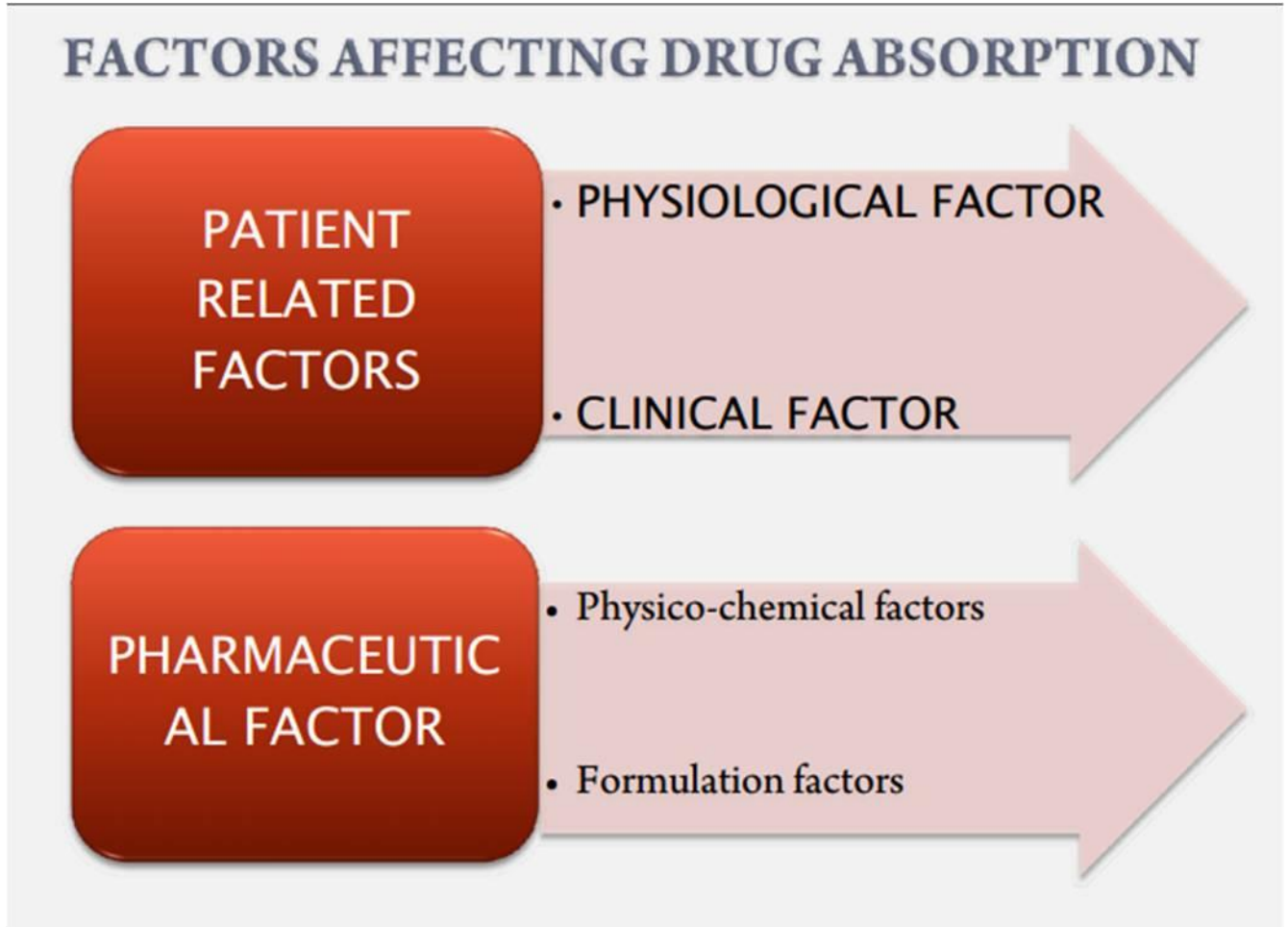

FACTORS AFFECTING DRUG ABSORPTION
PATIENT RELATED FACTORS
• PHYSIOLOGICAL FACTOR
• CLINICAL FACTOR
PHARMACEUTICAL FACTOR
• Physico-chemical factors
• Formulation factors

Physicochemical properties of drugs affecting absorption

1. Drug solubility and dissolution rate
2. Particle size and effective surface area
3. Polymorphism and amorphism
4. Salt form of the drug
5. Lipophilicity of the drug
6. Drug stability
7. pH-partition theory: pka of the drug and pH

pH-partition theory

Drugs are absorbed from the biological membranes by passive diffusion depending on the fraction of un-ionized form of the drug at the pH of that biological membrane. Degree of ionization depends on both drugs pKa and the solution pH. Ionized drugs are more hydrophilic and have minimal membrane transport compared to the un-ionized form of the drug. Solution pH will affect the overall partition coefficient of an ionizable substance.

Brodie proposed the pH-partition theory to explain the influence of GI pH and drug pka on the extent of drug transfer or drug absorption.

pH-partition theory state that the process of absorption of drugs, which are lipid soluble with MW greater than 100 and transported by passive diffusion, is governed by:

1. The dissociation constant (pka) of the drug.
2. The lipid solubility of the unionized drug (a function of drug Ko/w).
3. The pH at the absorption site.

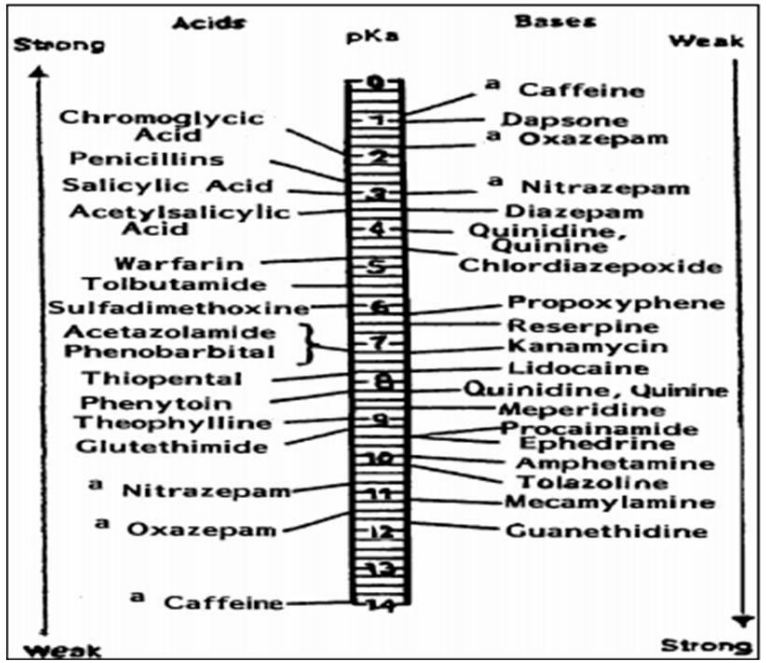
Determination of how much drug will be found on either sides of a membrane

Henderson-Hassel-balch equation for acid drug

The fraction of drug in solution that exist in the unionized form is a function of both dissociation constant of the drug and the pH of the solution.

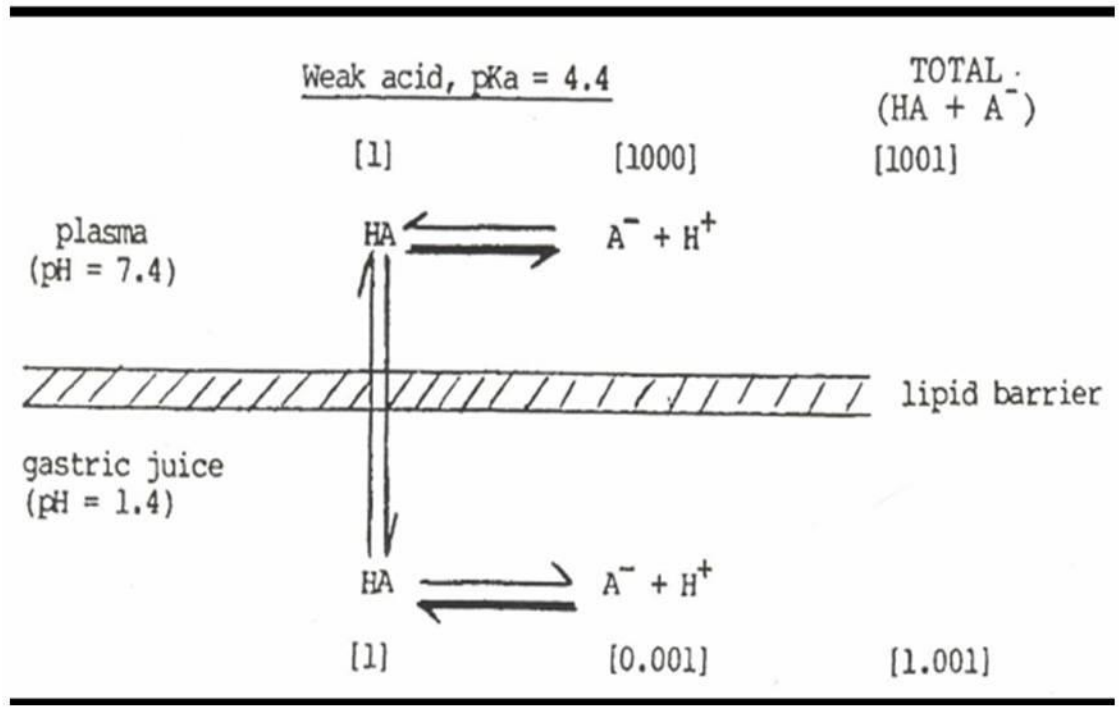
The dissociation constant is often expressed for both acids and bases as pKa (the negative logarithm of the acidic dissociation constant.)

The lower the pKa of an acidic drug, the stronger the acid i.e., greater the proportion of ionized form at a particular pH. The higher the pKa of a basic drug, the stronger the base.



From the knowledge of pka of the drug and pH at the absorption site (or biological fluid), the relative amount of ionized and unionized drug in solution at a particular pH and the percent of drug in solution at this pH can be determined by Henderson-Hasselbach equation for an acid:

$$pH = pKa + \log \frac{[A^-]}{[HA]}$$



A weak acid such as aspirin (pKa 3.5) is approximately 99 % unionized in the gastric fluid at pH 1.5, but only 1.0% of aspirin is unionized at pH 6.5 (small intestine)

Drugs	PKa	PH/site of absorption
Very weak acids e.g. pentobarbital Hexobarbital	>8	Unionized at all pH values; Absorbed along the entire length of GIT
Moderately weak acids e.g. aspirin Ibuprofen	2.5 – 7.5	Unionized in gastric pH& ionized in intestinal pH; better absorption from stomach
Stronger acids E.g. disodium cromoglycate	< 2.0	Ionized at all pH values; Poorly absorbed from GIT
Very weak bases e.g. theophylline Caffeine	< 5.0	Unionized at all pH values; Absorbed along entire GIT
Moderately weak bases e.g. codeine	5 – 11	Ionized at gastric pH, unionized at intestinal pH; better absorption from intestine.
Stronger bases e.g. guanethidine	> 11	Ionized at all pH values; Poorly absorbed from GIT

Formulation factors affecting absorption include:

a) Manufacturing/Processing variables: Method of granulation and compression force.

b) Pharmaceutical ingredients/excipients/ adjuvants: Absorption is altered by various excipients.

-- Vehicle, Diluents, Binders & granulating agent, Disintegrants, Lubricants, Suspending agents/viscosity agent, Surfactants, Colourants etc.

c) Nature and type of dosage form: Disintegration rate. **Bioavailability in the following order -** Solutions>suspensions>capsules>tablets>coated tablets > enteric coated tablet

d) Product age and storage conditions: A number of changes can result due to aging and alteration in storage conditions which can adversely affect absorption.