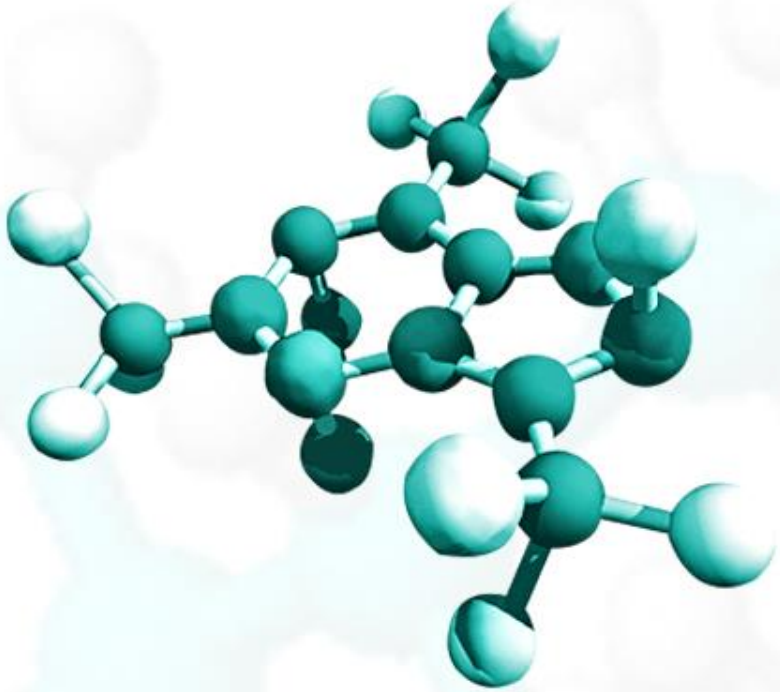

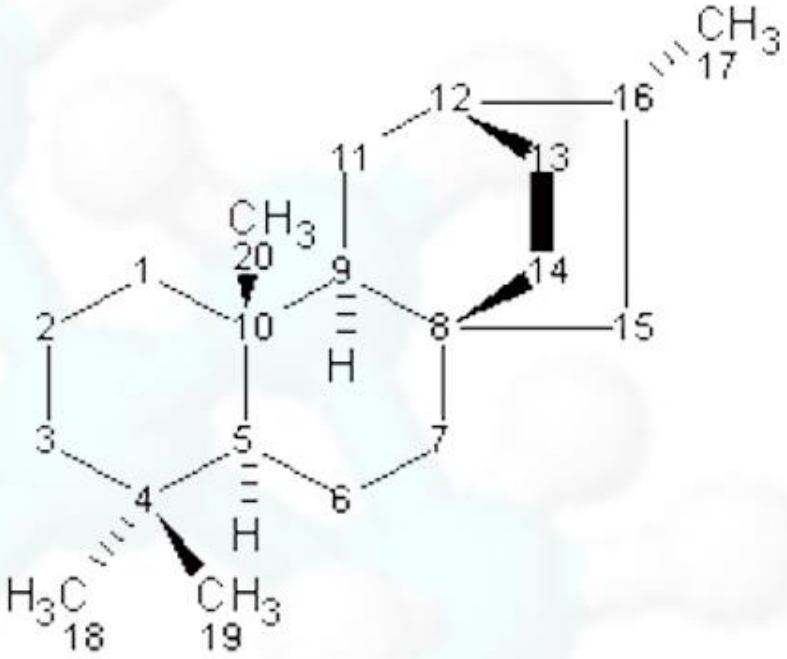


# Medicinal Chemistry 1
# 0914101 & A0914101


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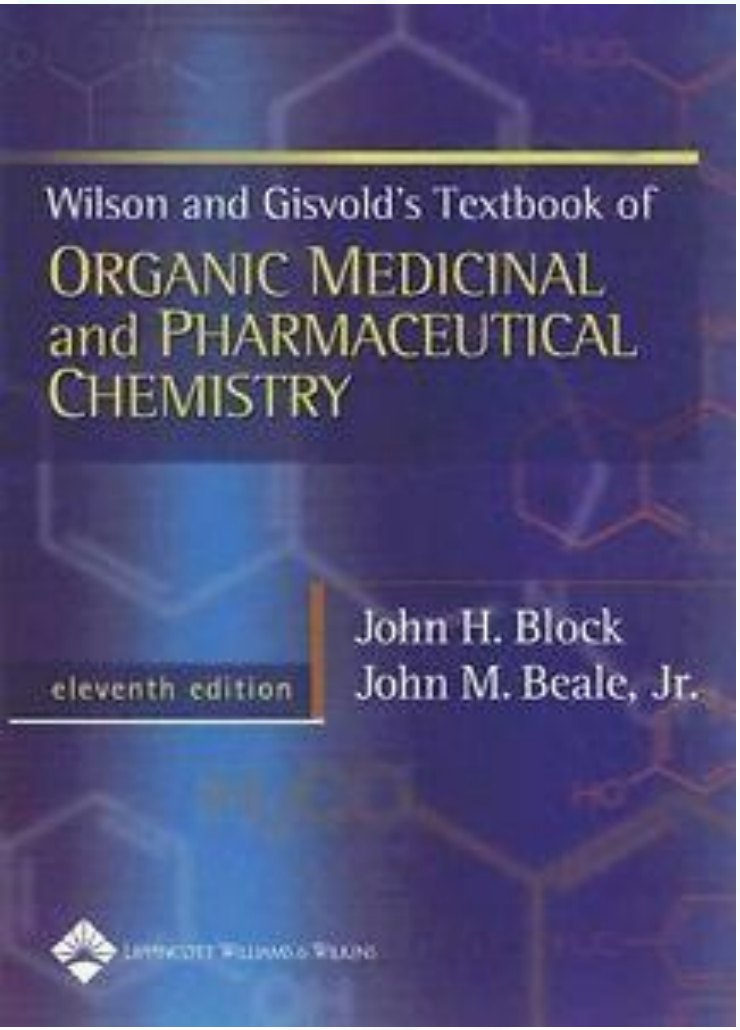
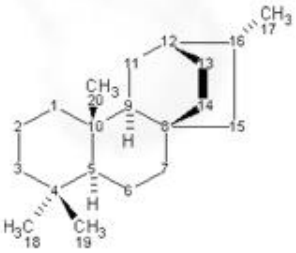
Dr. Belal Omar Alnajjar

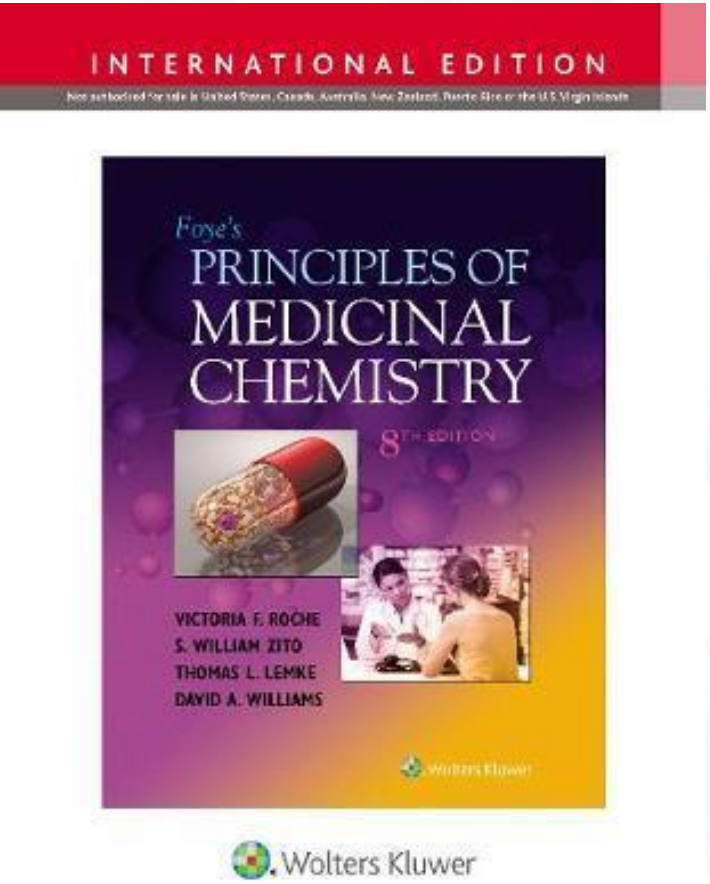
# Resources



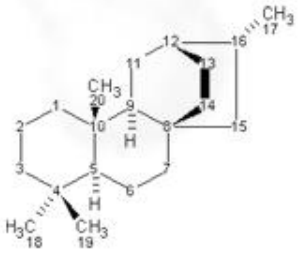

- **Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry**



# Resources

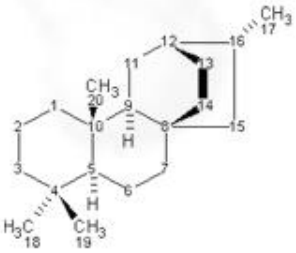



- **Foye's Principles of Medicinal Chemistry**



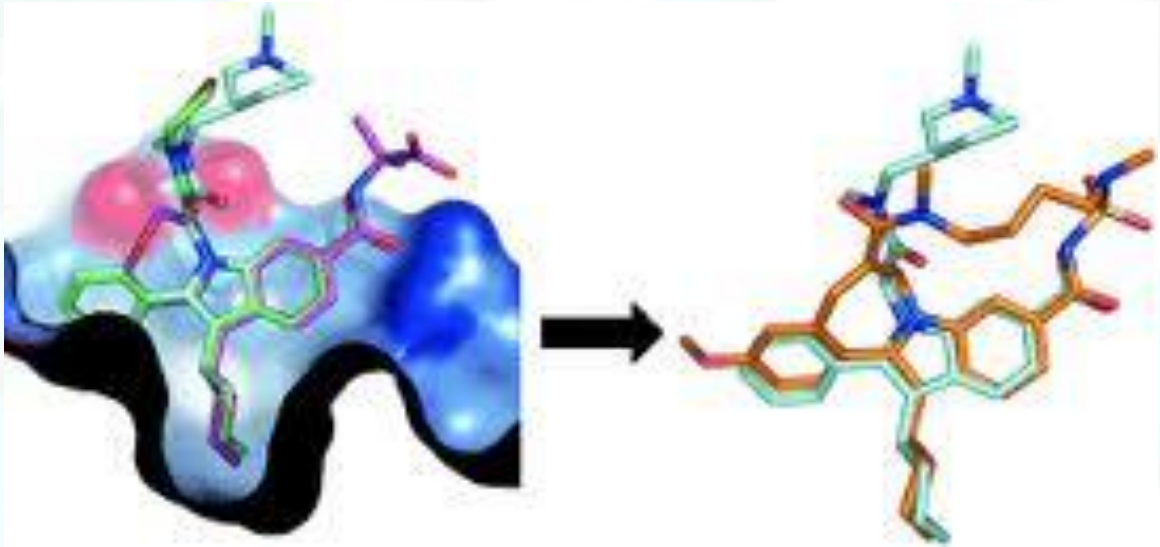
# What You Will Learn

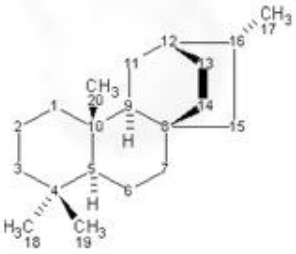
Overview and Introduction



# What You Will Learn

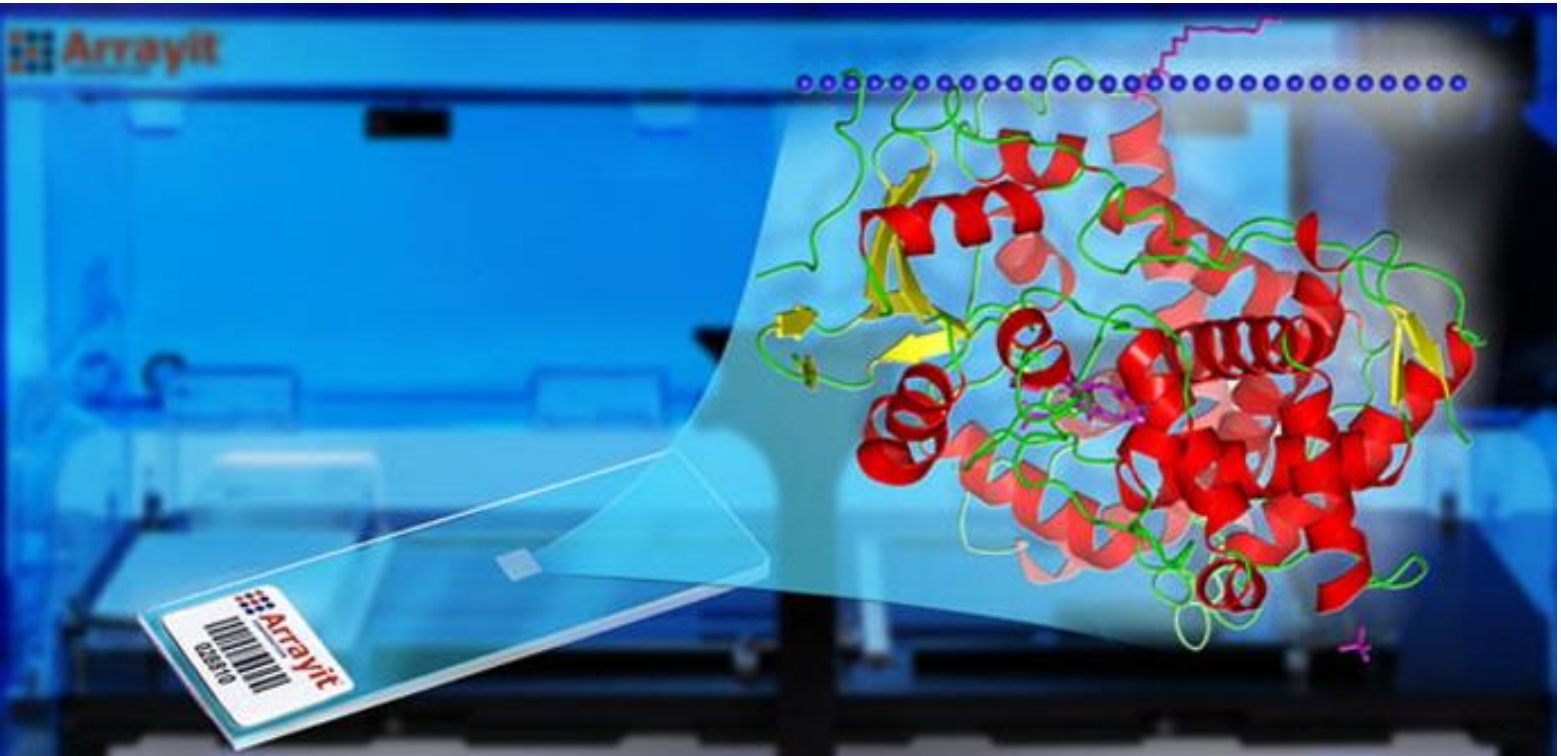
- **Physicochemical Properties in Relation of Drug Action**

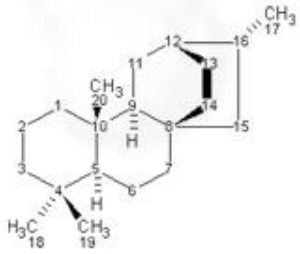




# What You Will Learn

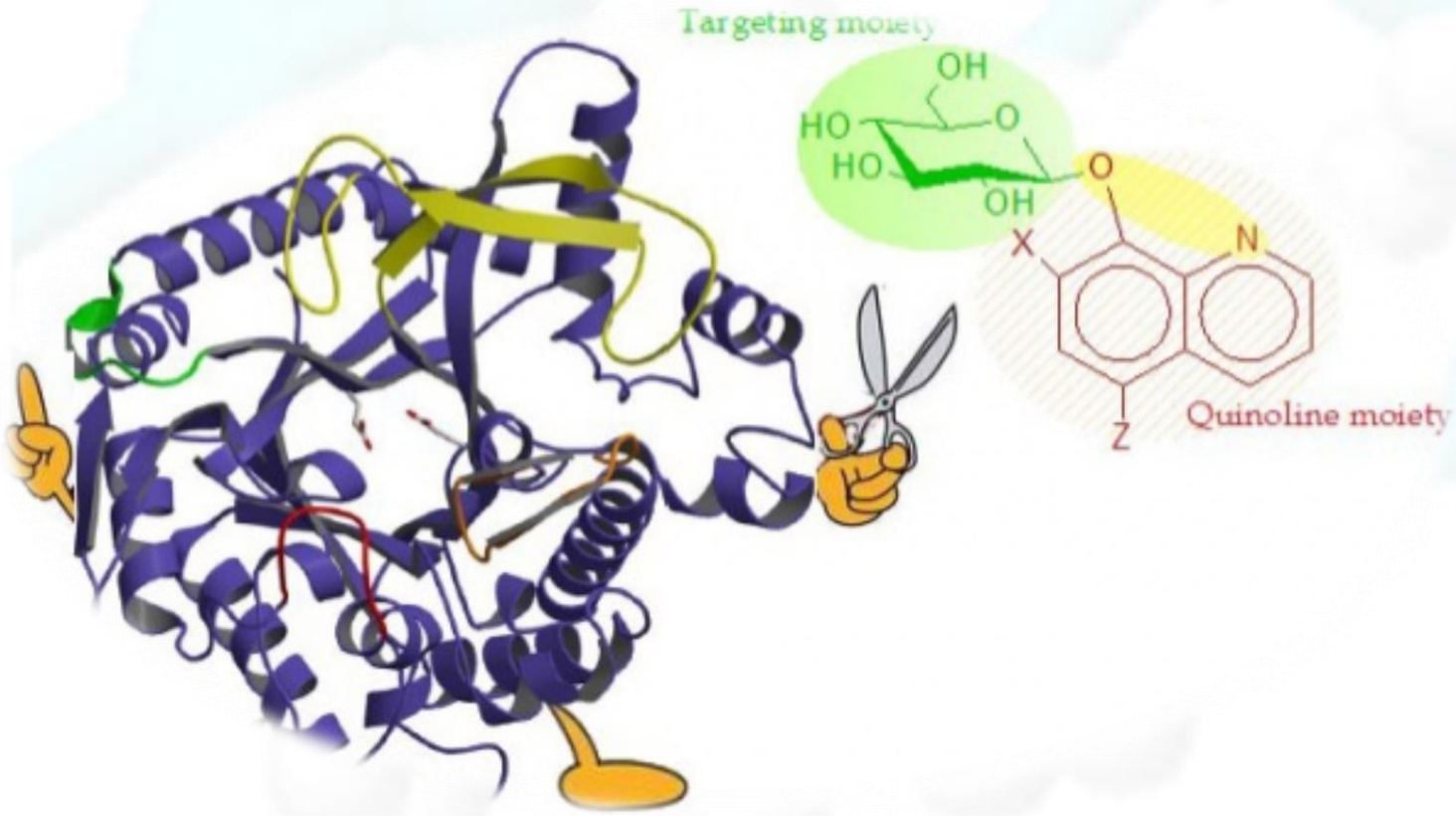
- Metabolic Changes of Drugs and Other Organic Compounds

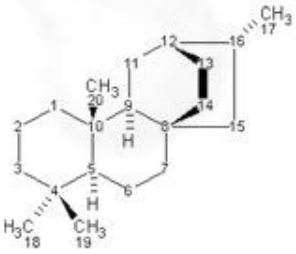


# What You Will Learn

- Pro-Drugs



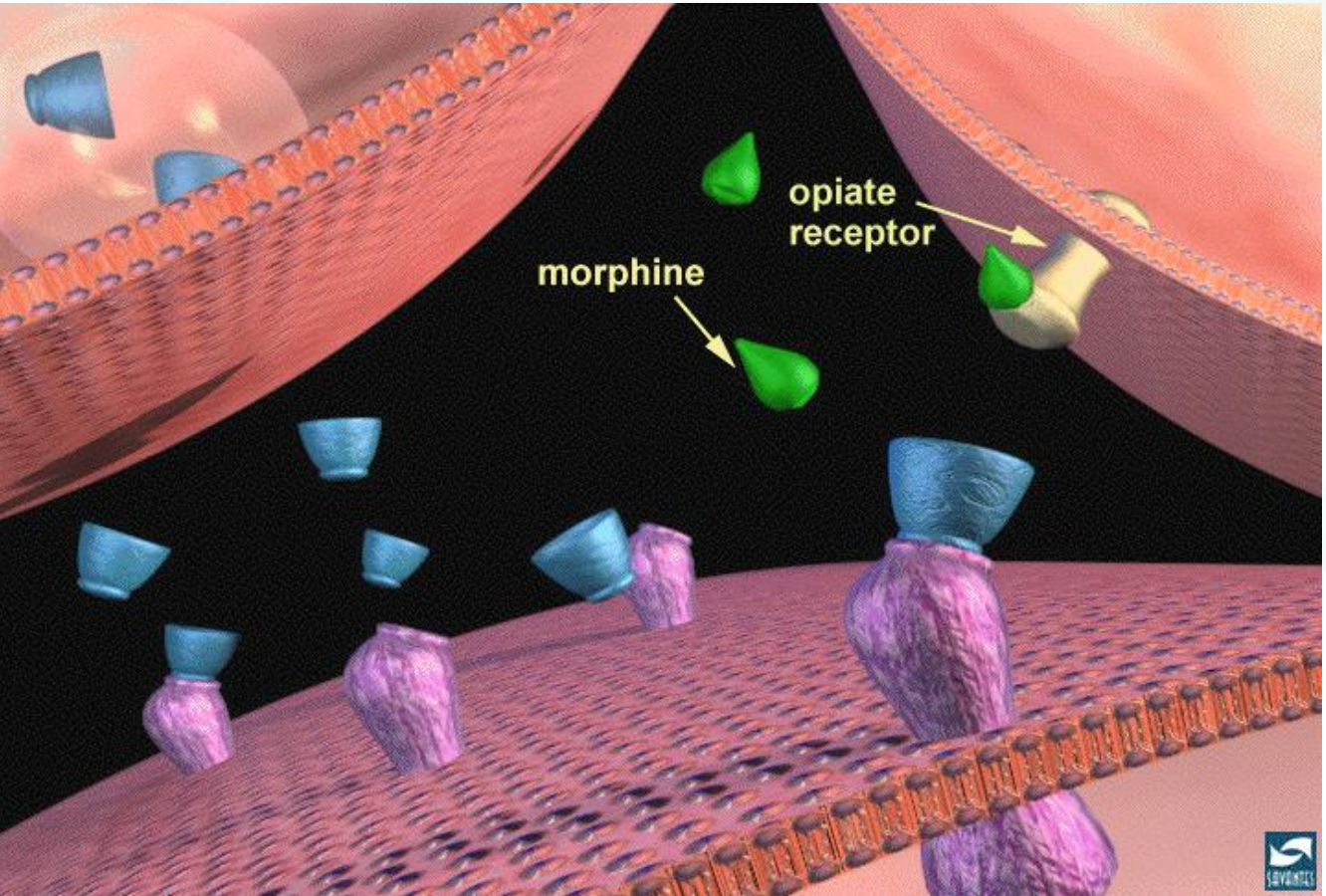



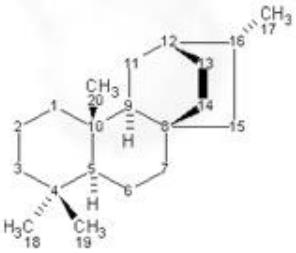
# What You Will Learn

- Central Nervous System (CNS) Drugs

# What You Will Learn

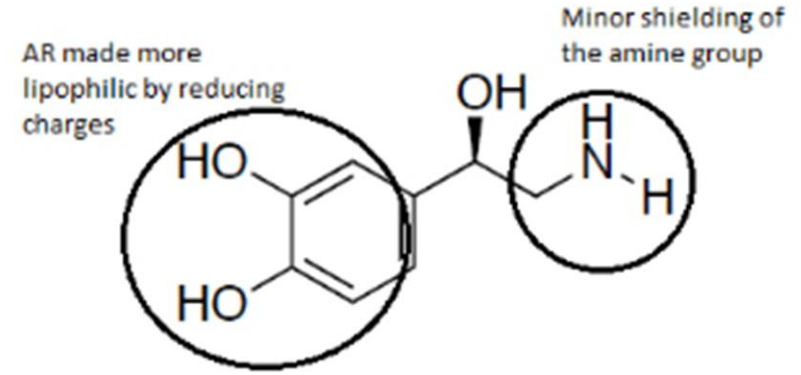
- Opioid Analgesics

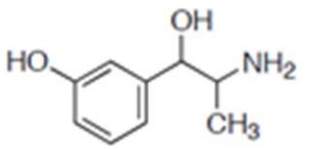


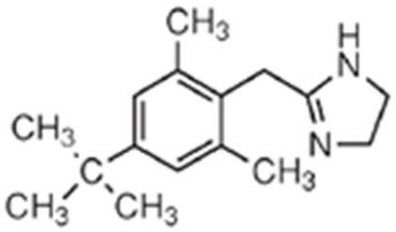
# What You Will Learn

- Adrenergic Agents



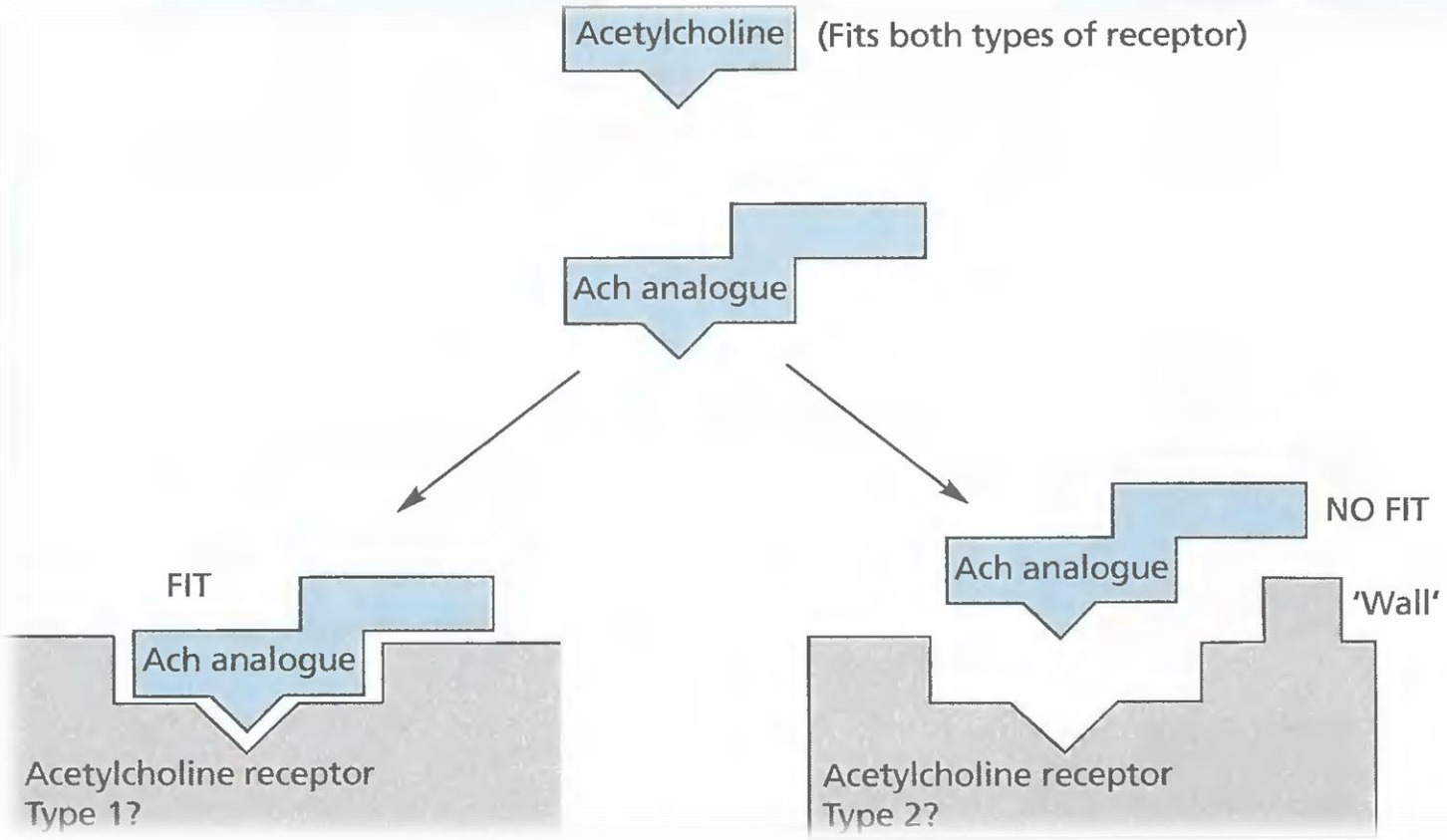

Metaraminaol

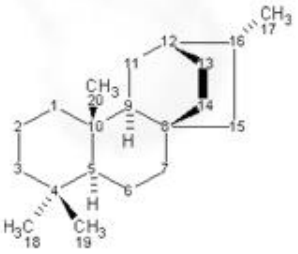


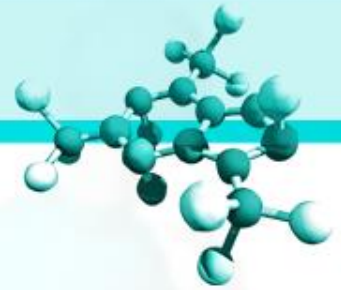

Xylometazoline

# What You Will Learn

- Cholinergic Agents

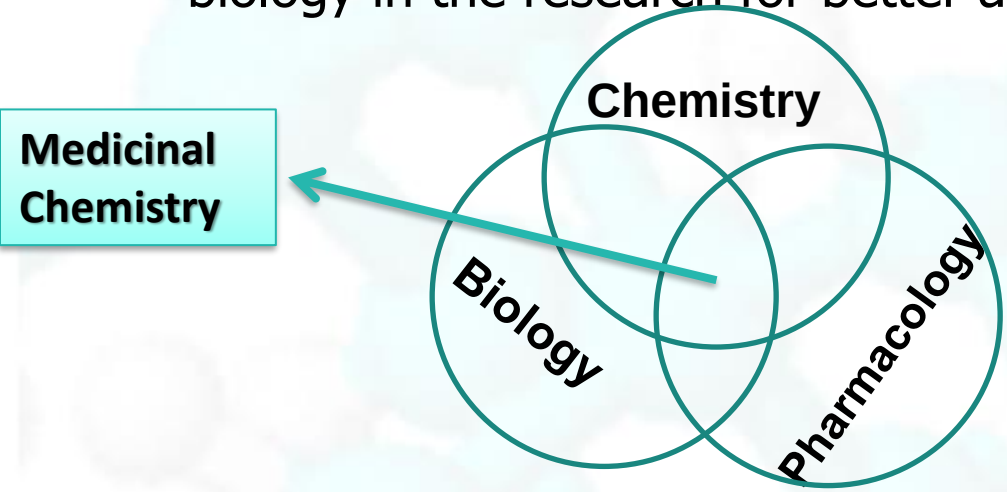


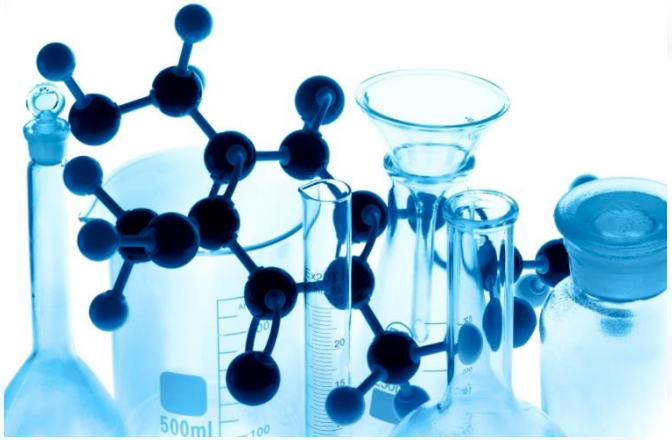





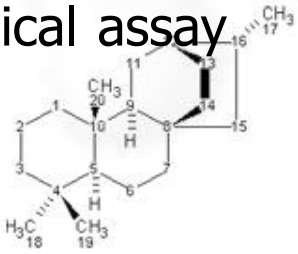
# Definition

- **Medicinal chemistry** is best to be **defined** as an interdisciplinary research area incorporating different branches of chemistry and biology in the research for better and new drugs (Drug Discovery).



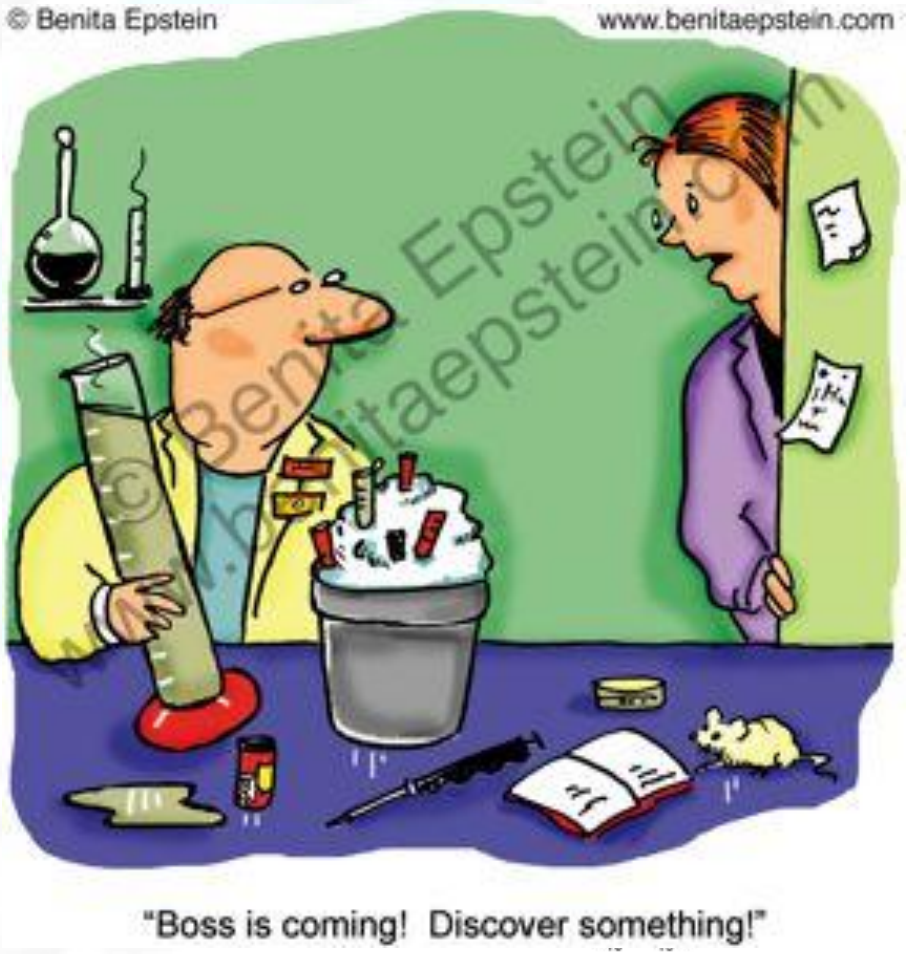




- **WHO's definition:** Medicinal chemistry is the science which deals with the synthesis, chemistry of mode of action and chemical assay of drug substance



# What Medicinal Chemist Can Do?

- **Generally Medicinal Chemists can:**
- **Make new compounds**
- **Determine their effect on biological processes.**
- **Alter the structure of the compound for optimum effect and minimum side effects.**



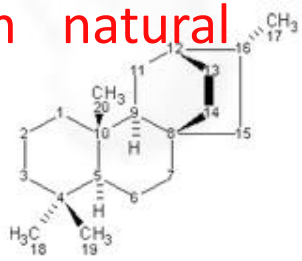
# medicinal chemistry covers three critical steps

1. **A discovery step, consisting**

   – The choice of the therapeutic target (receptor, enzyme, transport group, cellular or in vivo model)

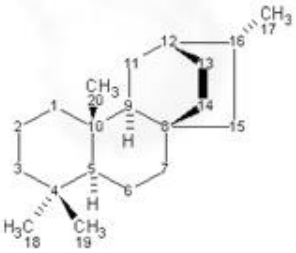
   – The identification (or discovery ) and production of new active substances interacting with the selected target.

   – Such compounds are usually called lead compounds, they can originate from synthetic organic chemistry, from natural sources, or from biotechnological processes.



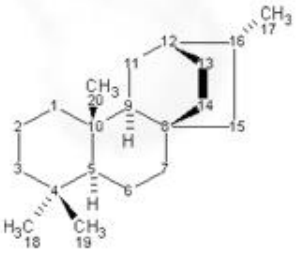
2. **An optimization step,**

- Improvement of the lead structure. The optimization process takes primarily into account the increase in potency, selectivity and toxicity.
- Its characteristics are the establishment and analysis of Structure-Activity Relationship

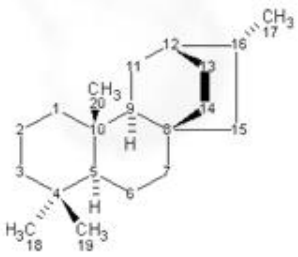


## 3. A development step

- Optimization of the synthetic route for bulk production
- The continuation of the improvement of the pharmacokinetic properties and the fine tuning of the pharmaceutical properties
- Water-soluble derivatives



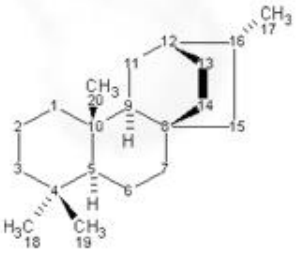
- **A certain number of terms more or less synonymous with medicinal chemistry are used:**
  - Pharmacochemistry,
  - Molecular Pharmacochemistry,
  - Drug Design
  - Pharmaceutical Chemistry



# Classification systems

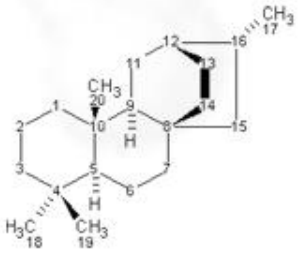
- **Drugs can be classified under the following Categories**

1. The Origin of the Drug
2. The Mode of Action
3. The Nature of Illness
4. The Chemical Structure

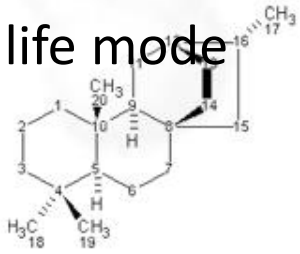


- **The Origin of Drug:**

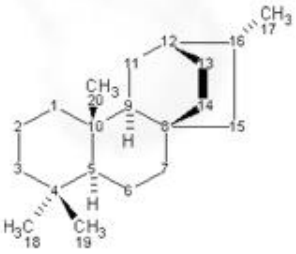
  a. Drug from natural origin: Herbal or plant or mineral origin.
  b. Drug derived from chemical synthesis.
  c. Drug derived by biotechnology genetic-engineering, hybridoma technique



- **The Mode of Action**
  1. **Medicine that treat the cause of the Disease**
     - Called "True Drugs"
     - Chemotherapeutics, antibacterial, antifungal, etc.
  2. **Medicine that Compensate for the deficiency**
     - Take the place of missing substances (vitamins, insulin)
  3. **Medicine that Alleviate the symptoms**
     - Symptomatic treatments attenuate or neutralize a disorder in a disease state (ibuprofen)
     - Do not cure the patient but rather to render daily life mode more comfortable.



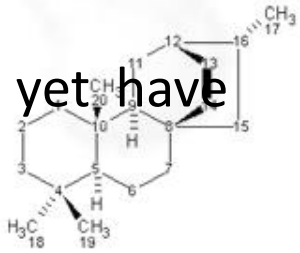
- **The Nature of Illness**
  - The World Health organization in 1968 adopted this physiological classification which classifies drugs by the body system on which they act



- **Chemical structure**
  - Many drugs which have a common skeleton are grouped together,
  - e.g. penicillins, barbiturates, opiates, steroids, catecholamines, etc

» There is a danger that one could be confused into thinking that all compounds of a certain chemical group have the same biological action.

» For example, barbiturates may look much alike and yet have completely different uses in medicine.



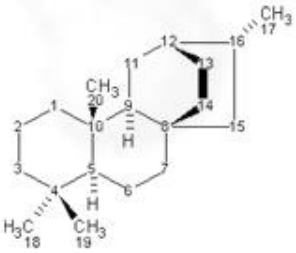
# Common Medicinal Chemistry Classification

I. **Pharmacodynamics Agents**
   - Antiarrhythmic
   - Vasodilators
   - Antihypertensive
   - Antiallergics

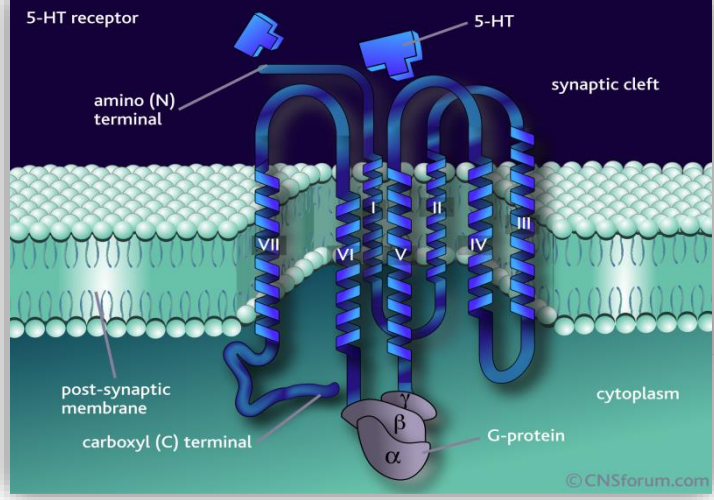
II. **Chemotherapeutic Agents**
   - Antibacterial,
   - Antiviral,
   - Antifungal

III. **Agents acting on metabolic disease on endocrine function**
   - Antidiabetics
   - Hypolipiemics
   - Steroid Hormones

IV. **Agents acting on the Central Nervous System**
   - Antidepressants
   - Antipsychotics
   - Sedatives
   - Hypnotics



# Important Definitions




- **Receptor:** A protein with which a chemical messenger or drug can interact to produce a cellular response.

**Drugs**: chemical compounds produce their biological effects via binding to a "receptive molecule" or "receptor". A term first coined by Paul Ehlrich

# Important Definitions

- **Agonist** : A chemical compound that binds to a receptor and produces the biological activity (*POSITIVE intrinsic activity*).
- **Partial Agonist** : A chemical compound that binds to a receptor and capable of producing a partial biological activity (less than 80% of *POSITIVE intrinsic activity*).
- **Antagonist** : A chemical compound that binds to a receptor, but does NOT activate the receptor or produce the biological activity (*ZERO intrinsic activity*).

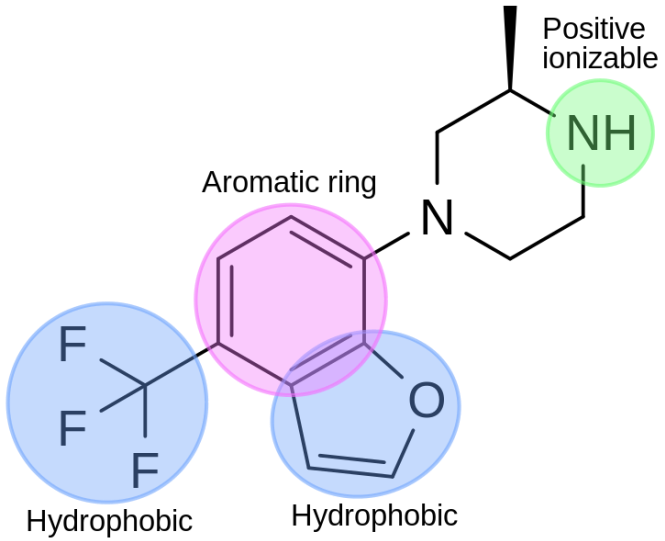
# Important Definitions

- **Enzyme**: A protein that acts as a catalyst for a reaction.
- **Inhibitor:** An agent that binds to an enzyme and inhibits its activity.
- **Inhibition constant (Ki):** A measure of the equilibrium between an enzyme–inhibitor complex and the uncomplexed enzyme and inhibitor.
- **$IC_{50}$ :** The concentration of an inhibitor required to inhibit an enzyme by 50%.

# Important Definitions

- **Ligand** : A chemical compound/substance that binds to a receptor.

- **Pharmacophore** : Groups or part of molecule essential for activity.

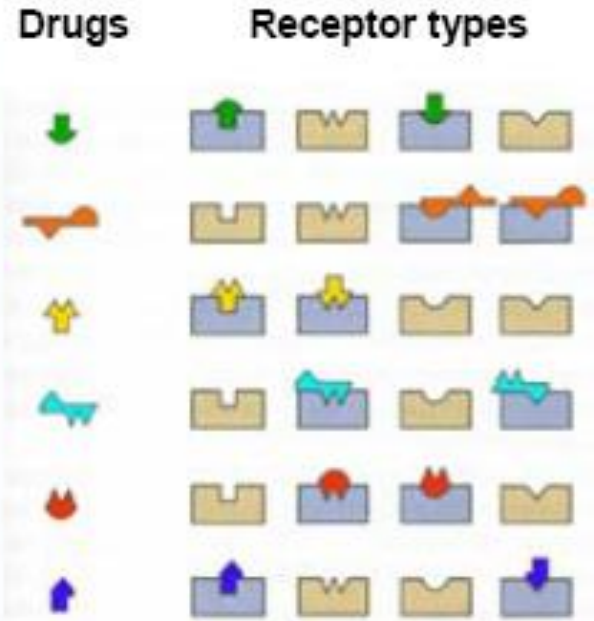


# Important Definitions

- **Structurally non-specific drugs:** are those which the drugs interaction with the cell membrane depends more on the drug molecule's Physical characteristics (solubility, partition coefficient, acidity, basicity) than on its chemical structure. Example hypnotics, general anesthetic agents, bactericidal agents
- **Structurally specific drugs:** are those for which pharmacological activity is determined by the drugs ability to bind to a specific endogenous receptor. Activity is primarily determined by the drug's chemical structure, examples: NSAID, antihistaminic etc…

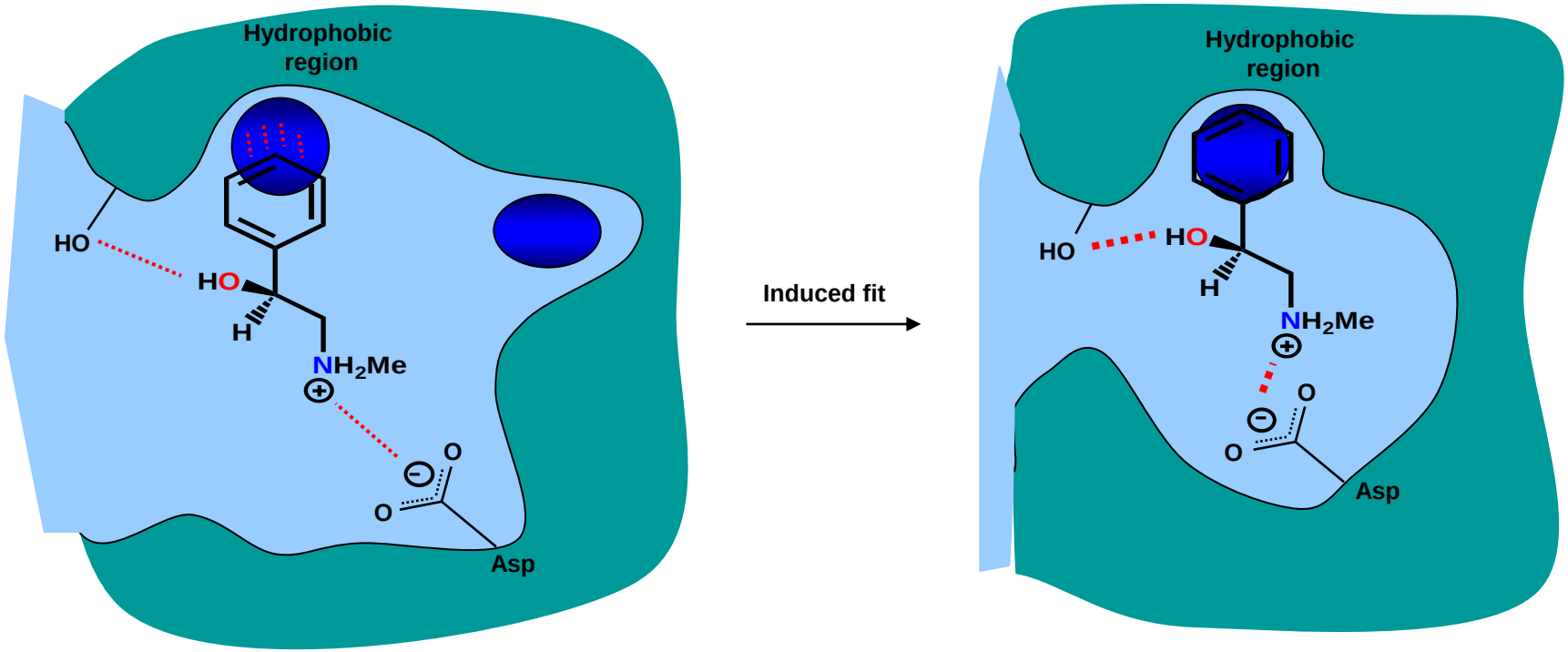
# Drug-receptor Interactions

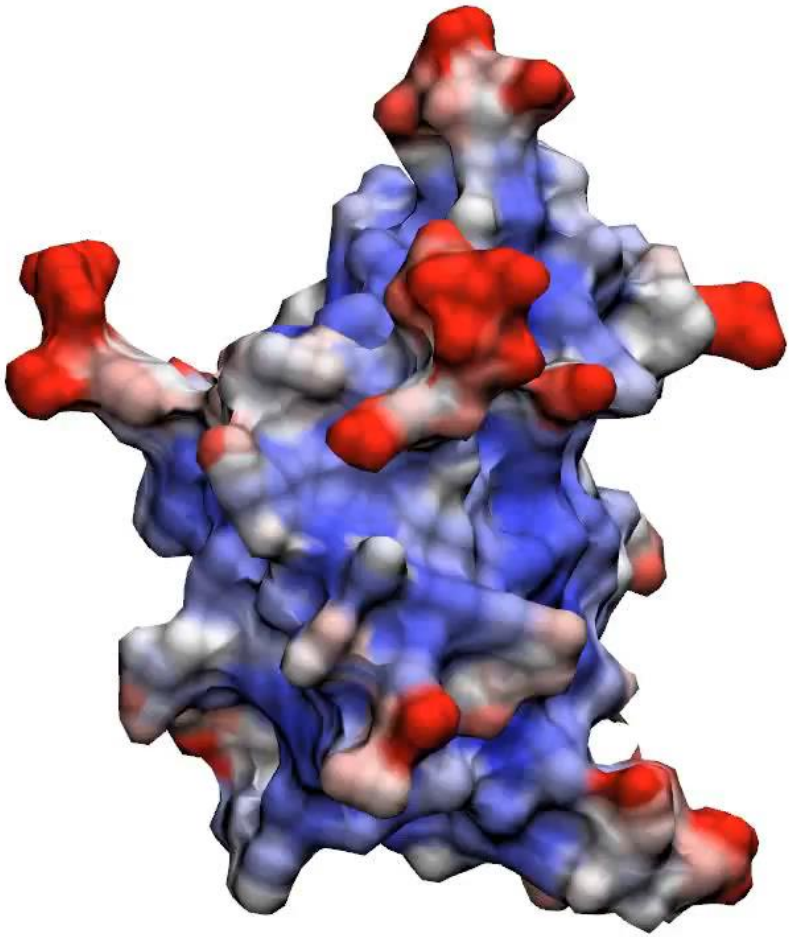
- *Lock and Key Concept*

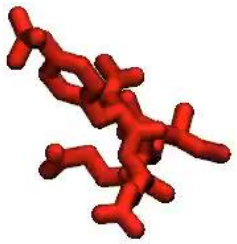



# Drug-receptor Interactions

- In Reality → Both of R & D are Flexible → binding of the drug to a receptor is dynamic process







- Affinity of Drug (ligand) or how strongly D is binding to the binding site is determined by:

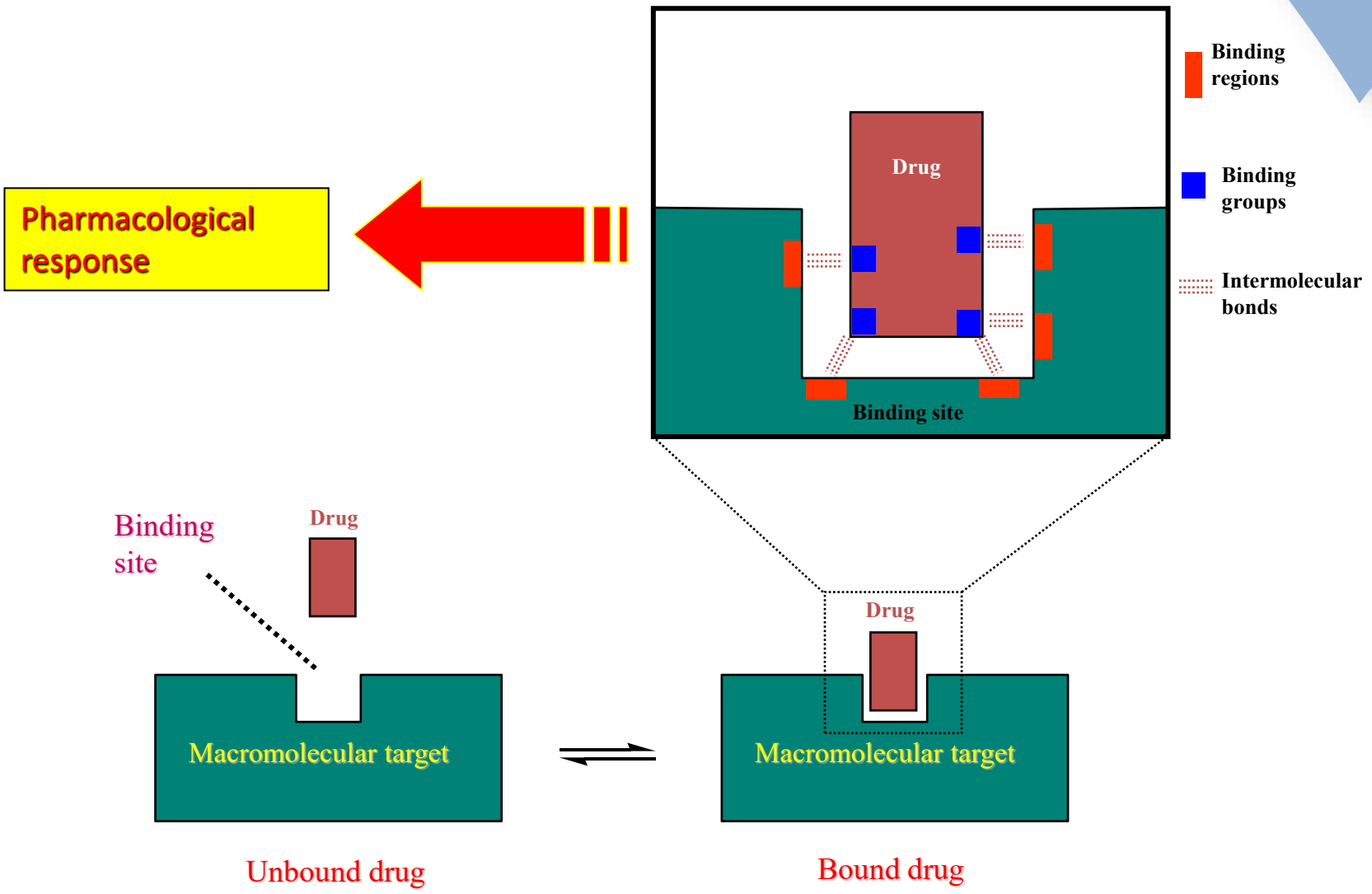
$$\Delta G = \Delta H - T\Delta S$$

**Δ*G* – free energy difference**
**Δ*H* – enthalpy**
**Δ *S* – entropy**

$$\Delta G = -2.303\ RT\ logK$$

$$[D] + [R] \underset{}{\overset{K}{\rightleftharpoons}} [DR]$$

# DRUG-RECEPTOR INTERACTIONS



# Drug-Receptor Interactions

- **Covalent interaction (bond)**
- **Ionic interaction**
- **Hydrogen bonding**
- **Hydrophobic interaction**
- **Van der Waals forces**