Pharmacokinetics

ABSORPTION I

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- **Sources**
- **Lippincott Illustrated Reviews: Pharmacology 7th Edition**
- **Katzung ; Basic & Clinical Pharmacology 14th Edition**
- **Bennett & Brown ; Clinical pharmacology 11th edition**
- **Essentials of Medical Pharmacology; Lafi 09**

Pharmacokinetics

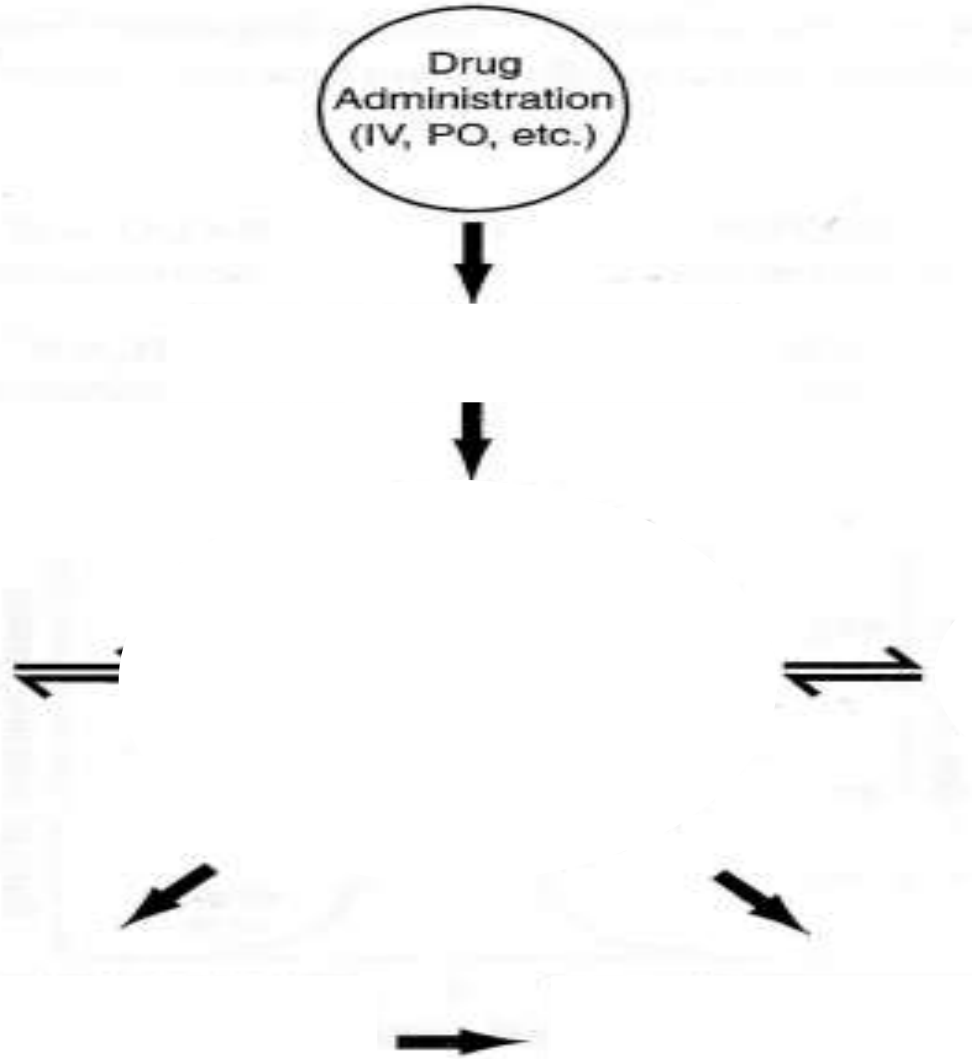
Pharmacokinetic characteristics of drug molecules concern the processes of absorption, distribution, metabolism, and excretion.

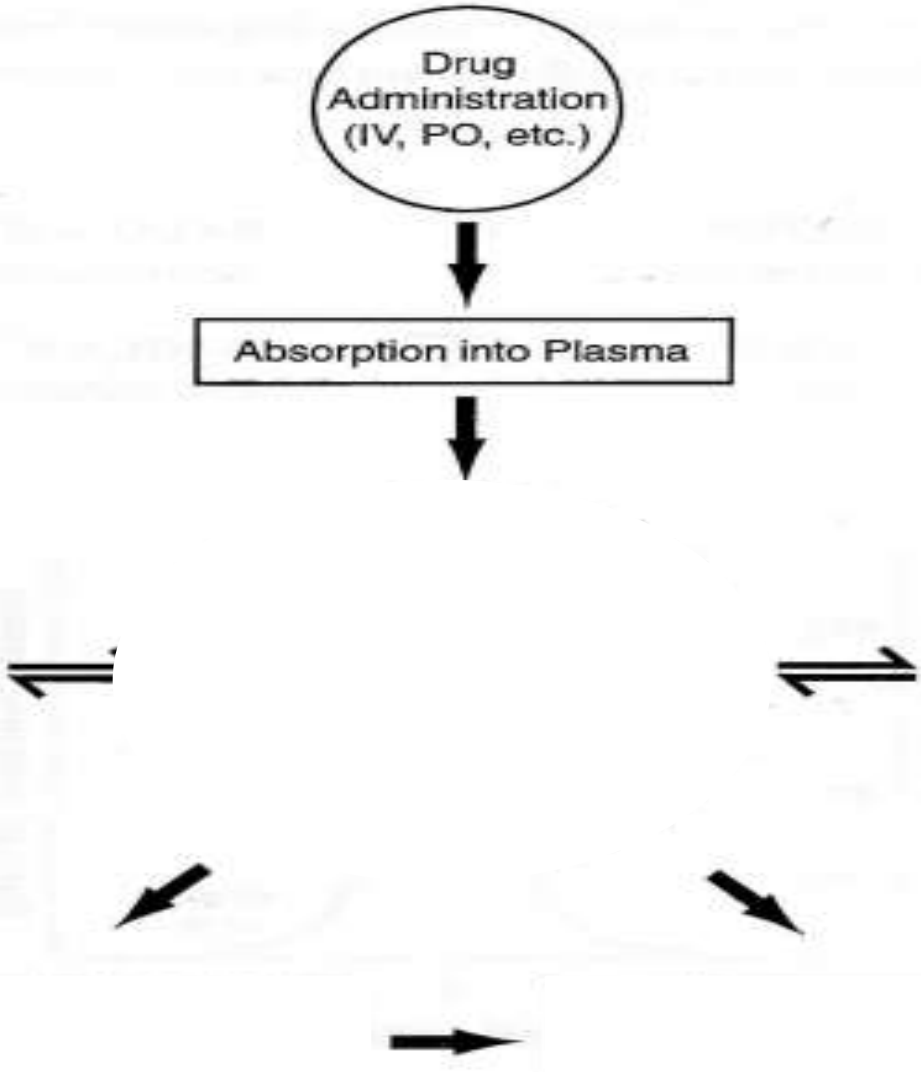
ABSORPTION

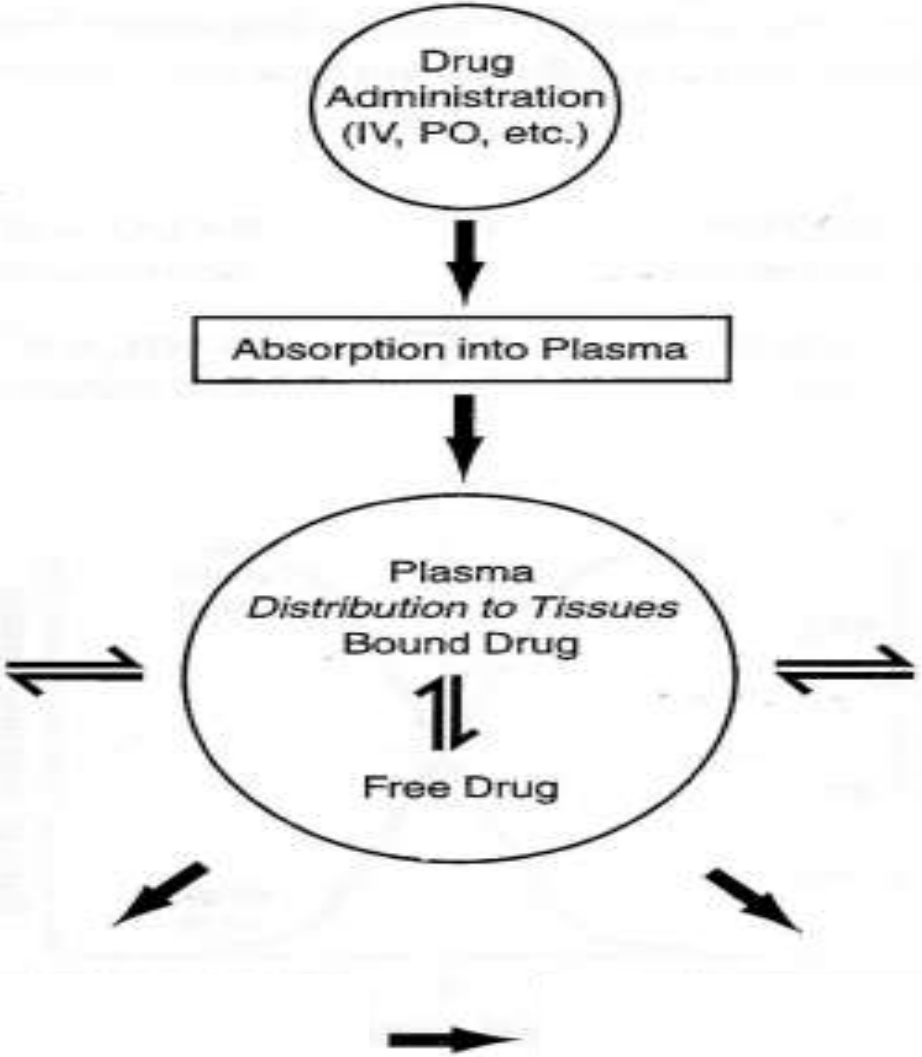
DISTRIBUTION

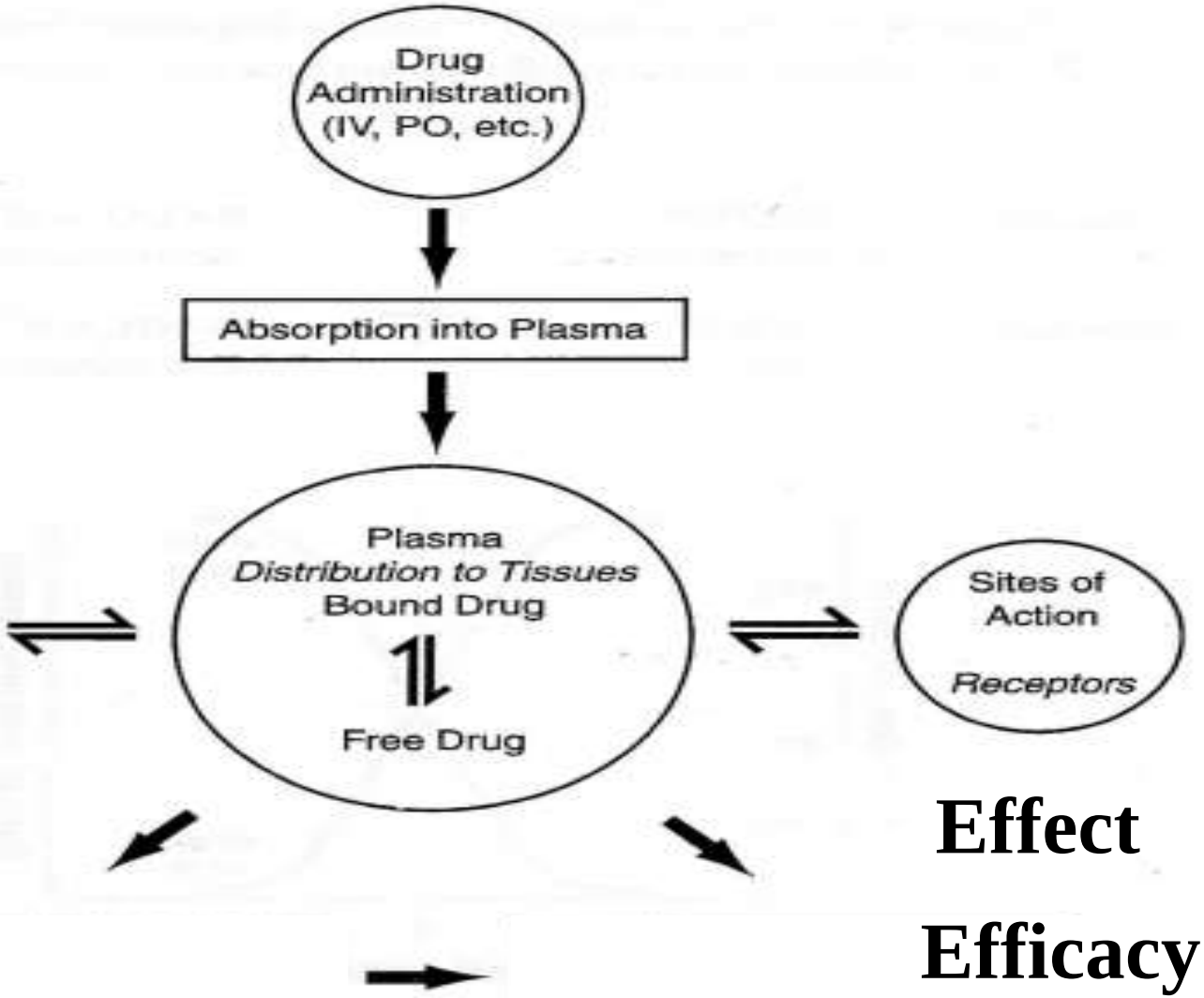
METABOLISM

Excretion


Drug
Administration
(IV, PO, etc.)

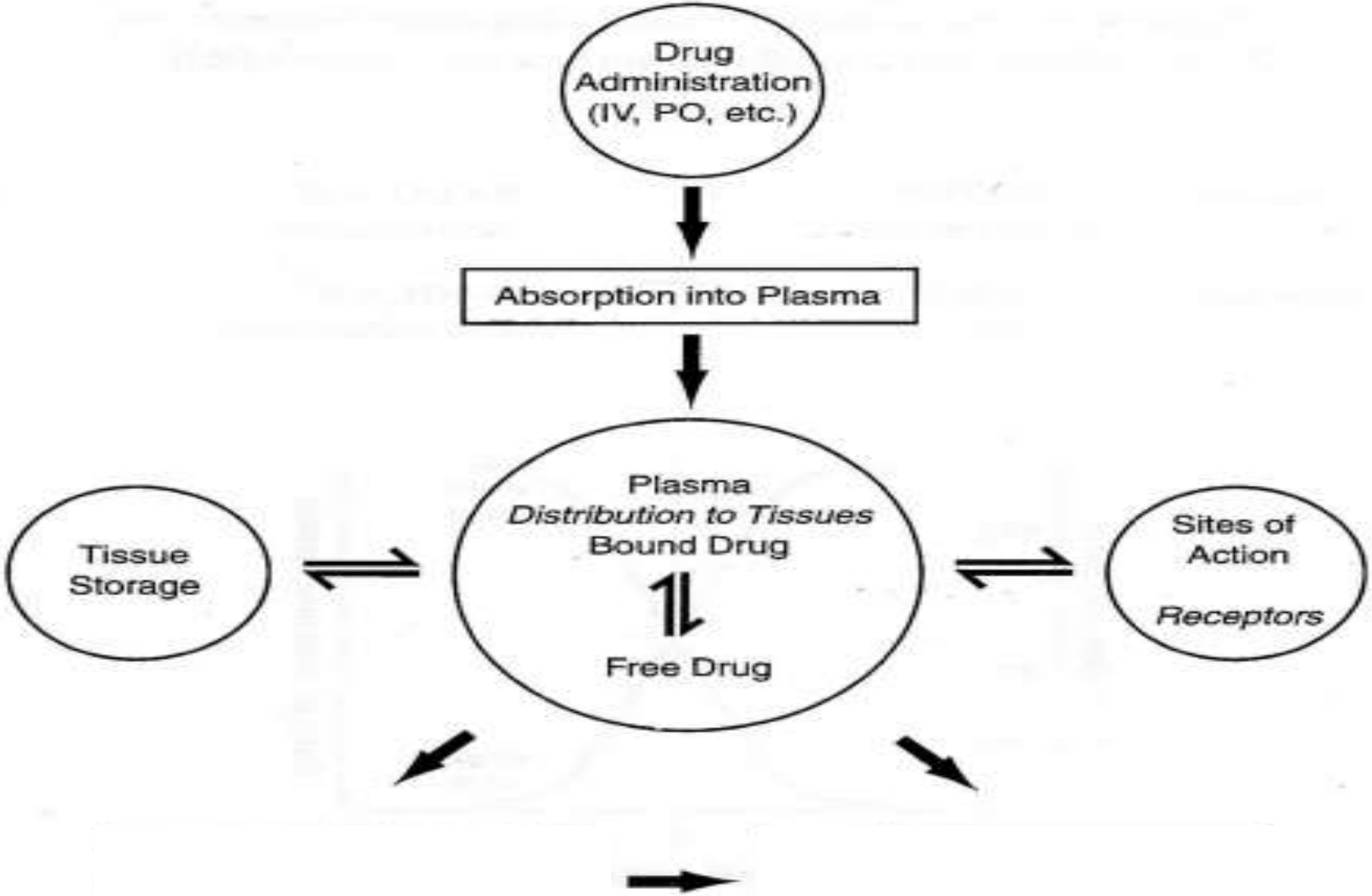

Drug
Administration
(IV, PO, etc.)
Absorption into Plasma

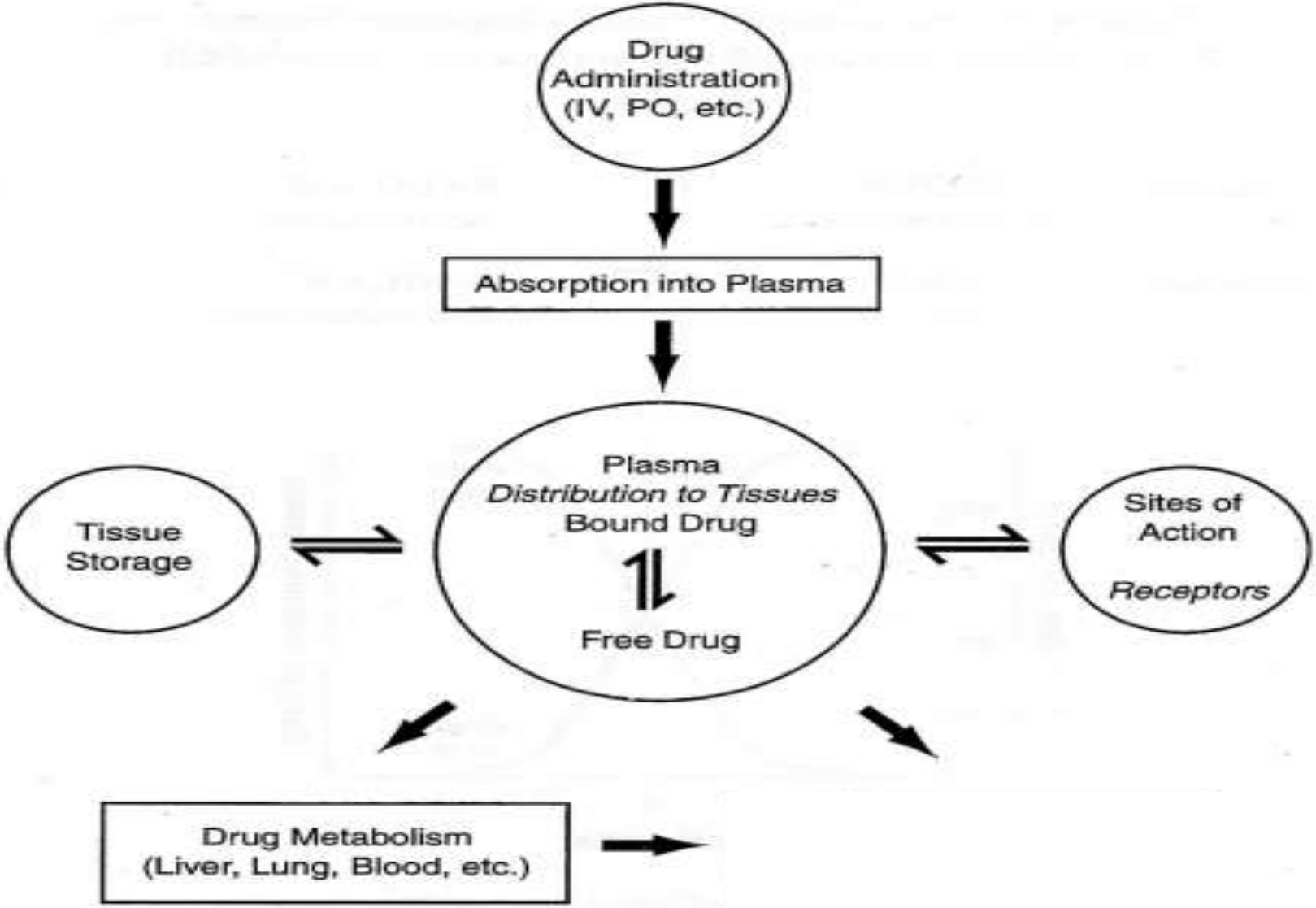

Drug
Administration
(IV, PO, etc.)
Absorption into Plasma
Plasma
Distribution to Tissues
Bound Drug
Free Drug

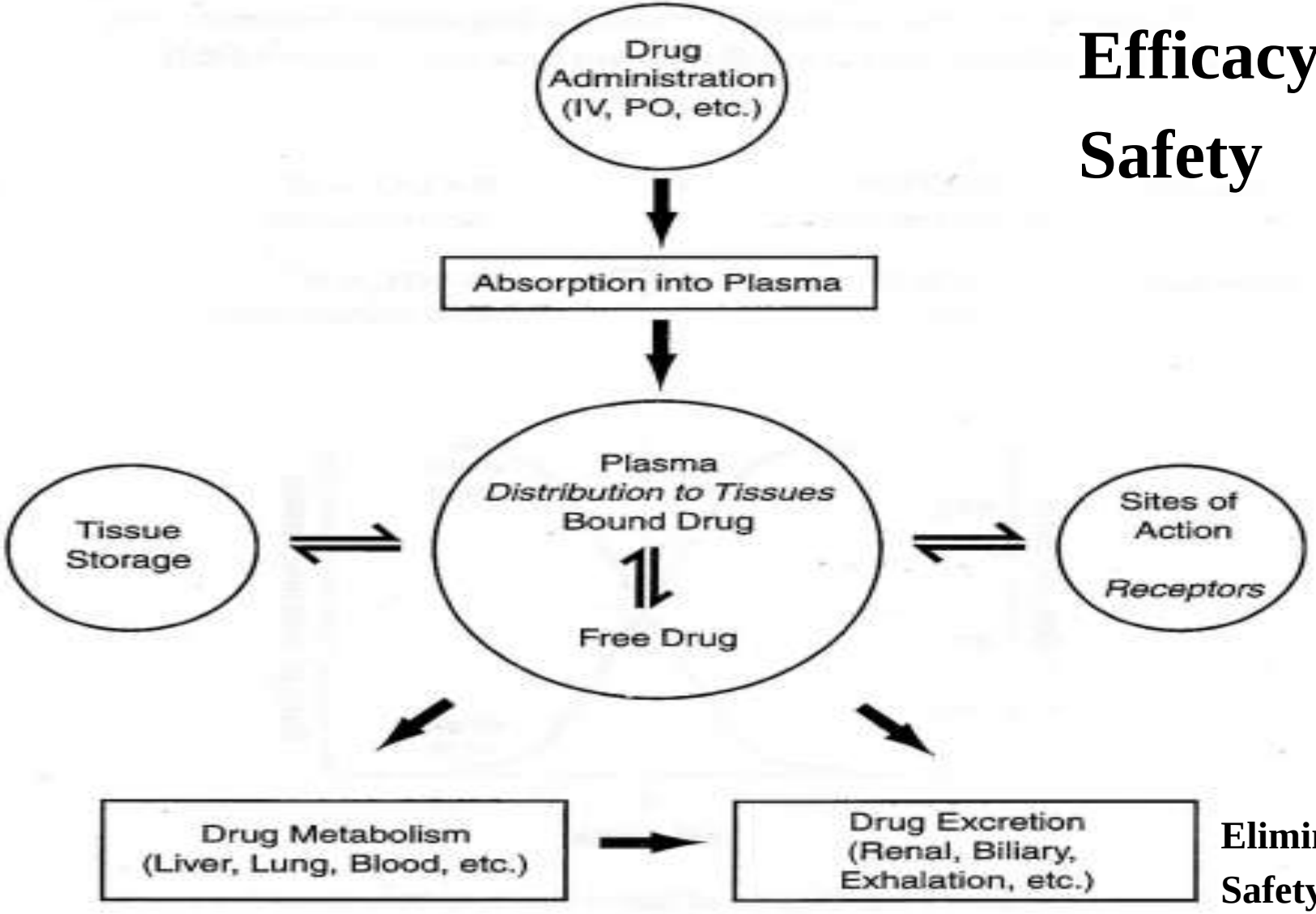


Effect

Efficacy


Drug Administration (IV, PO, etc.)
Absorption into Plasma
Plasma
Distribution to Tissues
Bound Drug
Free Drug
Tissue Storage
Sites of Action
Receptors


Drug Administration (IV, PO, etc.)
Absorption into Plasma
Plasma
Distribution to Tissues
Bound Drug
Free Drug
Tissue Storage
Sites of Action
Receptors
Drug Metabolism (Liver, Lung, Blood, etc.)



Efficacy

Safety

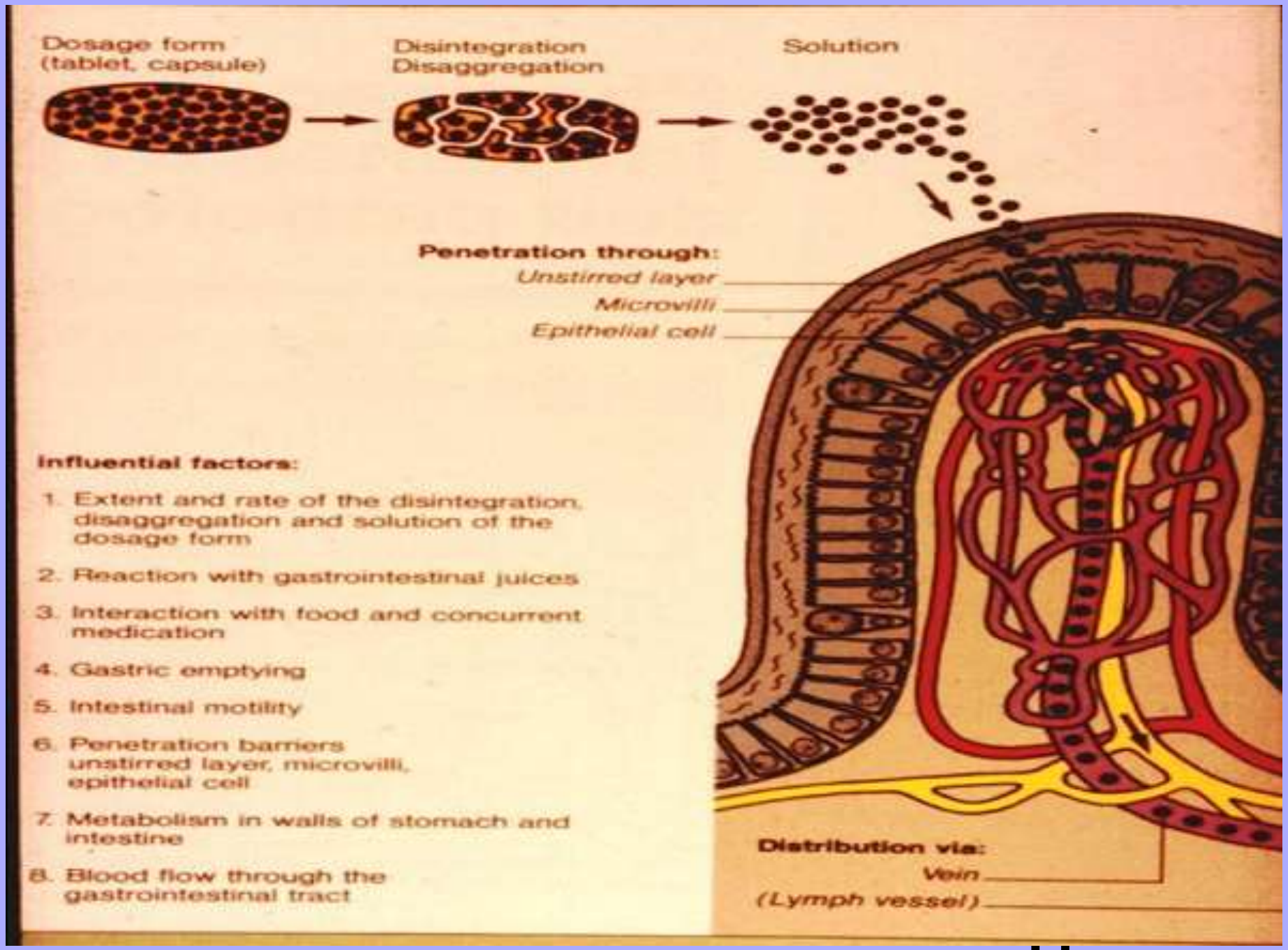
Elimination

Safety

The biodisposition of a drug involves its permeation across cellular membrane barriers.

ABSORPTION

- **Concerns the processes of entry of a drug into the systemic circulation from the site of its administration .**



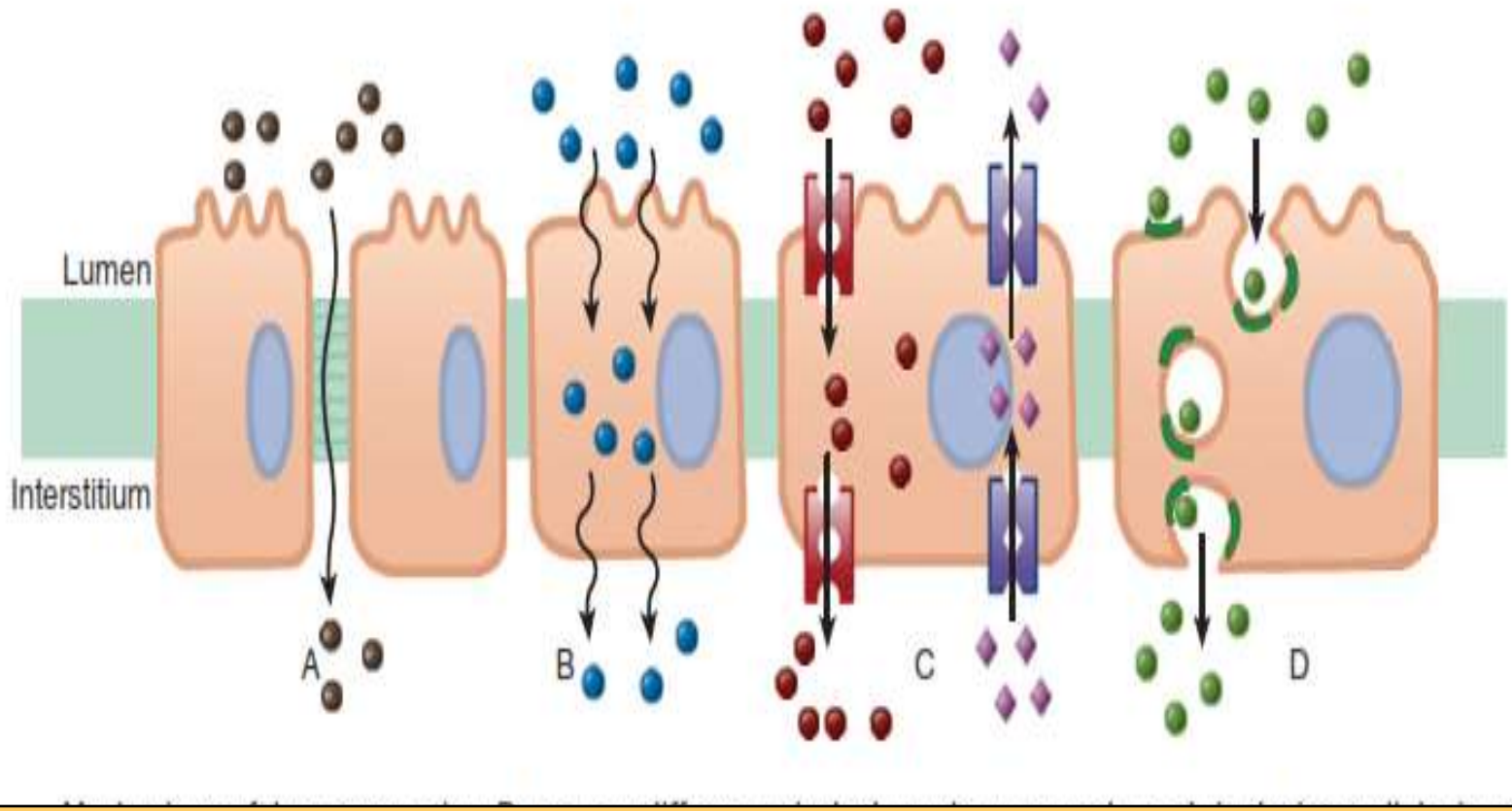
Influential factors:

1. Extent and rate of the disintegration, disaggregation and solution of the dosage form
2. Reaction with gastrointestinal juices
3. Interaction with food and concurrent medication
4. Gastric emptying
5. Intestinal motility
6. Penetration barriers unstirred layer, microvilli, epithelial cell
7. Metabolism in walls of stomach and intestine
8. Blood flow through the gastrointestinal tract

Q1- Drug transport across membranes by :

1. *Diffusion of unionized drugs*
2. *Diffusion of drugs that are weak electrolytes*
3. *Active transport*
4. *Filtration*
5. *Facilitated diffusion*

Q1- Drug transport across membranes by :

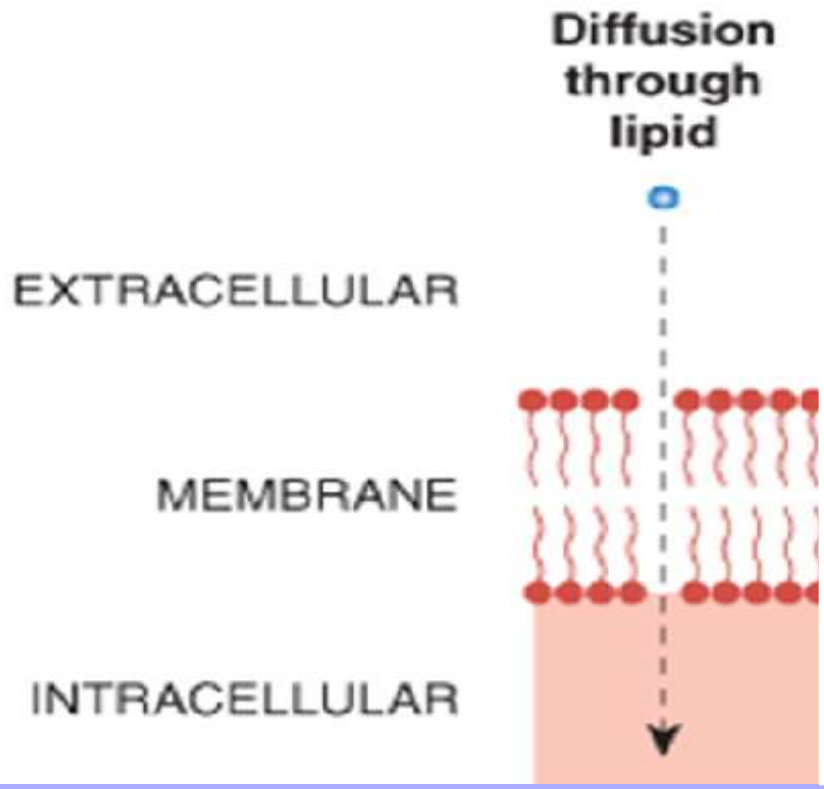


- **Three (of four) ways for drugs to cross lipid membranes.**
- **Diffusion through lipid membrane** is **the most important.**

Three (of four) ways for drugs to cross lipid membranes.

1. **Diffusion through lipids (lipid membrane)** is **the most important.**
2. **Diffusion through aqueous channels is not important** because the channels are only 0.4nm wide and most drugs are at least 1nm in diameter.
3. **Carrier mechanisms** for specific compounds like **A.A and sugars.**
4. **Pinocytosis** which is important for large lipid soluble molecules like **some vitamins**

1-Diffusion of unionized drugs



1-Diffusion of unionized drugs is **the most common and most important** mode of traversing **biologic (Lipid) membranes**;

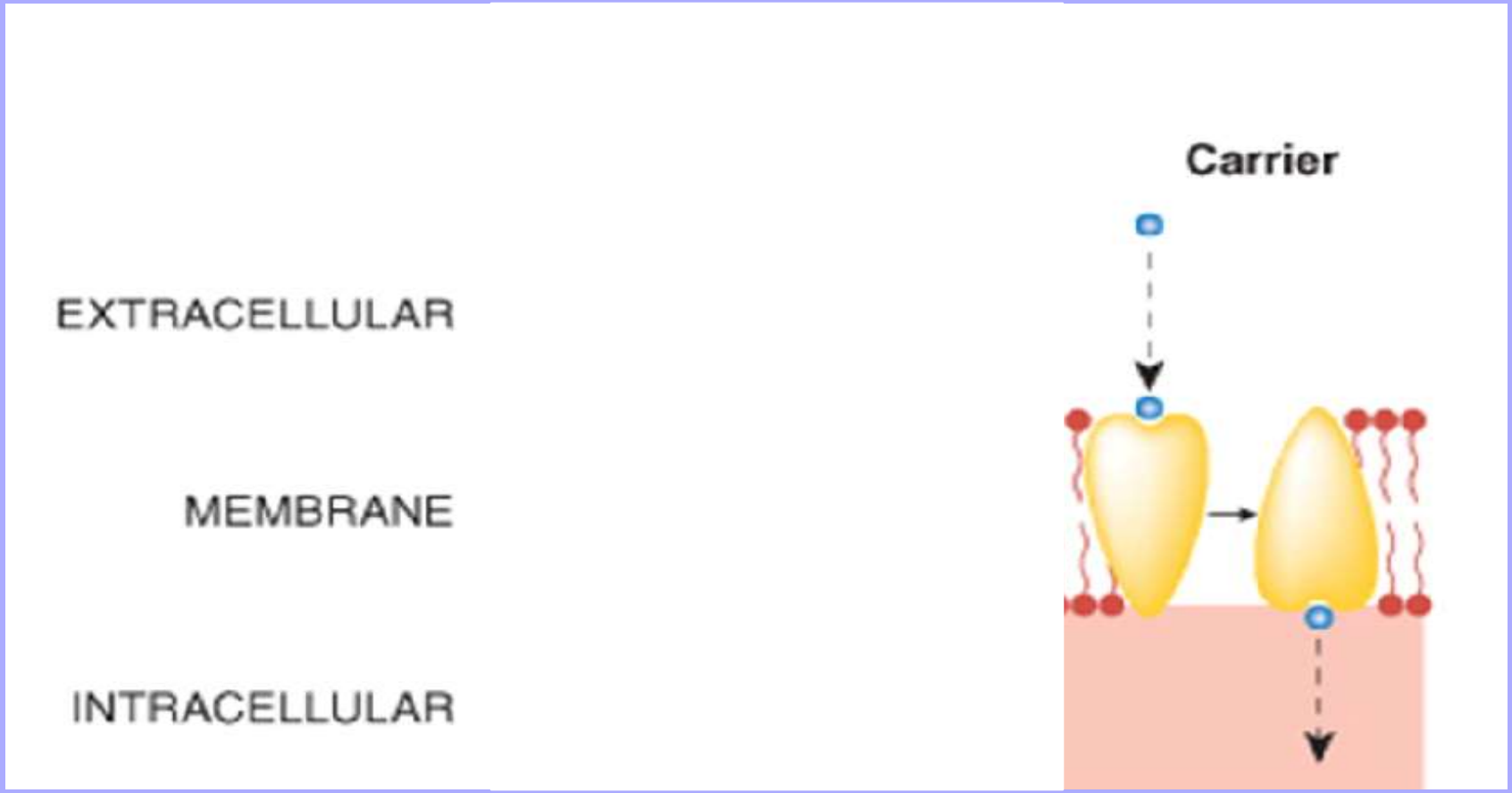
drugs diffuse passively down their concentration gradient.

2-Diffusion of drugs that are weak electrolytes

- **Many drugs are**
- **weak acids** (proton donor)
- **weak bases** (proton acceptor)
- **=weak dissociation in solvent**
- **(organic VS aqoues solvents)**

- **it can exist in either**
- **non ionized**
- **ionized**

3. Active transport



3. ***Active transport*** *is an energy-dependent process that can move drugs* ***against a concentration*** **gradient,** as in protein-mediated transport systems. Active transport occurs in **only one direction and is saturable.** sugars, amino acids,and nucleosides.

4. Filtration at the capillary walls

Because both ionised and unionised solutes readily pass across the capillary wall,

the influence of pH on intramuscular and subcutaneous absorption of drugs is likely to be far less significant.

4. Filtration at the capillary walls

a much more loosely knit structure than the epithelial lining of the gastrointestinal tract, allows the rapid passage of all molecules below a molecular weight of about 5000, whether ionised or unionised.

5. Facilitated diffusion

is movement of a substance down a concentration gradient.

Facilitated diffusion is

- **carrier-mediated,**
- **specific, and**
- **saturable;**
- **it does not require energy.**

2-Diffusion of drugs that are weak electrolytes

- **Many drugs are**
- **weak acids** (proton donor)
- **weak bases** (proton acceptor)
- **=weak dissociation in solvent,**

- **thus it can exist in either**
- **non ionized**
- **ionized forms**

2-Diffusion of drugs that are weak electrolytes

- **Many drugs are weak acids** (proton donor) **or weak bases** (proton acceptor) **=weak dissociation in solvent, thus it can exist in either non ionized or ionized forms in an equilibrium , depending on;an equilibrium , depending on;**

  - **the pH of the environment (stomach is acidic & SI is ?**
  - **the pKa (the pH at which the molecule is 50% ionized and 50% non ionized)**

- **Only the unionized form** of a drug can diffuse to any significant degree across **biologic (Lipid) membranes.**

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pH

- Physiologic pH is about 7.35
  - –Slightly alkaline

pKa

- Is the pH at which the molecule or drug is completely balanced between the
- uncharged (lipid soluble) and the
- charged (water soluble) form.

Henderson
Hasselbalch

$$\log [RH]/[R] = pKa\text{-}pH$$

Focus

Drugs must be
Absorbed

- A drug must be able to be absorbed by the body.

Drugs must have
Delivery

- A drug must be able to be delivered to site of action.

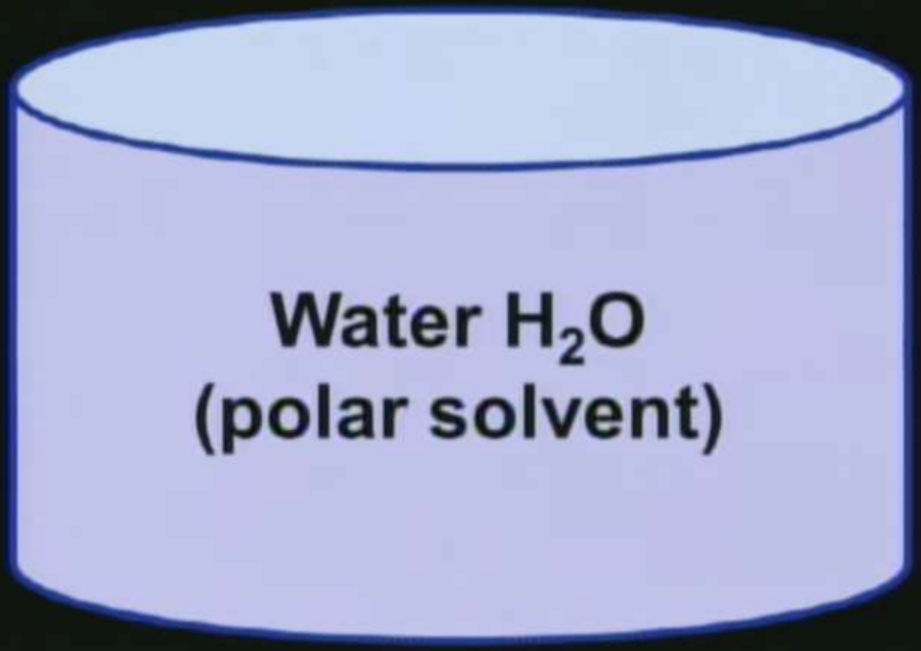
Drugs must have
Elimination

- Drugs must be eliminated at a reasonable rate.

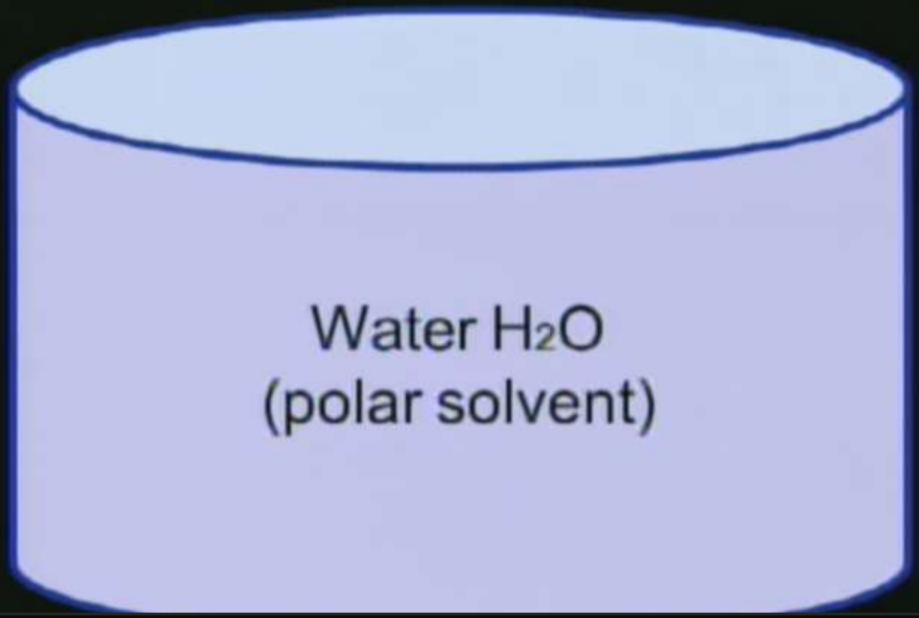
- Most drug are weak acids or weak bases

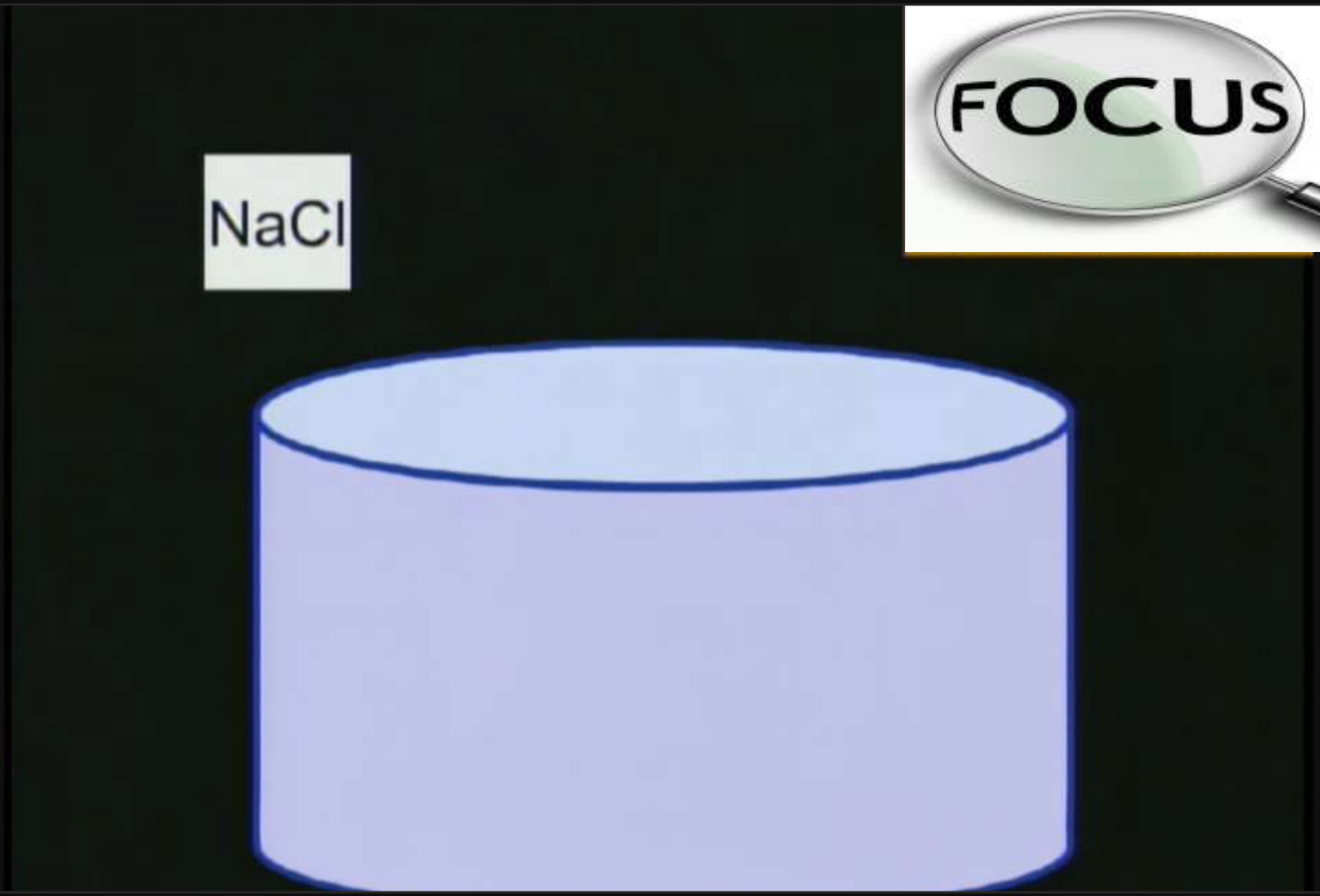
Weak vs. Strong

Beaker of water

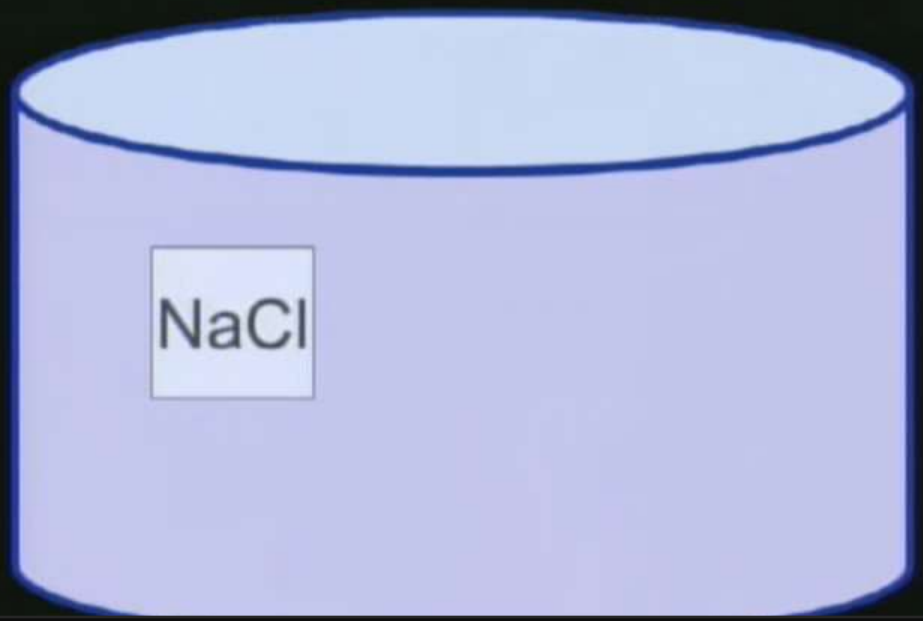


NaCl (Table salt)
White powder




FOCUS
NaCl

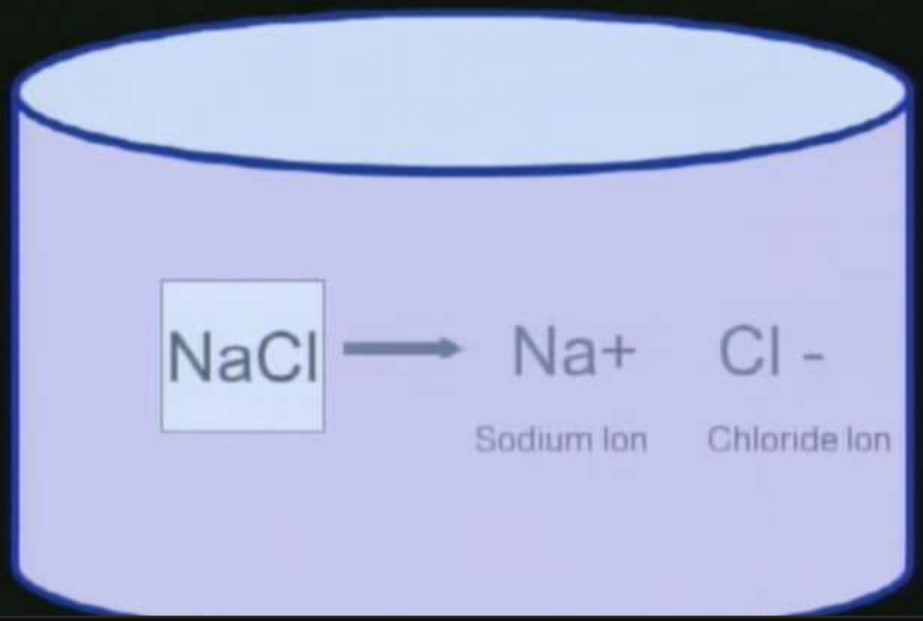

FOCUS


NaCl

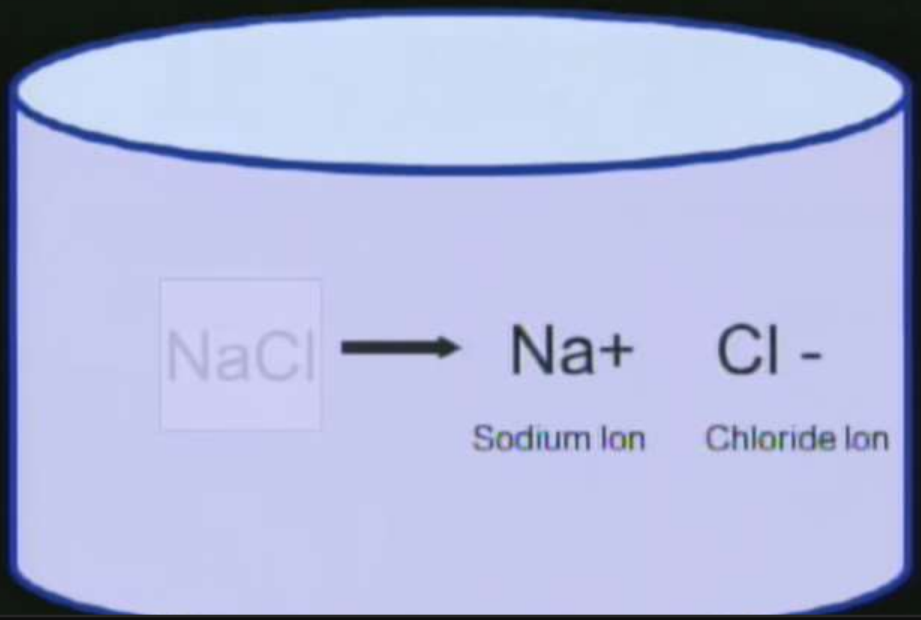

FOCUS


NaCl


FOCUS


NaCl
Na+
Sodium Ion
Cl -
Chloride Ion


FOCUS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Na+
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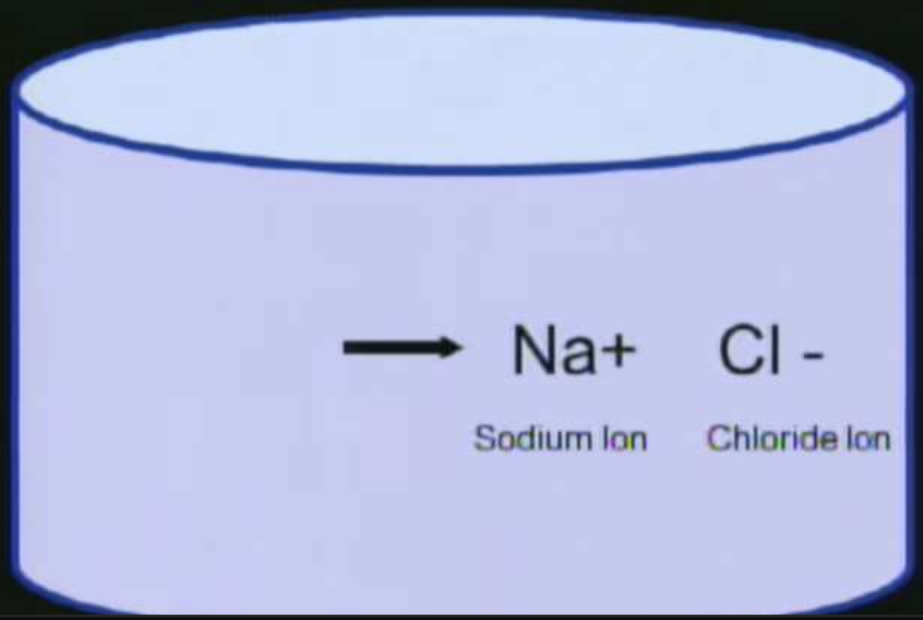
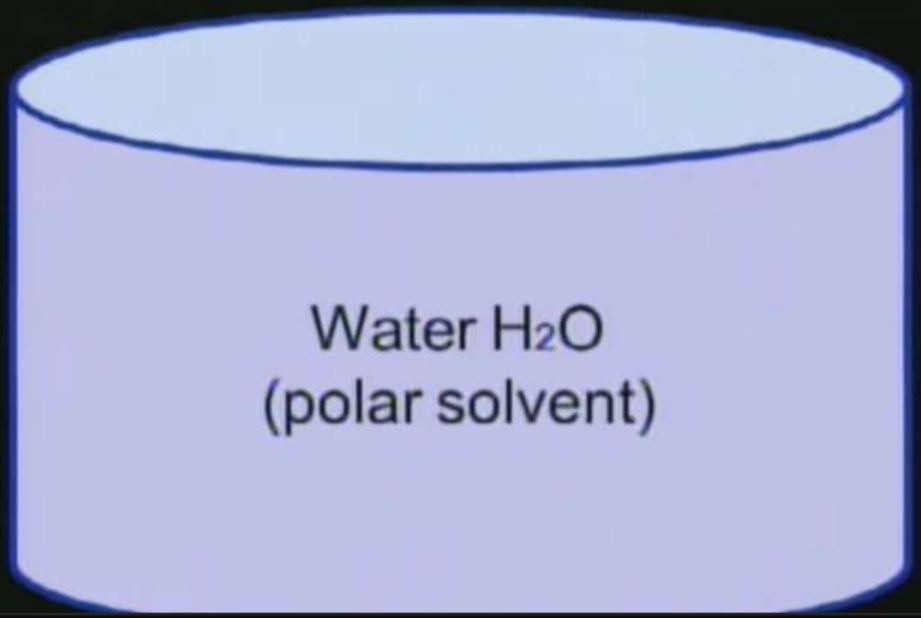

Na+
Cl -
Sodium Ion
Chloride Ion

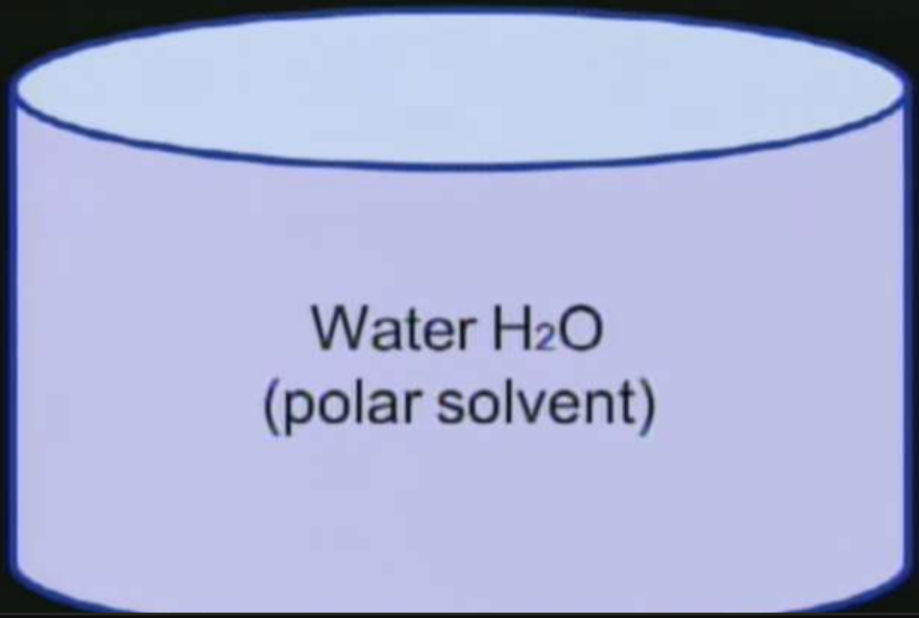
Stronger means more
Complete Dissociation

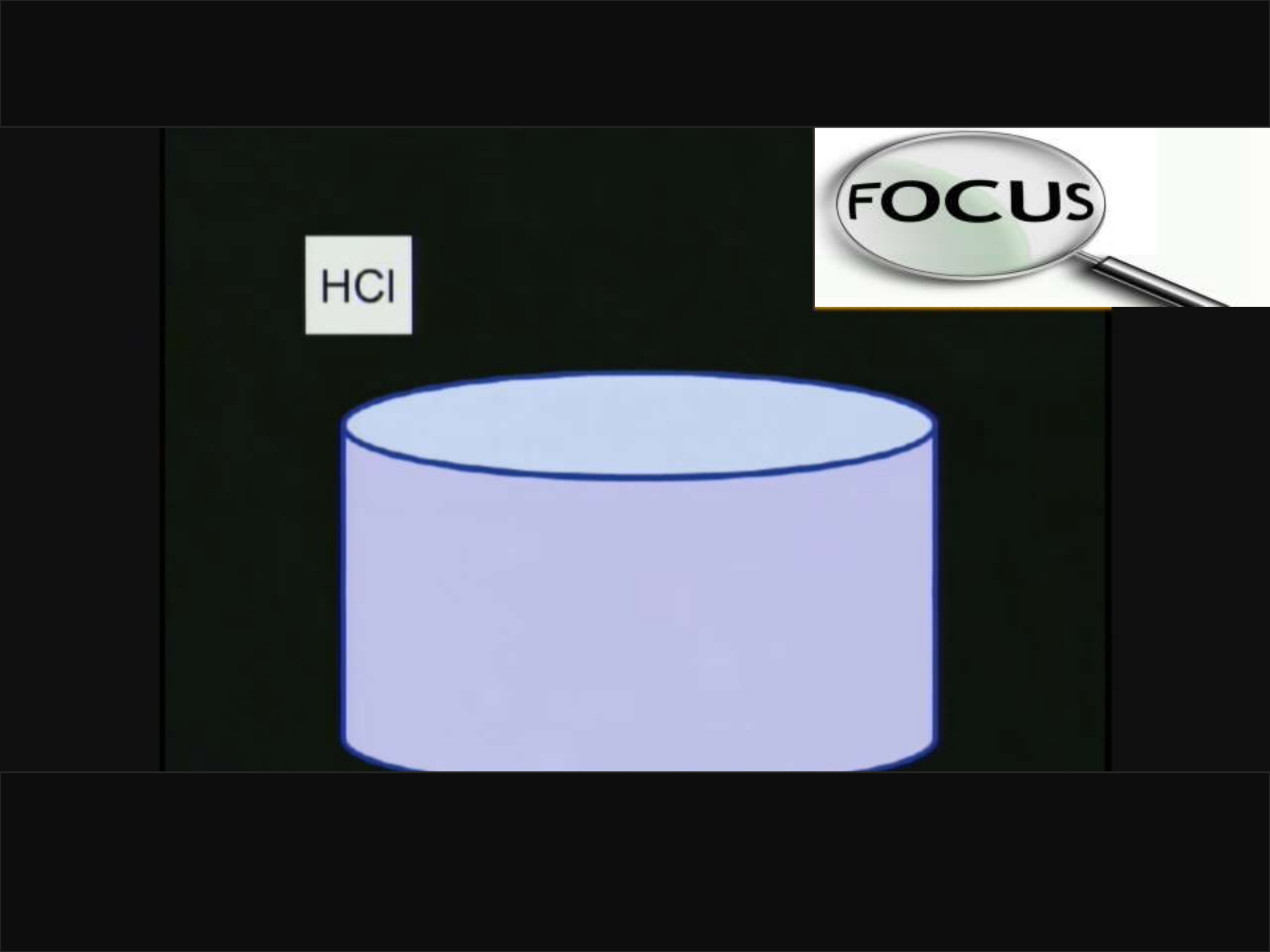
$$NaCl \longrightarrow Na^{+} \quad Cl^{-}$$

STRONG ACID

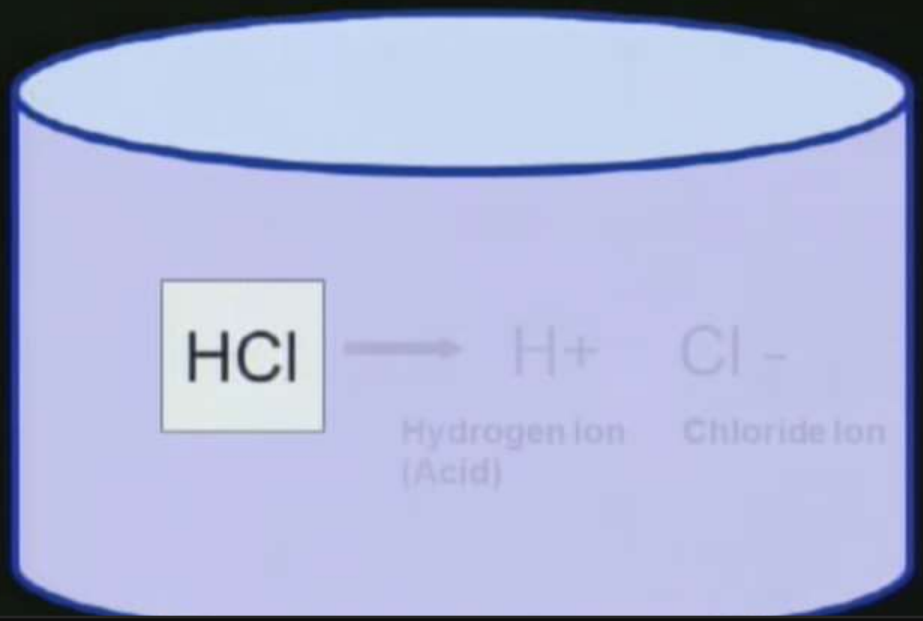


HCl (Hydrogen Chloride)
White powder

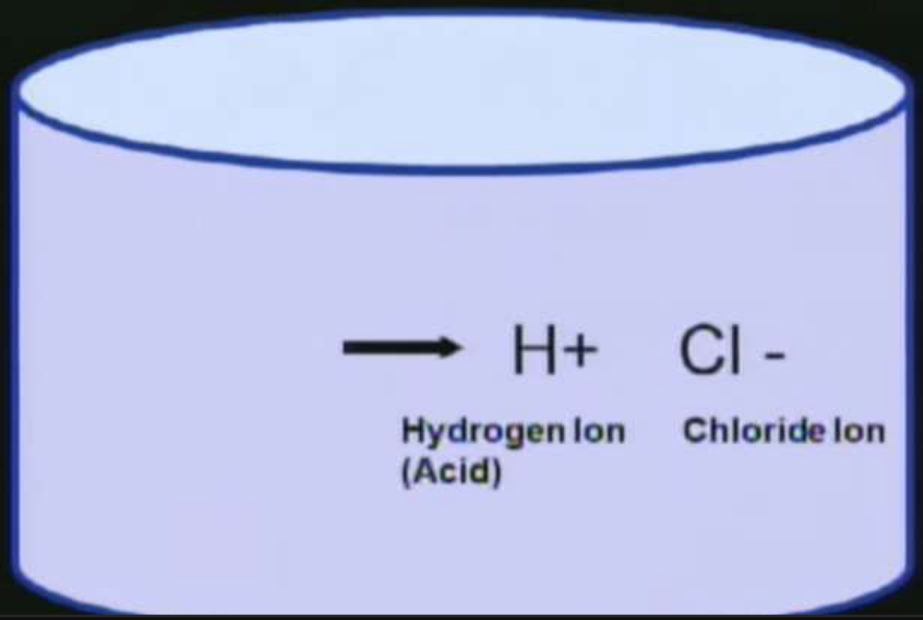



FOCUS
HCl


FOCUS


HCl
H+
Hydrogen ion
(Acid)
Cl -
Chloride ion


FOCUS

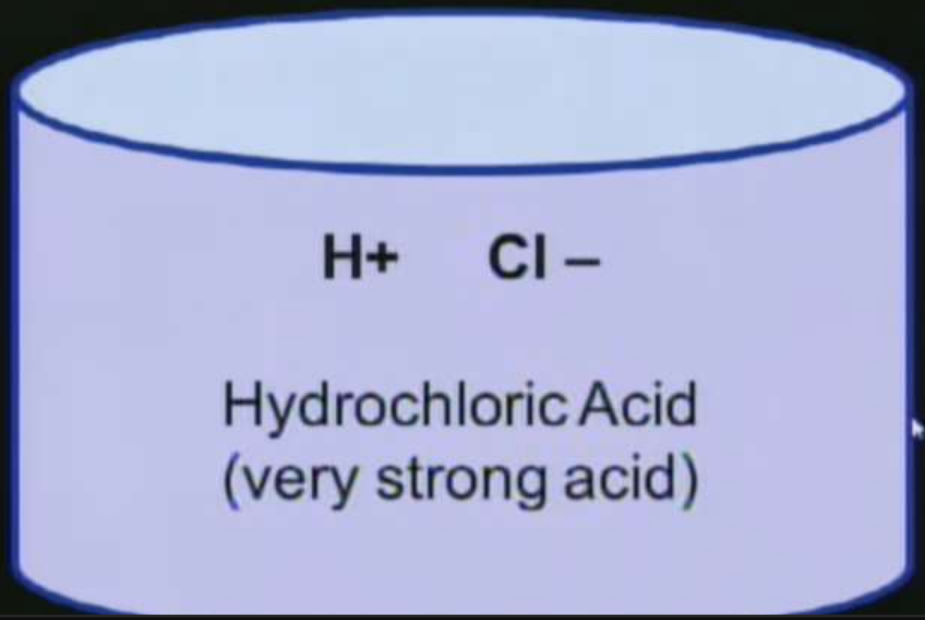

H+
Cl -
Hydrogen Ion
(Acid)
Chloride Ion

Stronger means more complete dissociation

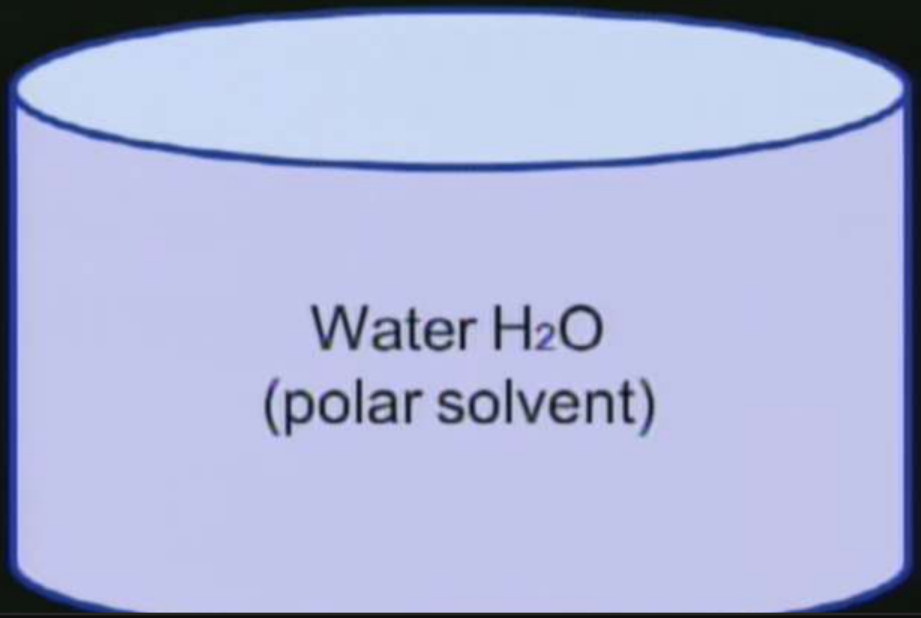
not how much it burns!

$$HCl \longrightarrow H^+ \quad Cl^-$$

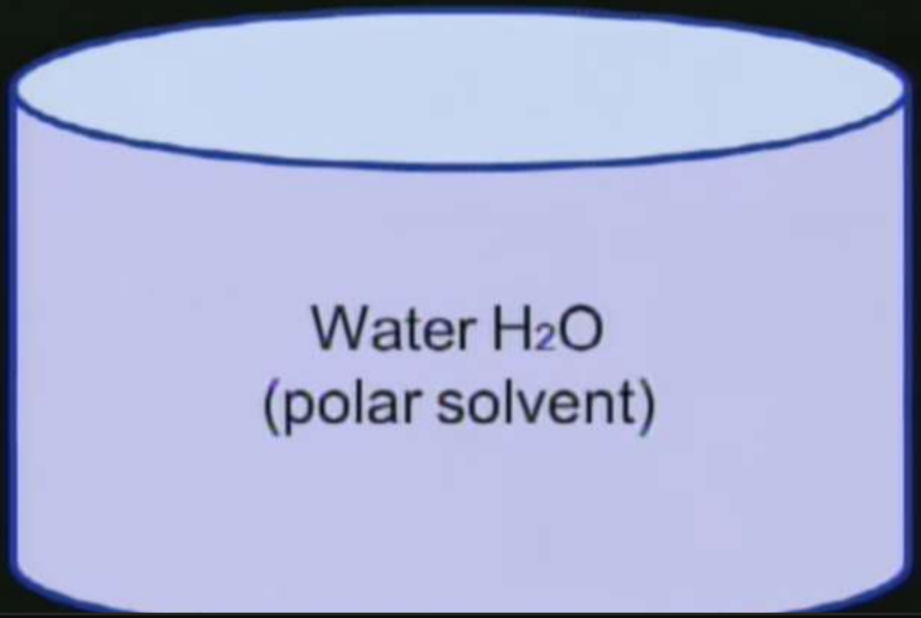

FOCUS

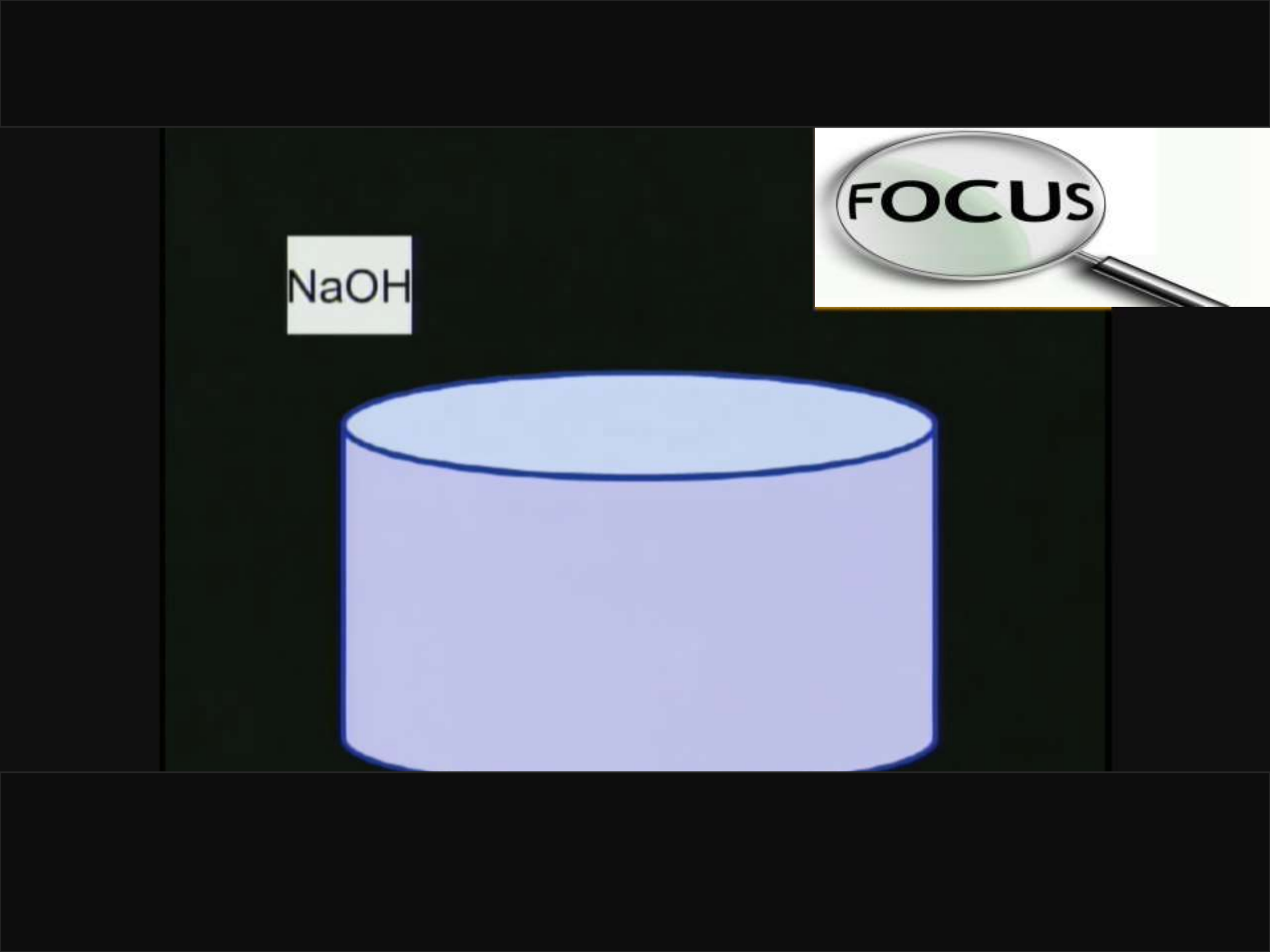

H+ Cl –
Hydrochloric Acid
(very strong acid)

STRONG BASE

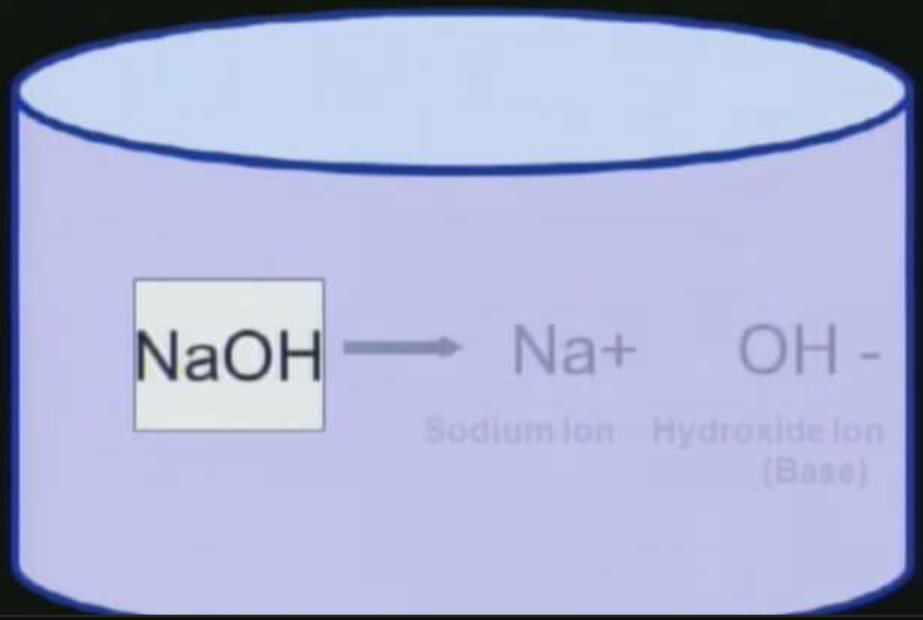


NaOH (Sodium Hydroxid
White powder

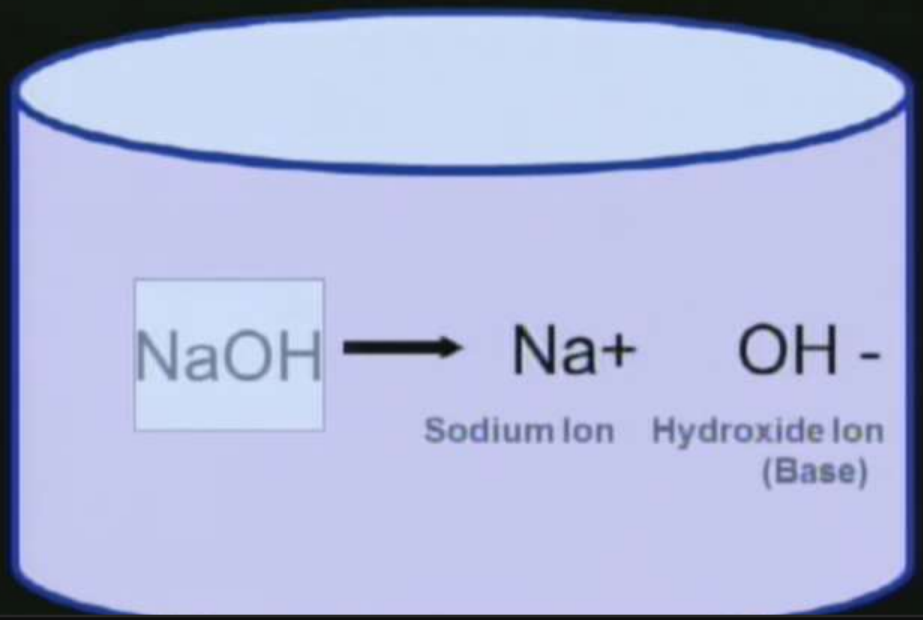



FOCUS
NaOH


FOCUS


NaOH
Na+
OH -
Sodium Ion
Hydroxide Ion
(Base)


FOCUS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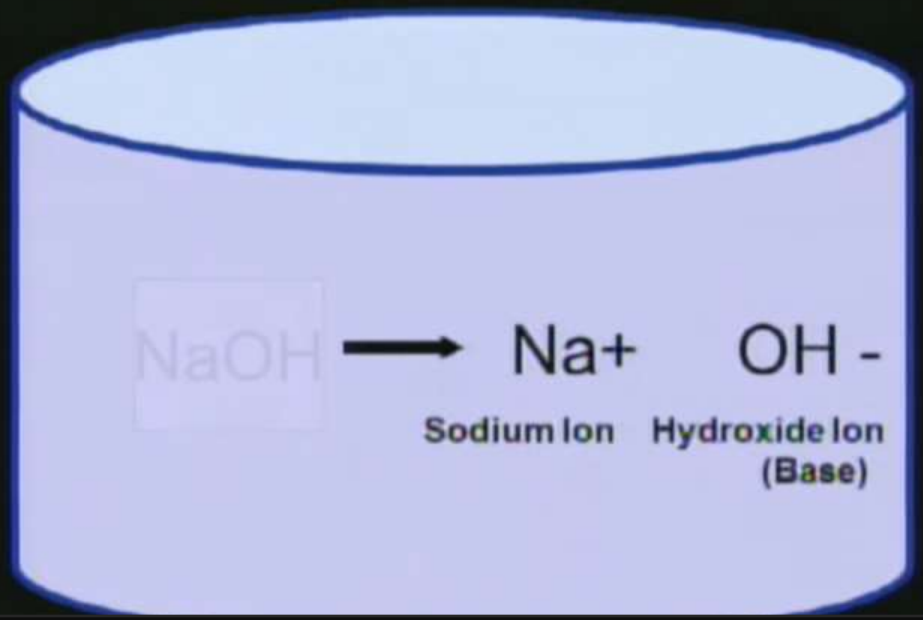
NaOH
Na+
OH -
Sodium Ion
Hydroxide Ion
(Base)

Stronger means more complete dissociation

not how much it burns!

$$NaOH \longrightarrow Na^+ + OH^-$$


To be continued