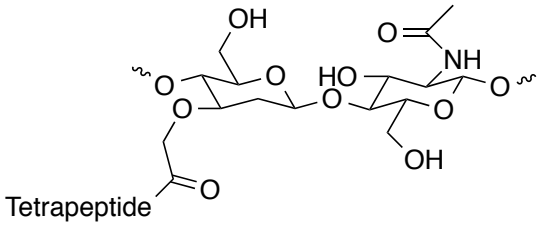
Isopenicillin N



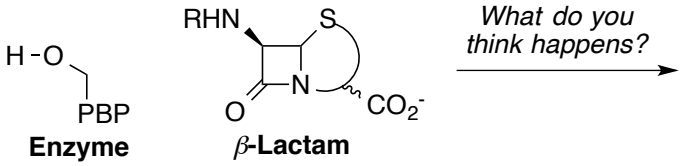


Penicillin's Mechanism of Action: Deactivation of Bacterial Transpeptidase

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



Peptidoglycan Layer
(repeating unit)



Enzyme **β-Lactam**