Physicochemical Properties in Relation to Biological Activity

Drug Design Approaches

1-Empirical

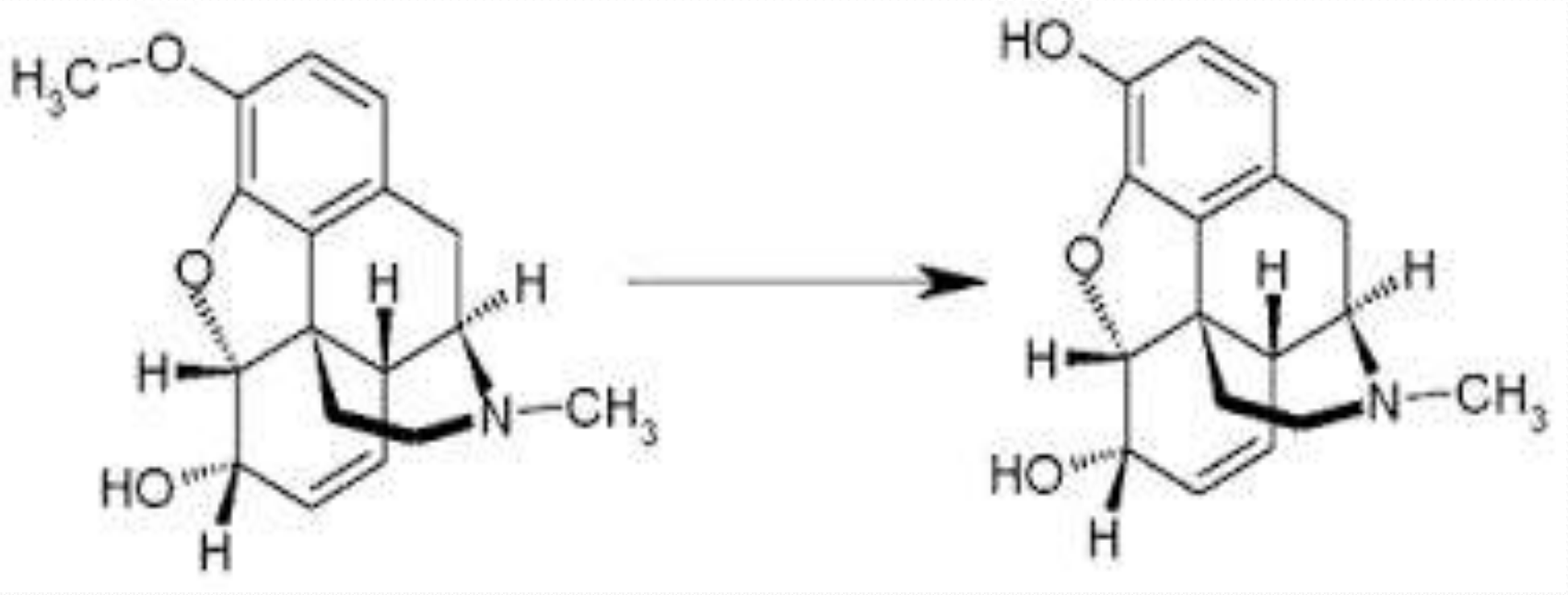
2-Semempirical

3-Rational Drug Design

4-Combintorial chemistry.

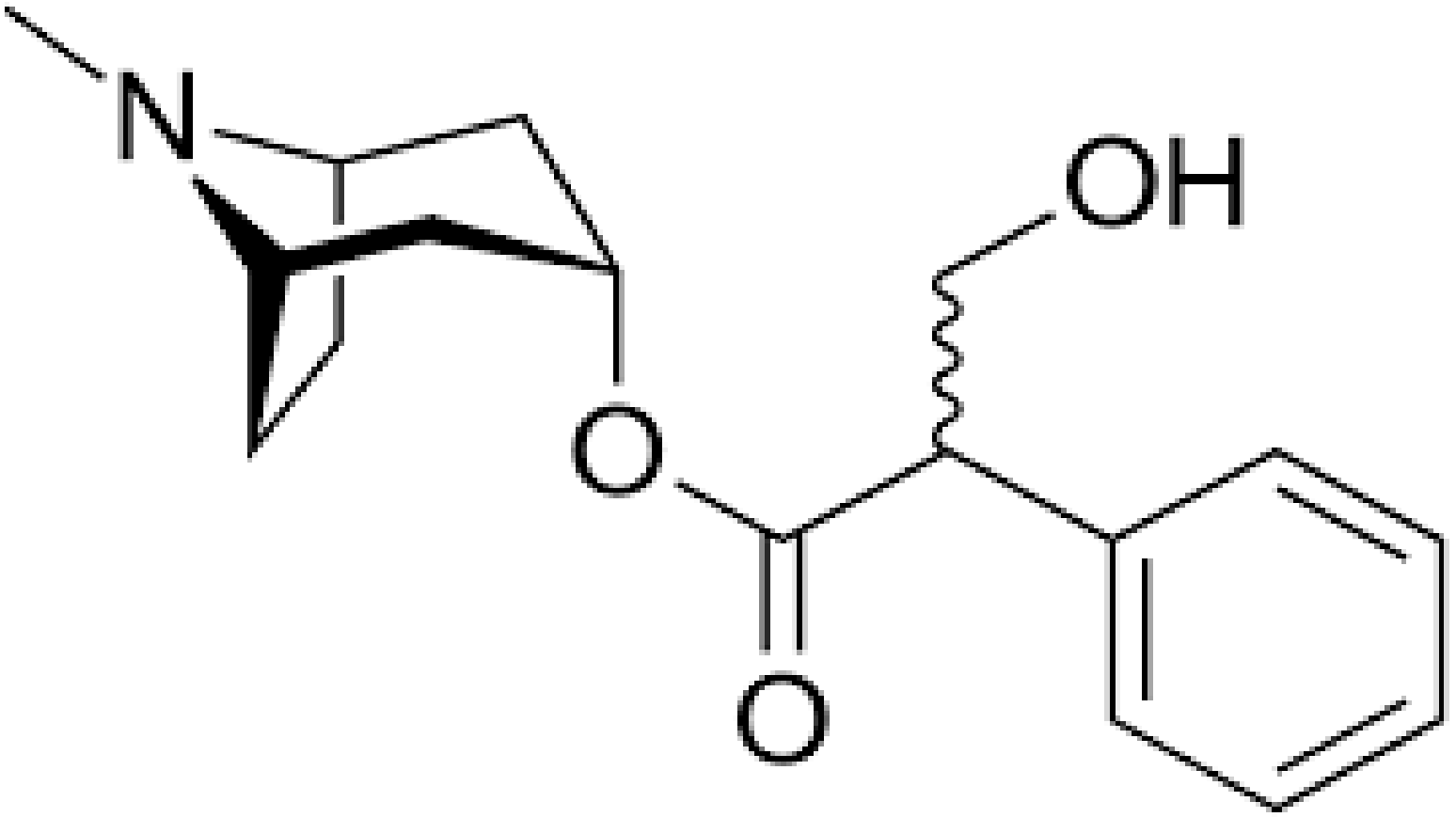
There are several changes to improvement biological activity or bioavailability of isolated or synthetic drugs.

1-Change in the functional group. Codeine converted to morphine

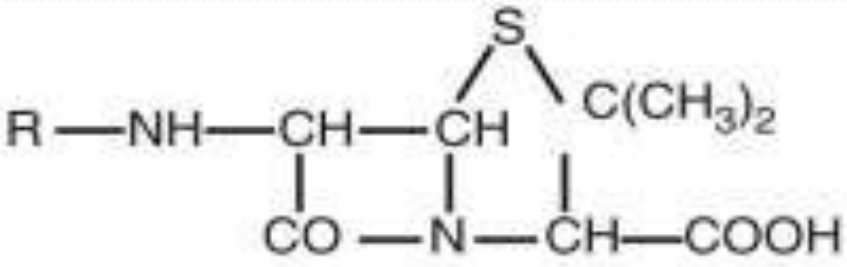


2-Changes in stereochemistry.

Epimerization of ester group from alpha to beta in atropine lead to loss or decrease activity .

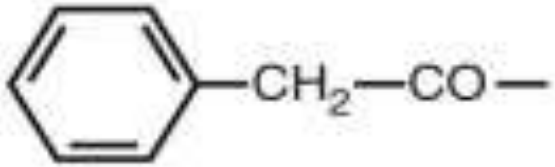


3-Change in functional group to enhance oral stability.

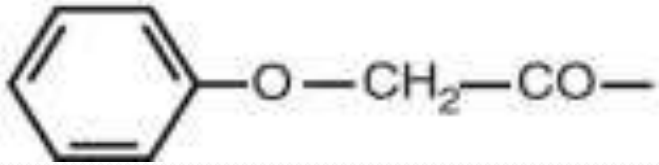


Structure of side chain R

Penicillin G
benzylpenicillin



Penicillin V
phenoxymethylpenicillin

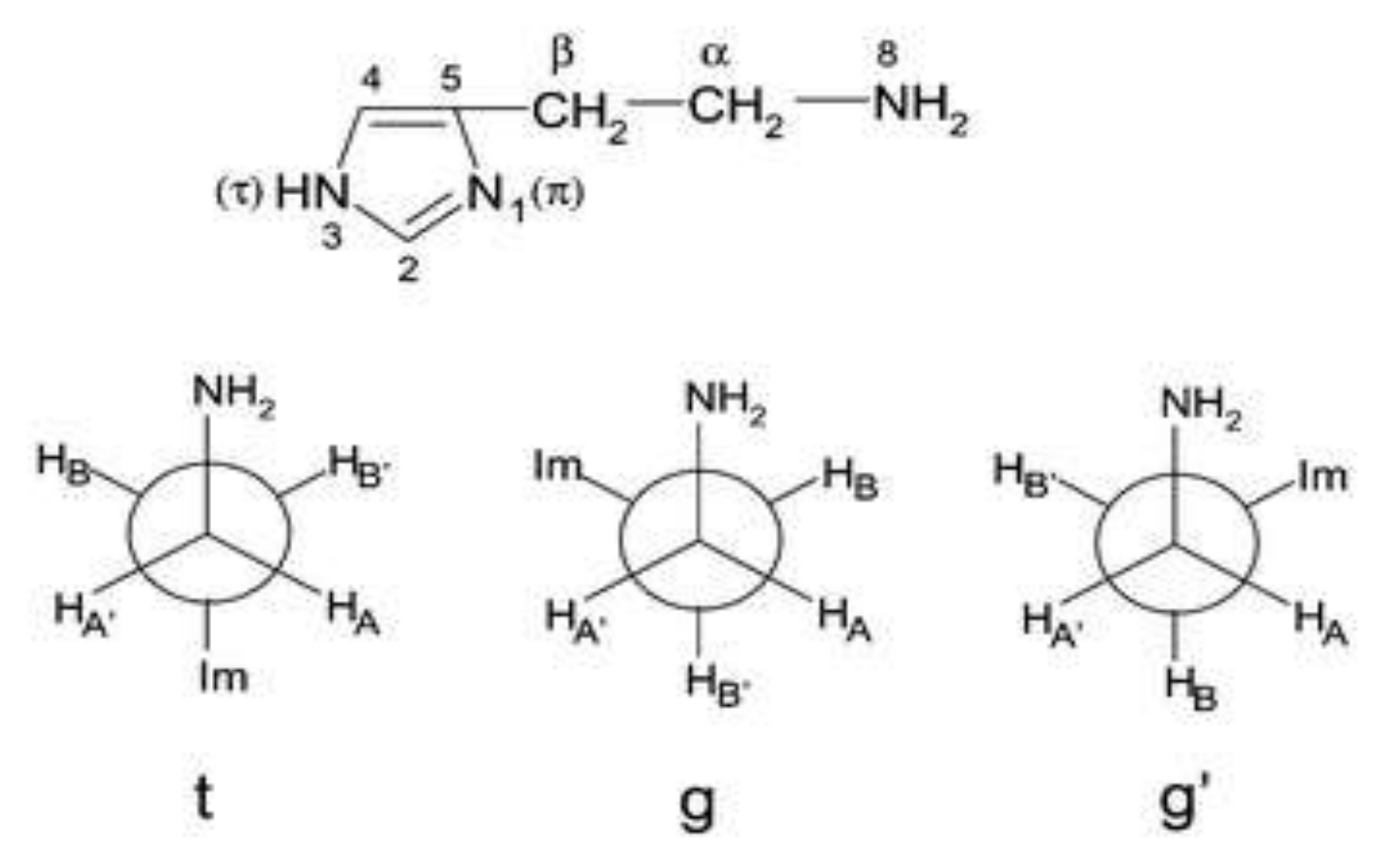


4-Conformational changes and specific receptors .

Histamine has two form ,

trans extended form for H1-Rec.activity.

Gauch folded form for H2-Rec.



The criteria must meet in the drug to be effective

1-Drug must be soluble in the body fluid.

2-Passes various membrane barriers*PC*.

3-Endure metabolic attach .

4-Eescape excessive distribution.

5-Pentrate to the site of action

Routes of Administration

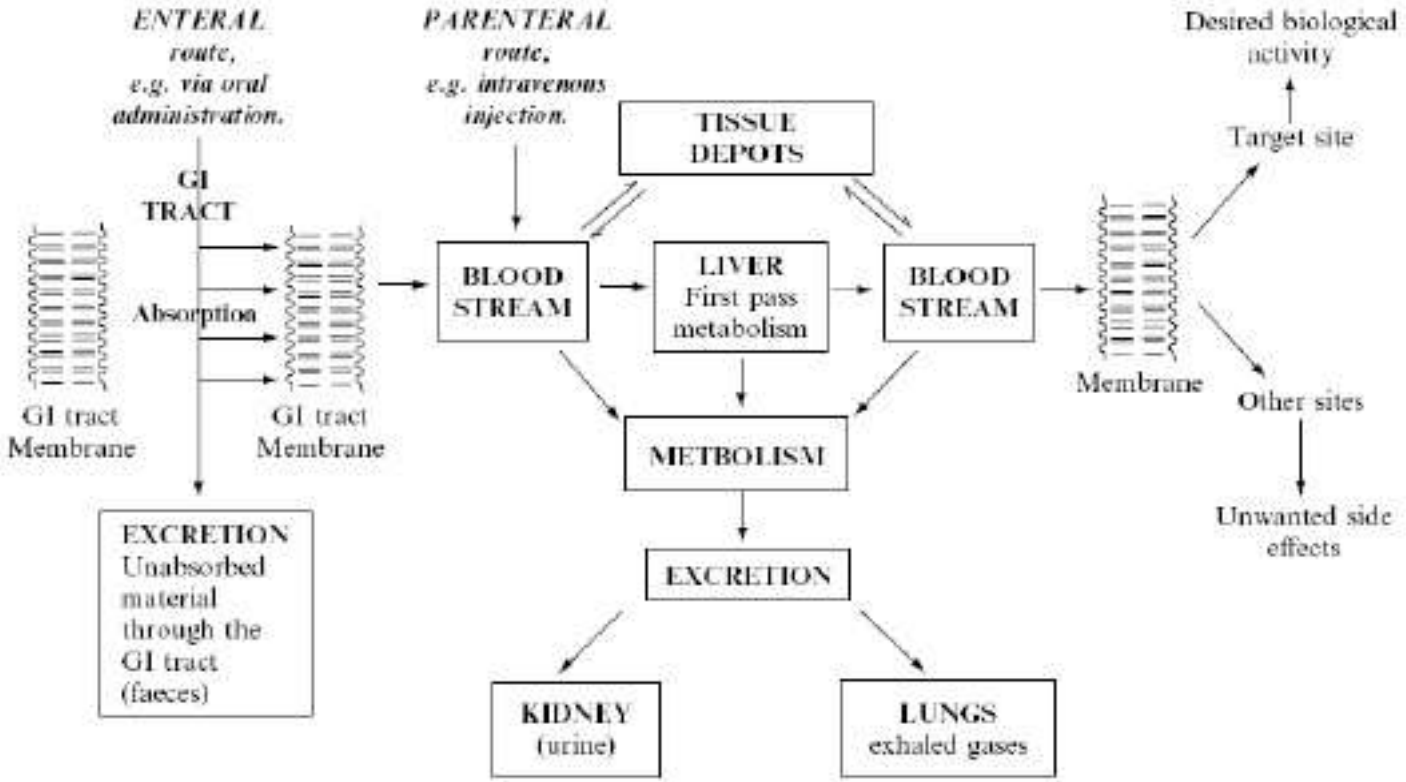


Figure 2.3 The main routes of drug administration and distribution in the body. The distribution of a drug is also modified by metabolism, which can occur at any point in the system

Pharmacokinetics Phase

- The pharmacokinetic phase of drug action includes the Absorption, Distribution, Metabolism and Elimination (ADME) of the drug.

Absorption

Absorption is the passage of the drug from its site of administration into the plasma after enteral administration.

It involves the passage of the drug through the appropriate membranes.

Distribution

- Distribution is the transport of the drug from its initial point of administration or absorption to its site of action.
- The main route is the circulatory system; however, some distribution does occur via the lymphatic system.

Metabolism

- Drug metabolism is the biotransformation of the drug into other compounds referred to as metabolites.

- These biotransformations occur mainly in the liver but they can also occur in blood and other organs such as the brain, lungs and kidneys.

Elimination

- Elimination is the collective term used for metabolic and excretion processes that irreversibly remove a drug from the body during its journey to its site of action. It reduces the medical effect of the drug by reducing its concentration at its site of action.
- Slow Elimination
- Rapid Elimination

Bioavailability of Drugs

- The bioavailability of a drug is defined as the fraction of the dose of a drug that is found in general circulation It is influenced by such factors as ADME.
- Bioavailability is not constant but varies with the body's physiological condition.

Drug crossing cell membrane:

3 possible routes through w- drugs can cross cell membrane.

1.passive diffusion of water-soluble drug through an aqueous channel or pore.

2.passive diffusion of a lipid-soluble drug dissolved in a membrane.

3. carrier-mediated active transport of drug(e.g. prot. transporter)

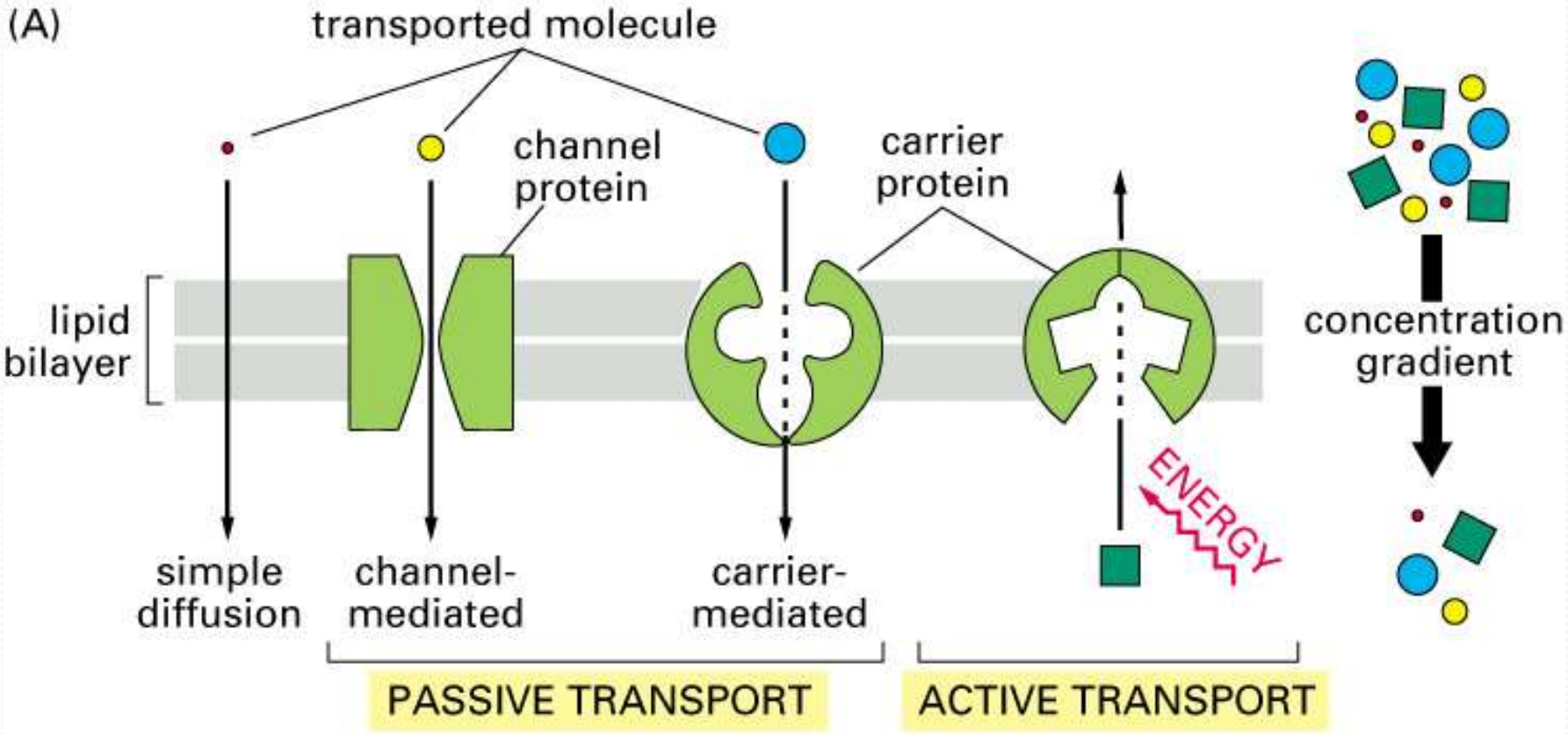


Figure 11–4 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Tissue Depots

*drug can also be stored in tissue depots.

Neutral fat a depot of considerable importance.

* more lipophilic the drug, →more likely it will concentrate in these pharmacologically inert depots.

Drug +Fat → Drug-Fat [Adipose tissue is another site of drug loss]