PHYSICOCHEMICAL PRINCIPLES

Drug molecules interact with biological structures

drug effect

lipoproteins/enzymes

membranes

nucleic acids

DRUG EFFECT

Drug effect is preceded by drug transport

from site of application to site of action

and is dependent on

physicochemical properties

PHYSICOCHEMICAL PROPERTIES

Interatomic distances

Intermolecular forces

Stereochemistry

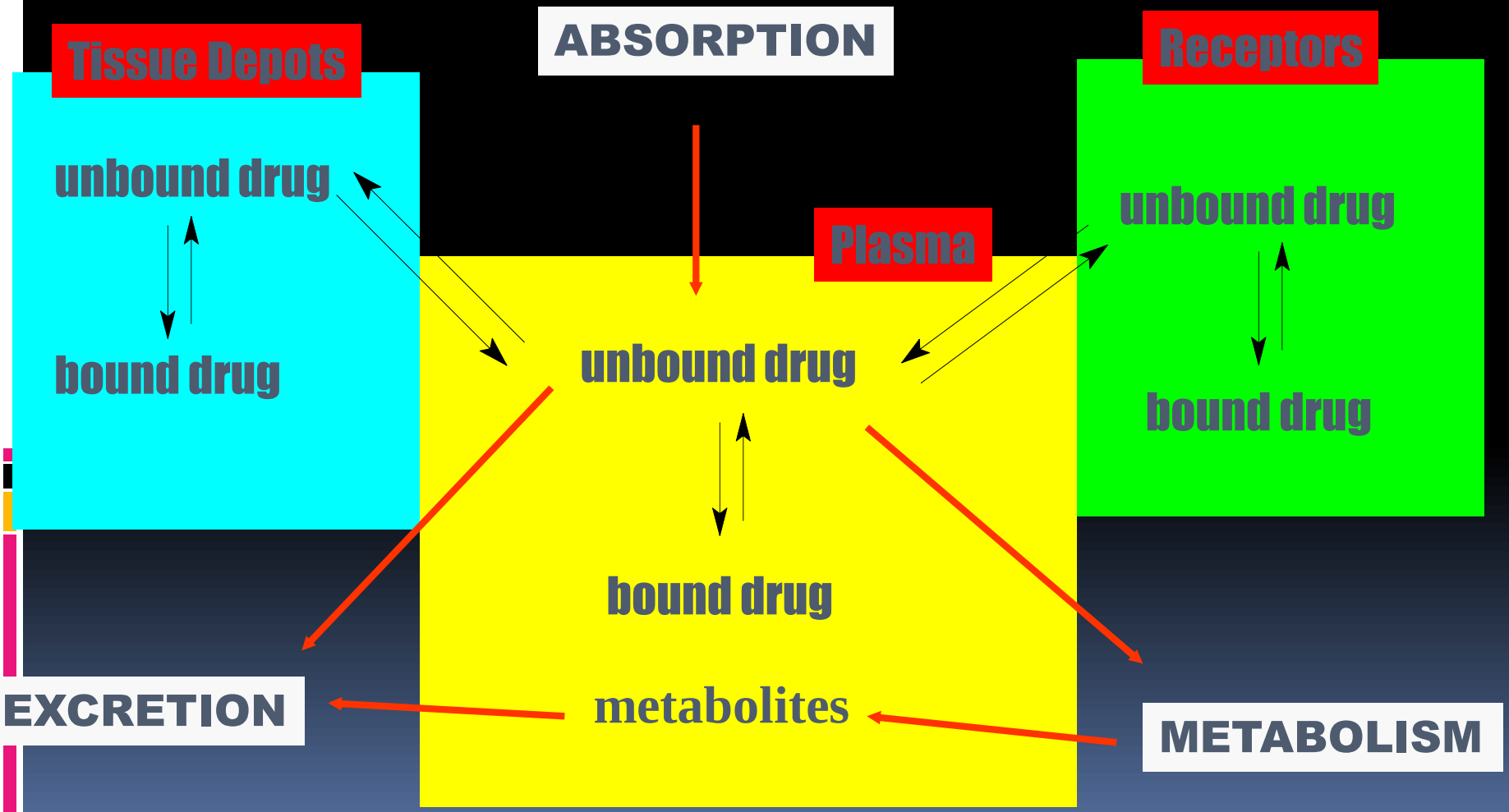
Partition coefficient

Solubility

Ionization

All affect pharmacokinetics

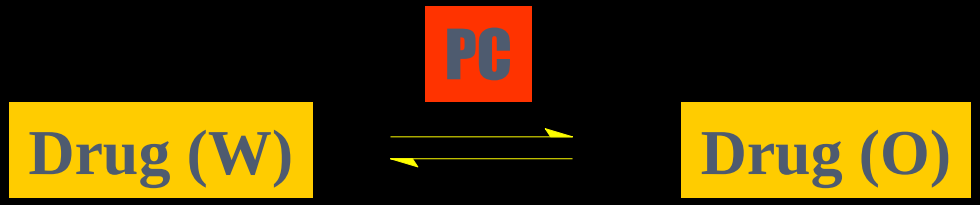
PHARMACOKINETICS



PARTITION COEFFICIENT

Hydrophobic bonding interactions are critical

Can be approximated by partition coefficient



$$PC = \frac{[drug]_O}{[drug]_W}$$

Thus, PC describes the entire drug.

Oral Administration
Absorption from stomach, intestine and other factors in the plasma befor getting to the site of action

Ex. Aniline ArNH2 Ka=4

Stomach pH=1 ratio ionized to unioize 1000 :1

Intestine pH=5 ratio ionized to unionize 1:10

Plasma pH=7ratio ionized to unionize 1:1000 means very small amount of aniline will return to the stomach.

For this reason if aniline adim.iv the stomach may be considered as the site of loss.

The relationship between pka ,pH of the body and the ratio of ionize to unionize of the drug can be calculated by Henderson-Hasselbulc

For a weak acid

$$pH - pK_a = \log \frac{[Ionized]}{[Un-ionized]}$$

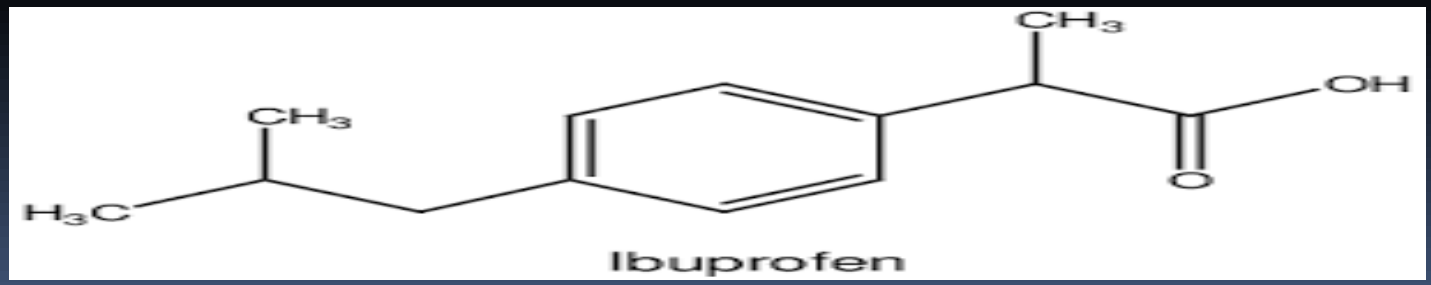
For a weak base

$$pH - pK_a = \log \frac{[Un-ionized]}{[Ionized]}$$

Example. Ibuprofen acidic drug with ka=5.2 ,pH=2.2 of gastric fluid predict the ratio and reflect possible site of absorption

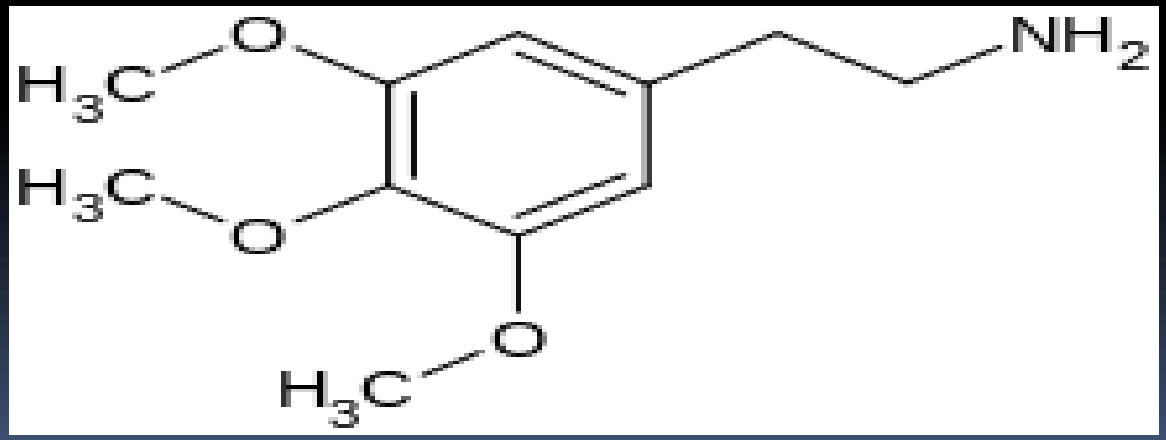
ratio=1 to 1000

site stomach



Ibuprofen

Basic drug mescaline pka=8.2 ,pH=6.2 for urine
ratio=1 to 100 un. to ion.
Degree of ionization play important role in the influencing the degree of absorption from the body



Factors effect of drug absorption

a)Drugs with same pka with different PC should different degree of absorption

Drugs	pka	PC	Absorption
Thiopental	7.6	100	Readily
Secobarbital	7.9	23	Less Readily
Barbital	7.8	0.7	slowly

B)Non absorbable complex formation

Oral adim. quaternary ammonium salt, formation non absorbable complex from interaction with the charge of carboxyl or sulfonic acid residue of intestinal mucosa. Anthelmintic drug ,prevent undesirable systemic effect and preserve high gastro-intestinal conc. for toxic intestinal parasite

c) Protein binding

Bind of the drug to the plasma protein has great influence on the

.biological activity

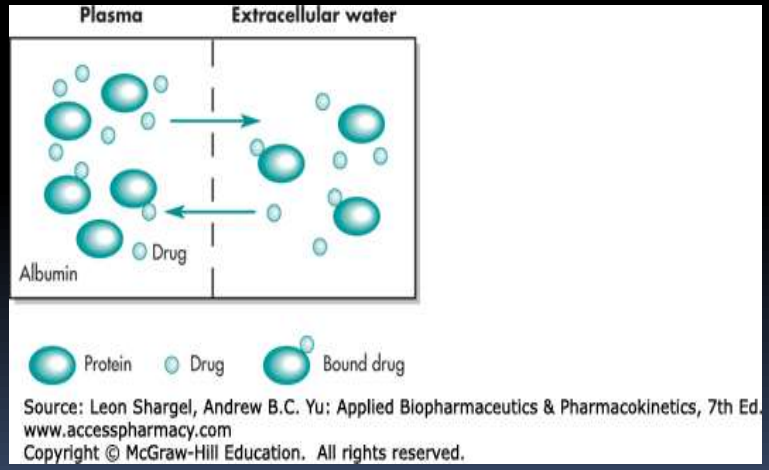
.transport metabolism

.absorption

.duration

.t. half

.Drug .Drug interaction



Source: Leon Shargel, Andrew B.C. Yu: Applied Biopharmaceutics & Pharmacokinetics, 7th Ed.
www.accesspharmacy.com

D) Neutral fat
Drugs with high PC are concentrate in the inert depots .. short duration of action of some drugs)