Introduction to Biopharmaceutics Absorption

For Class- B.Pharmacy 6th Semester

Subject- BIOPHARMACEUTICS AND PHARMACOKINETICS (BP604T)

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Introduction

Study of physicochemical properties of drugs & dosage forms and affects of routes of administration on the rate and extent of drug absorption.

Thus, biopharmaceutical factors influence the

- Protection and stability of the drug within the product
- Rate of drug release from the product
- Rate of dissolution of the drug at the absorption site
- Availability of the drug at its site of action

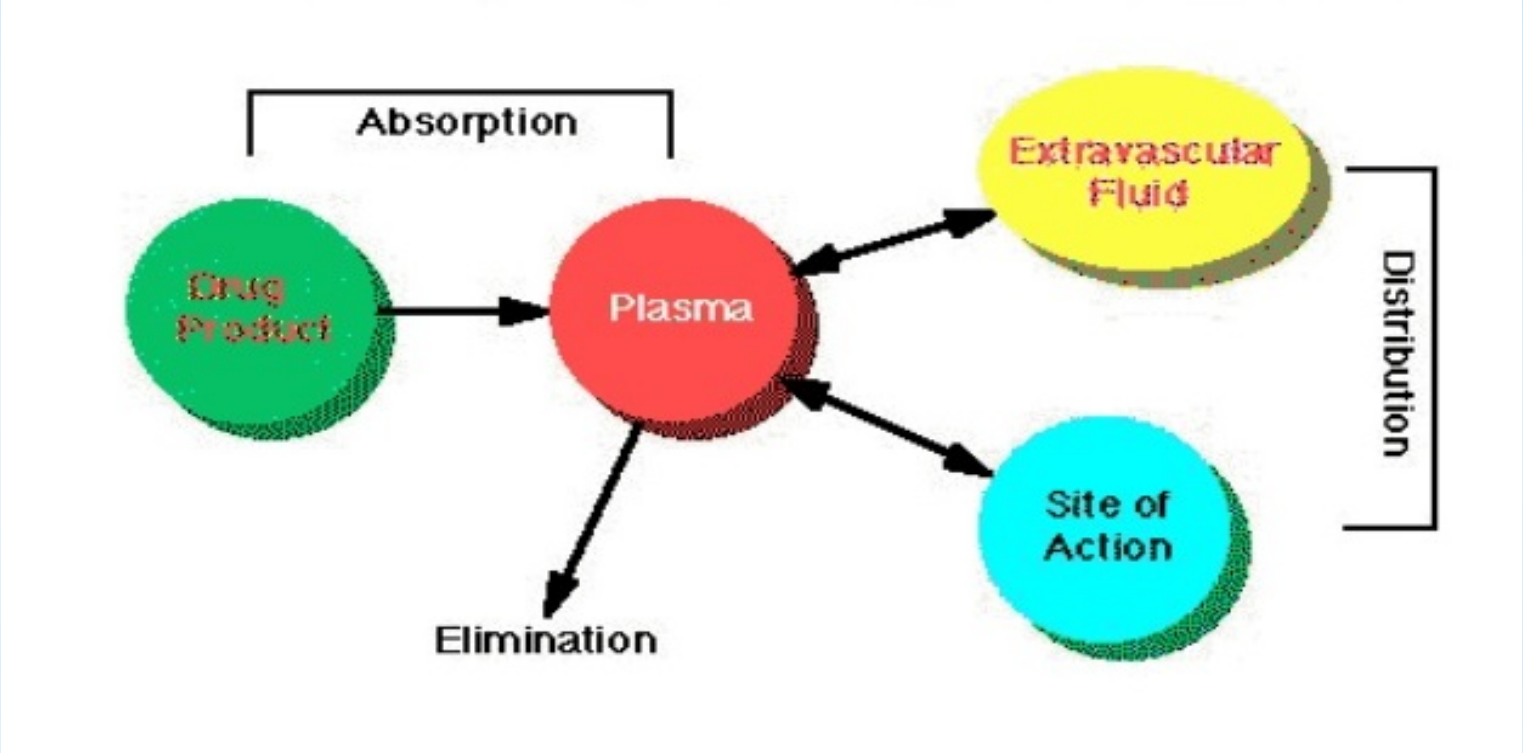


Figure- Schematic representation of the dynamic relationships between the drug, the product and pharmacologic effect.

ADME Process

Blood concentration of a drug are the result of four simultaneously occurring processes:

* Absorption
* Distribution
* Metabolism
* Excretion
* Besides the ADME process, an important factor of drug concentration is how drugs move through biological membranes by diffusion.

Absorption

Once a drug is released from its dosage formulation, the process that transfers it into the blood is called **absorption.**

One of the primary factors affecting **oral** drug absorption is the **gastric emptying time.**

* This the time that the drug remains in the stomach before it is emptied into the small intestine
* Most absorption occurs in the small intestine.
* Some factors increase the gastric emptying time, but most slow it.
* If a drug remains in the stomach too long, it can be degraded or destroyed, and its effect decreased.

Distribution

* Blood carries the drug throughout the body and to its sites of action.
* Drugs are rapidly distributed to organs having high blood flow rates such as the heart, liver and kidneys.
* Distribution to the muscle, fat, and skin is slower because they have lower blood flow rates.

Metabolism

* Drug metabolism refers to the body's process of transforming drugs.
* The transformed drug is called a **metabolite**.
* The primary site of drug metabolism is in the liver.
* When transformed in the liver a drug is broken down into inactive or active molecules. Inactive are excreted through the kidneys and active produce effects and excreted later.

Excretion

* Most drugs are excreted in the urine by the kidneys. The functional unit of the kidney is the **nephron**.
* Some oral drugs that are difficult to break down can be excreted in the feces (poop).
* The job of the kidney is to filter the blood and remove waste products.

MECHANISM OF DRUG ABSORPTION

- Passive diffusion
- Pore transport
- Carrier- mediated transport

*a) Facilitated diffusion

*b) Active transport

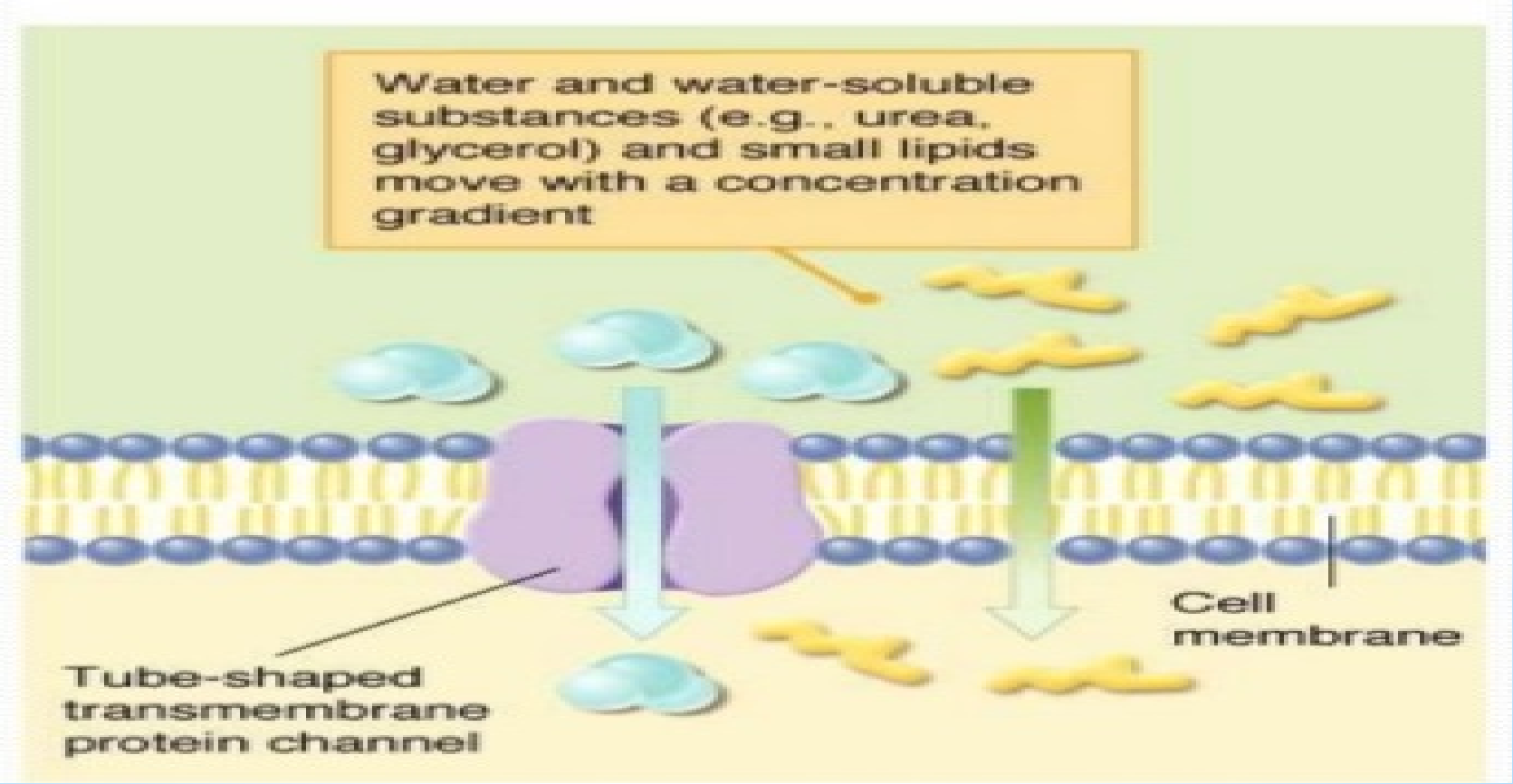
- Ionic or Electrochemical diffusion
- Ion-pair transport
- Endocytosis

Passive Diffusion

- Also known as non-ionic diffusion.
- It is defined as the difference in the drug concentration on either side of the membrane.
- Absorption of 90% of drugs.
- The driving force for this process is the concentration or electrochemical gradient.
- Passive diffusion is best expressed by Fick's first law of diffusion which states that the drug molecules diffuse from a region of higher concentration to one of lower concentration until equilibrium is attained & the rate of diffusion is directly proportional to the concentration gradient across the membrane.

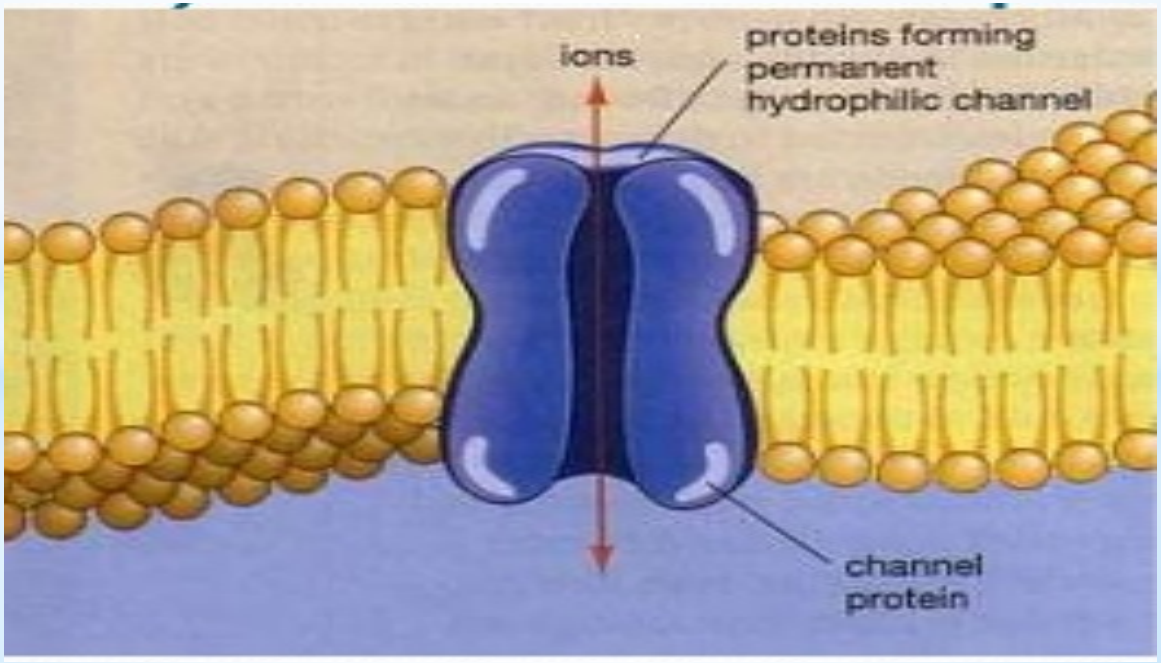
$$dQ/dt = D\ A\ Km/w/h\ (CGIT - C)$$

Passive Diffusion



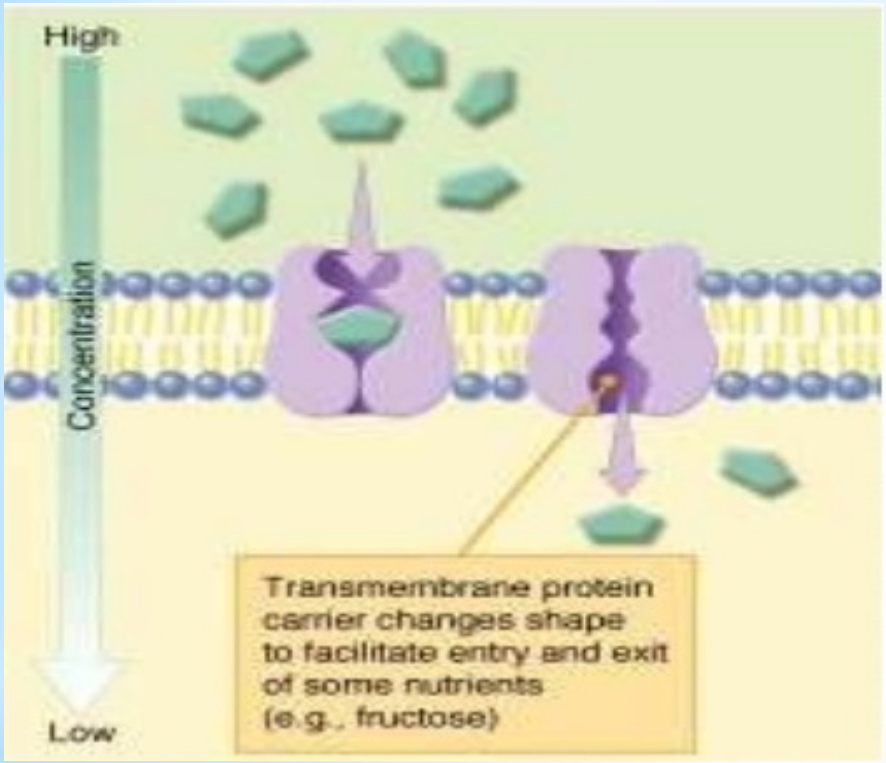
Pore transport

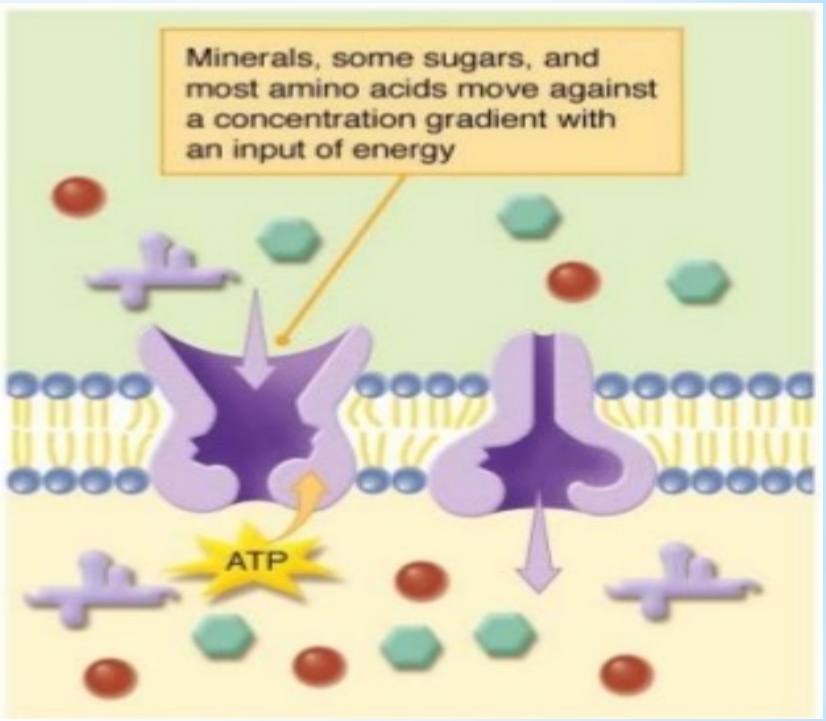
- It is convective transport, bulk flow or filtration.
- Important in the absorption of low mol. wt., low mol. size & generally water-soluble drugs e.g. urea, water & sugars.
- The driving force for the passage of the drugs is the hydrostatic or the osmotic pressure



Carrier Mediated System

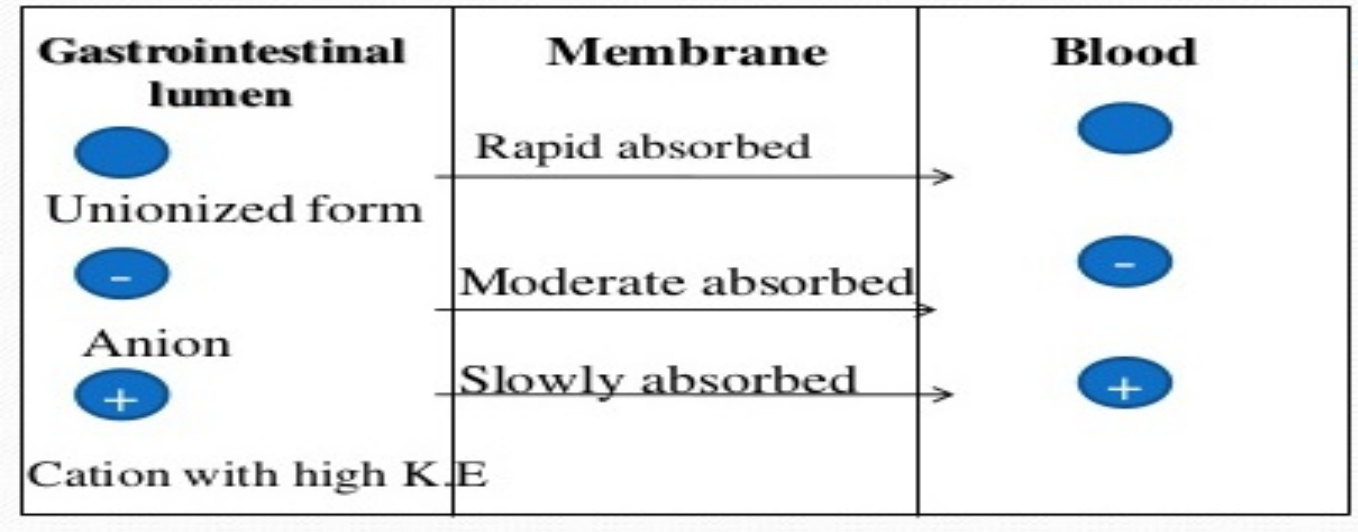
- Involves a carrier which binds reversibly with the solute molecules to be transported to yield the carrier solute complex which transverses across the membrane to the other side where it dissociates to yield the solute molecule
- The carrier then returns to its original site to accept a fresh molecule of solute.
- There are two types of carrier mediated transport system:
  - ✓ a) facilitated diffusion
  - ✓ b) active transport


High
Concentration
Low
Transmembrane protein carrier changes shape to facilitate entry and exit of some nutrients (e.g., fructose)

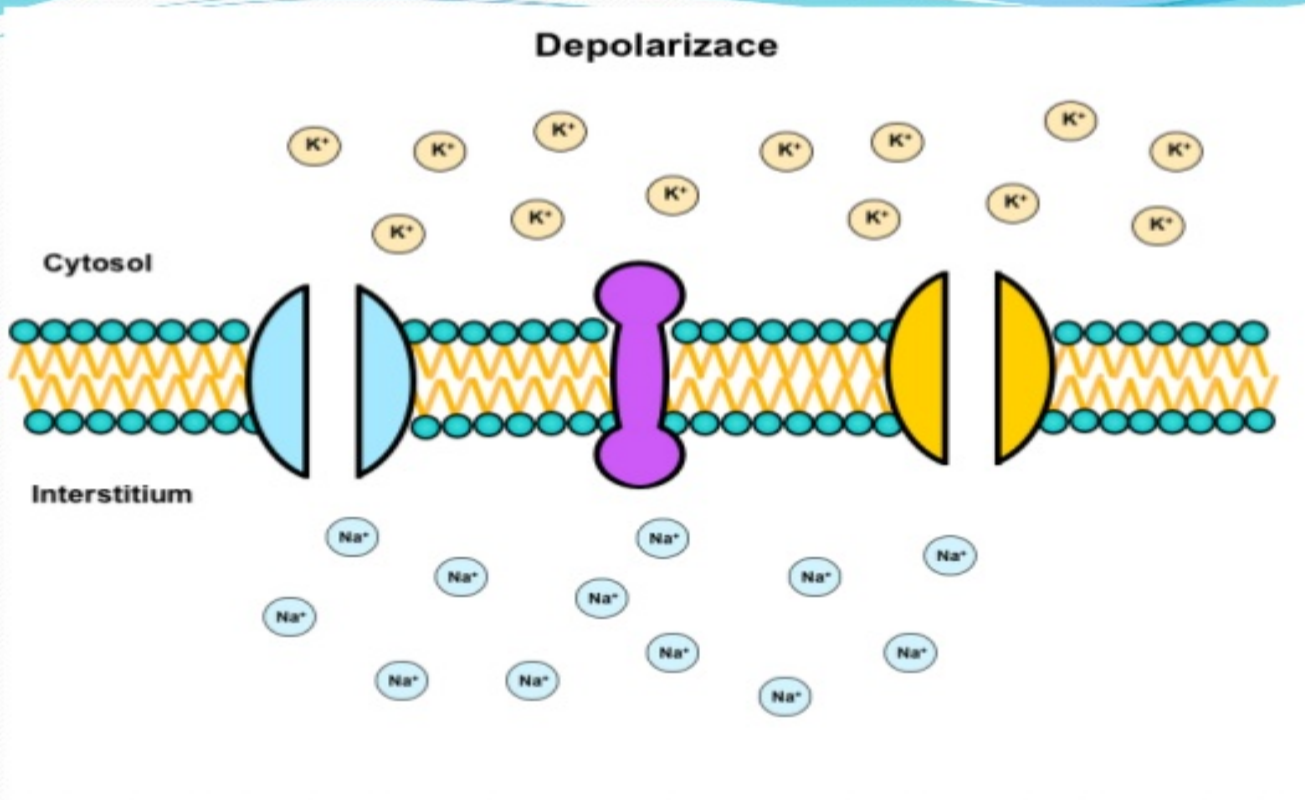

Minerals, some sugars, and most amino acids move against a concentration gradient with an input of energy
ATP

Ionic or electrochemical diffusion

- The charge on membrane influences the permeation of drugs.
- Molecular forms of solutes are unaffected by the membrane charge & permeate faster than cationic forms.
- Thus, at a given pH, the rate of permeation may be as follows: Unionized molecule > anions > cations



Ionic or electrochemical diffusion



Ion pair transport

- It is another mechanism is able to explain the absorption of such drugs which ionize at all pH condition.
- Transport of charged molecules due to the formation of a neutral complex with another charged molecule carrying an opposite charge.
- Drugs have low o/w partition coefficient values, yet these penetrate the membrane by forming reversible neutral complexes with endogenous ions. e.g. mucin of GIT.
- Such neutral complexes have both the required lipophilicity as well as aqueous solubility for passive diffusion. E.g. propranol

Endocytosis

- It involves engulfing extracellular materials within a segment of the cell membrane to form a saccule or a vesicle (hence also called as corpuscular or vesicular transport) which is then pinched off intracellular.
- Sometimes ,an endocytotic vesicle is transferred from one compartment to another. Such phenomenon is called transcytosis.
- Endocytosis includes two types of processes

✓ Phagocytosis

✓ pinocytosis