تفريغ بيوفارما

اسم الموضوع: Absorption

إعداد الصيدلاني/ـة: سارة سميح السبع

Soul Academy

لجان الدفعات

Drug absorption

Absorption

Main factors affecting oral absorption:

1. I Physiological factors. — جسم الانسان
2. II Physical-chemical factors. — طبيعة الدواء
3. III Formulation factors. — تصنيع الدواء + اضافات عليه

I Physiological factors affecting oral absorption:

1- Membrane physiology.

2- Passage of drugs across membranes. — مرور — عبر

3- Gastrointestinal physiology. — الجهاز الهضمي

I. Characteristics of GIT physiology and drug absorption — خصائص — PH

II. Gastric emptying time and motility — وقت افراغ المعدة — حركتها

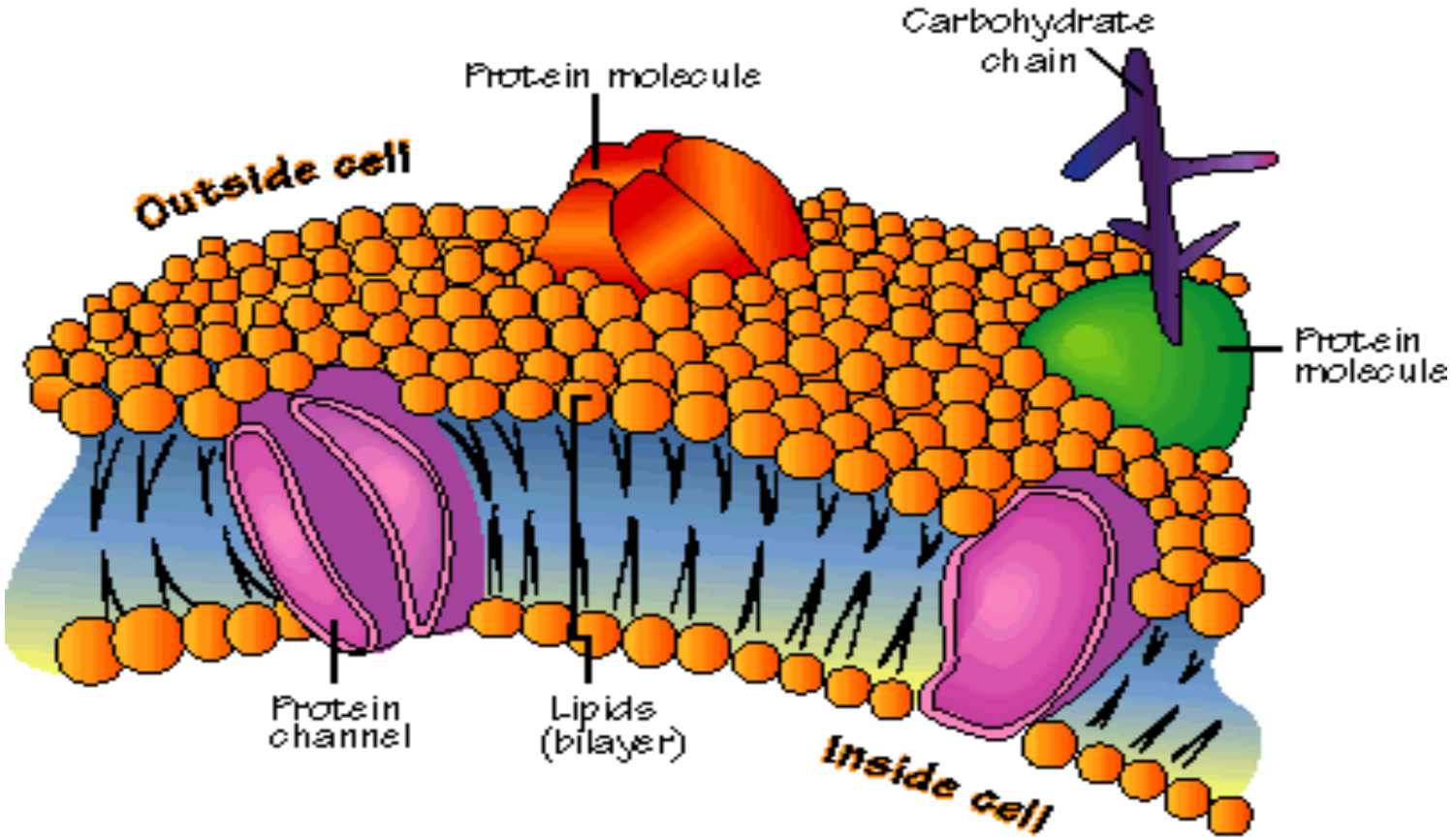
III. Effect of food on drug absorption — تأثير — مثل شاي هو دواء الحديد — حسب طبيعة الغذاء يصل تسريع أو إبطاء الامتصاص مثل الحليب + الحديد

عضو الامتصاص الرئيسي في GI هي small intestine

حسب نوع الأكل + اذا بضل بالمعدة فترة طويلة أو لا

Physiological factors influencing bioavailability

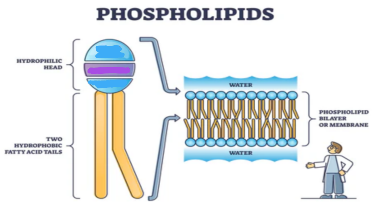
1- Membrane physiology:



1- Membrane physiology

- The cell membrane is the barrier that separates the inside of the cell from the outside.

- The cell membrane is made up of phospholipids, proteins, and other macromolecules.



- The phosopholipids make up a bilayer. It contains hydrophilic and hydrophobic molecules.

- The proteins in the cell membrane are located within the phospholipid bilayer.

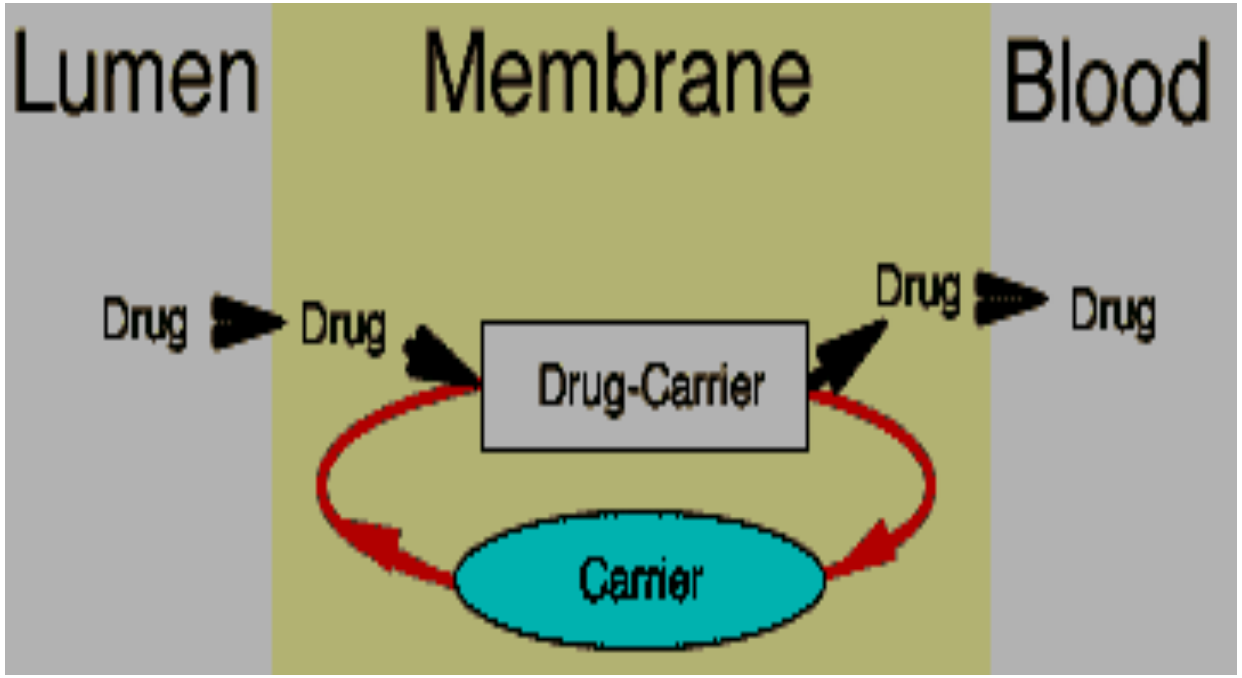
What is nature of biologic membrane?

- So, the biologic membrane is mainly lipid in nature but contains small aqueous channels or pores.

2-Passage of drugs across membranes

2- Transport across the membranes:

1- Carrier mediated:



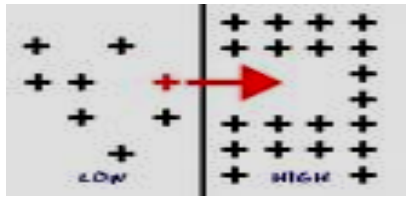
حفظ الأمثلة

2-Transport across the membranes

A- Active transport:

- A few lipid-insoluble drugs (e.g.5-flurouracil, L-dopa) that resemble (تشبه) natural physiologic metabolites (e.g. glucose, amino acids) are absorbed from the GIT by this process.

- Transport of a drug against concentration gradient (from regions of low drug concentrations to regions of high concentrations).

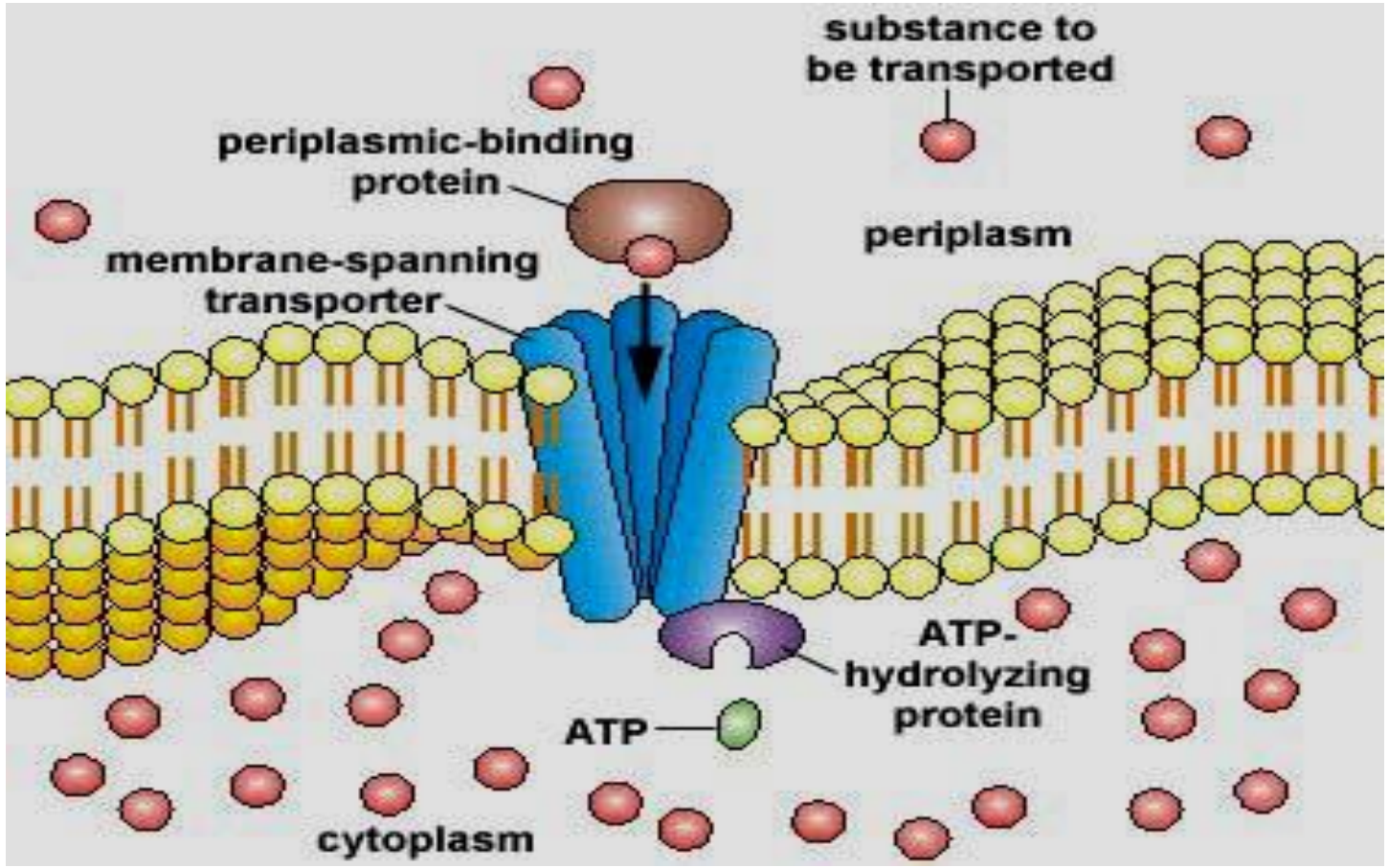


- It is an energy-consuming (مستهلك) system.

- The carrier molecule may be highly selective (انتقائي) for the drug molecule, therefore, drugs of similar structure may compete (تتنافس) for sites of adsorption (الارتباط) on the carrier (competitive inhibition is possible)

- Because only a certain amount of carrier is available (متوفرة), all the adsorption sites on the carrier may become saturated if the drug concentration gets very high.

2-Transport across the membranes



2-Transport across the membranes

تتشابه مع الـ active انها بدها Carryer + Saturable

تتشابه مع passive انها ما بدها طاقة

B- Facilitated diffusion:

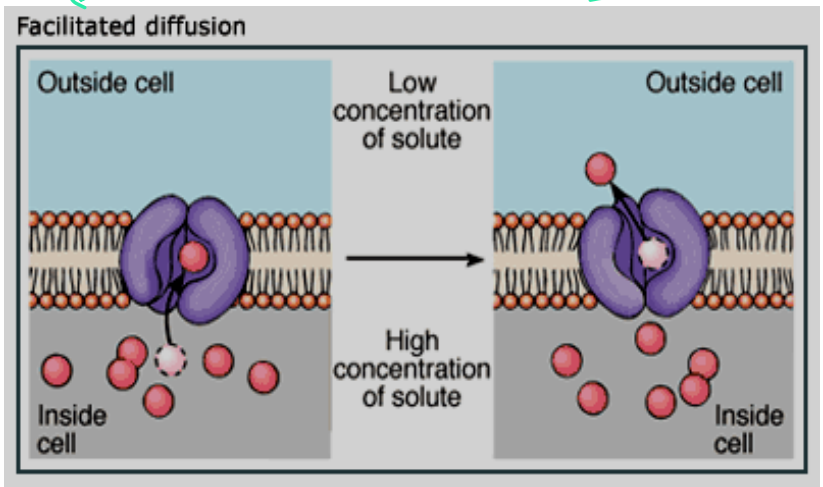
- Play a very minor role in absorption.

- A drug carrier is required but no energy is necessary. e.g. vitamin B12 transport.

- Saturable if not enough carrier and structurally selective for the drug and shows competition kinetics for drugs of similar structure.

- No transport against a concentration gradient only downhill but faster.

الى أسفل (يعني بنقل من اعلى تركيز لأقل تركيز)



مش مطلوب ولكن لزيادة الفهم

نشر الميسر

الانتشار الميسر يشبه الانتشار السلبي باستثناء أن البروتينات الحاملة المضمنة في الطبقة الثنائية للغشاء تسهل نقل المواد الكيميائية عبر الغشاء. فإن حركة المواد الكيميائية عبر الأغشية تكون من جانب التركيز العالي إلى جانب التركيز المنخفض دون إنفاق طاقة خلوية. الانتشار الميسر خاص إلى حد ما بالمواد الكيميائية القادرة على الارتباط ببروتين حامل. يحدث امتصاص العناصر الغذائية مثل الجلوكوز والأحماض الأمينية عبر الغشاء الظهاري للجهاز الهضمي عن طريق الانتشار الميسر. ونظرًا لأن عددًا محدودًا من البروتينات الحاملة متاح للنقل، فإن العملية قابلة للتشبع عند تركيزات عالية من المواد الكيميائية وقد يحدث التنافس على النقل بين جزيئات ذات بنية مماثلة.

2-Transport across the membranes

C- P-glycoprotein:

- P-glycoprotein transporters (PGP) are present throughout the body including liver, brain, kidney and the intestinal tract epithelia.

- Act as reverse pump generally inhibiting absorption.

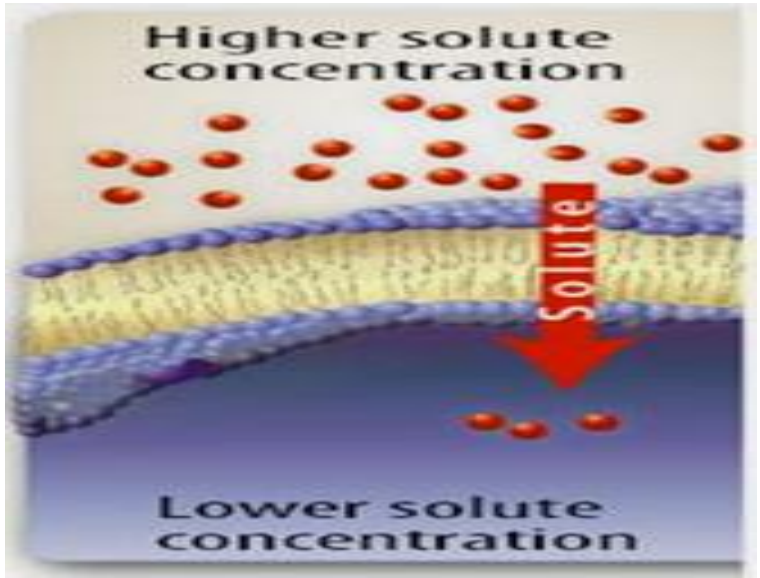
- This is an active, ATP-dependent process.

يطلعوا
عكس الامتصاص
(يطلعوا الدواء)

2-Transport across the membranes

2- Passive diffusion:

- Most drugs cross biologic membranes by passive diffusion.
- Diffusion occurs when the drug concentration on one side of the membrane is higher than that on the other side.
- The process is passive because no external energy is expended.
- The driving force for passive diffusion is the difference in drug concentrations on either side of the cell membrane.



2-Transport across the membrane

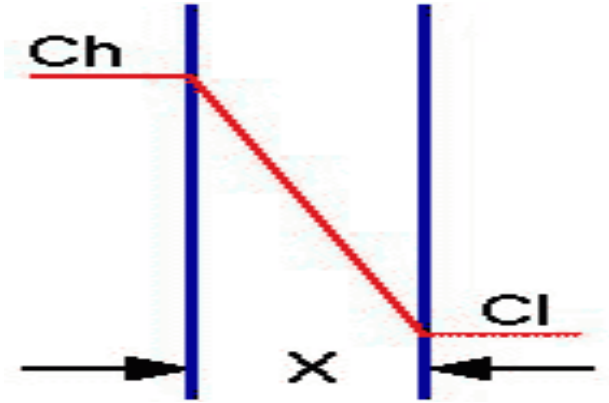


Diagram of Passive Transport with a Concentration Gradient

-The rate of transport of drug across the membrane can be described by Fick's first law of diffusion:-

أن اتجاه الانتشار عكس اتجاه زيادة التركيز

Fick's First Law, Rate of Diffusion

$$\text{Rate of diffusion} = \frac{dM}{dt} = -\frac{D \bullet A \bullet (Ch - Cl)}{x}$$

$\frac{dM}{dt}$ ← تغير في الكتلة

$\frac{dM}{dt}$ ← التغير بالزمن

2-Transport across the membranes

- The parameters of this equation are:-

D: diffusion coefficient. This parameter is related to the size and lipid solubility of the drug and the viscosity of the diffusion medium.

As lipid solubility increases or molecular size decreases then D increases and thus dM/dt also increases.

A: surface area. As the surface area increases the rate of diffusion also increase.

بطانة الأمعاء

The surface of the intestinal lining (with villae and microvillae) is much larger than the stomach. This is one reason absorption is generally faster from the intestine compared with absorption from the stomach.

2-Transport across the membranes

x: membrane thickness. The smaller the membrane thickness the quicker the diffusion process. As one example, the membrane in the lung is quite thin thus inhalation absorption can be quite rapid.

أسرع

جدًا

(Ch -Cl): concentration difference.

فرق

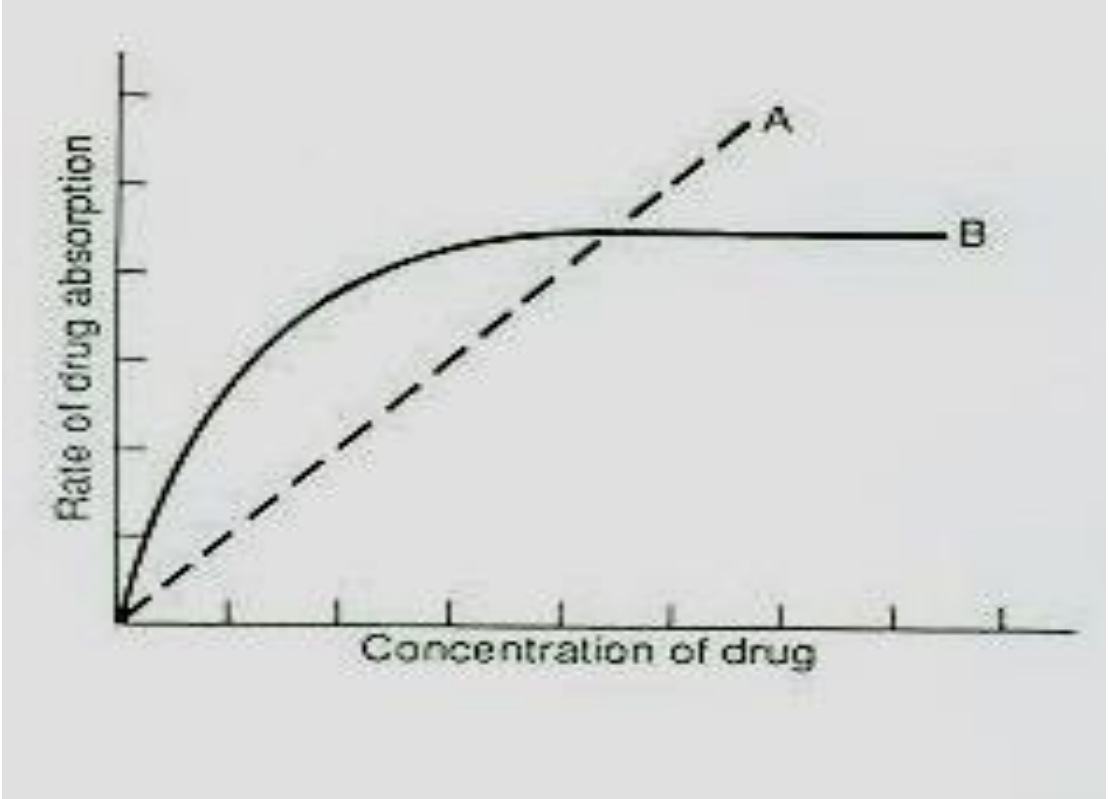
The drug concentration in blood or plasma will be quite low compared with the concentration in the GI tract. It is this concentration gradient which allows the rapid complete absorption of many drug substances.

- Normally Cl << Ch then:-

$$\frac{dM}{dt} = -\frac{D \bullet A \bullet Ch}{x}$$

constant, ka

2-Transport across the membranes



Relationship between drug concentration and absorption rate For a passive process (Curve A) and for a carrier-mediated Process (Curve B).

2-Transport across the membranes

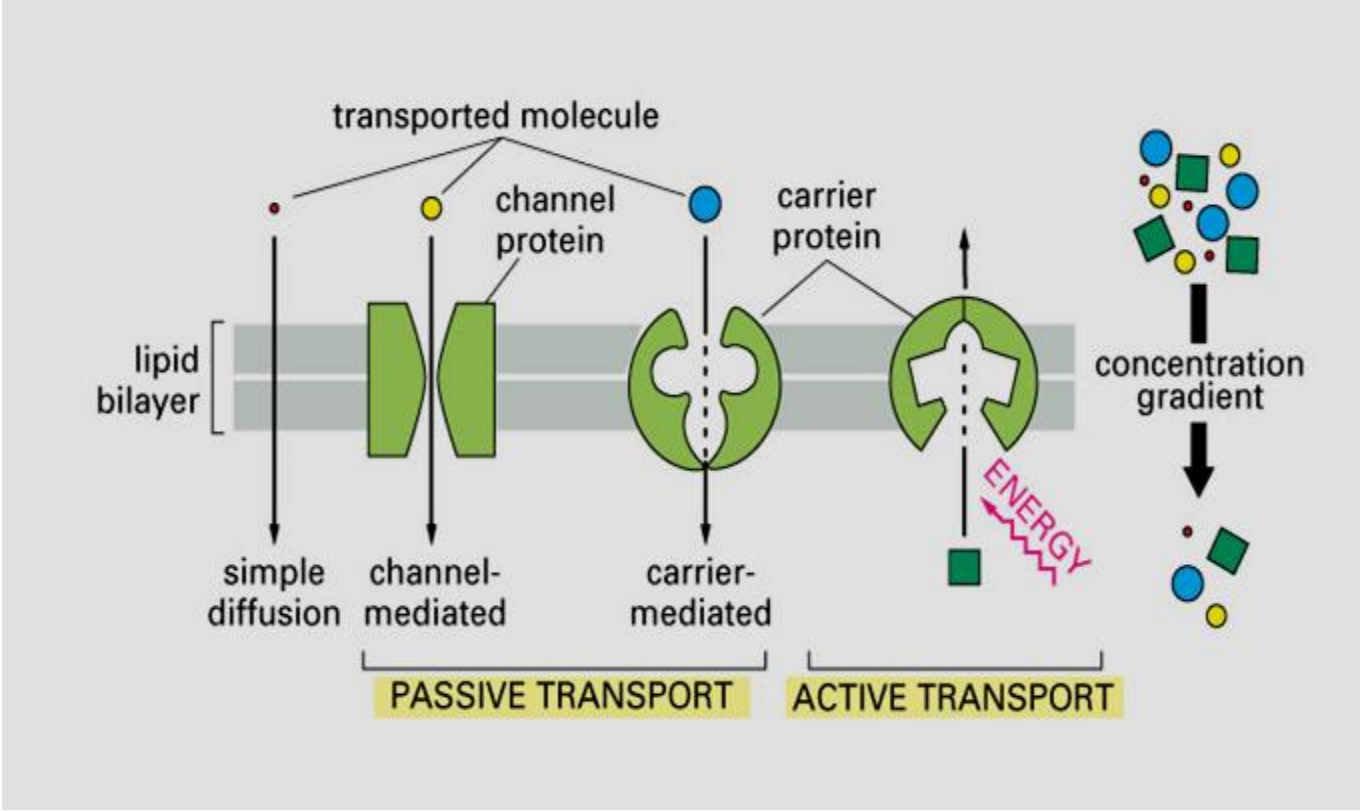


Illustration of Different Transport Mechanisms

2-Transport across the membranes

3- Vesicular transport:

- It is the process of engulfing particles or dissolved materials by the cell.

- Pinocytosis and phagocytosis are forms of vesicular transport that differ by the type of material ingested.

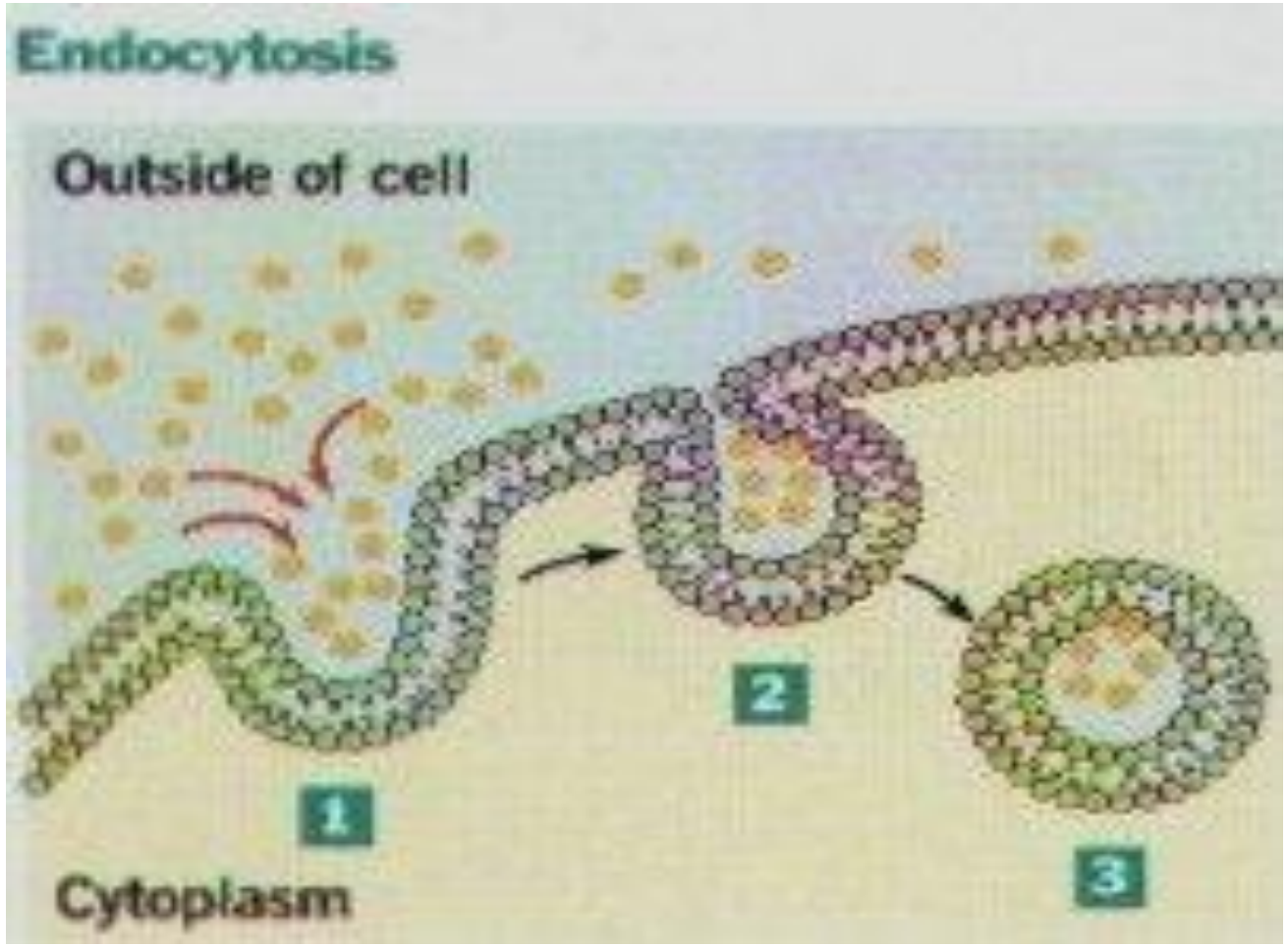
Pinocytosis: refers to the engulfment of small molecules or fluid.

Phagocytosis: refers to the engulfment of larger particles or macromolecules.

- During pinocytosis or phagocytosis, the cell membrane invaginates to surround the material, and then engulfs the material into the cell. Subsequently, the cell membrane containing the material forms a vesicle or vacuole within the cell.

- Vesicular transport is the proposed process for the absorption of Vitamin A, D, E, and K, peptides in new born.

2-Transport across the membranes



2-Transport across the membranes

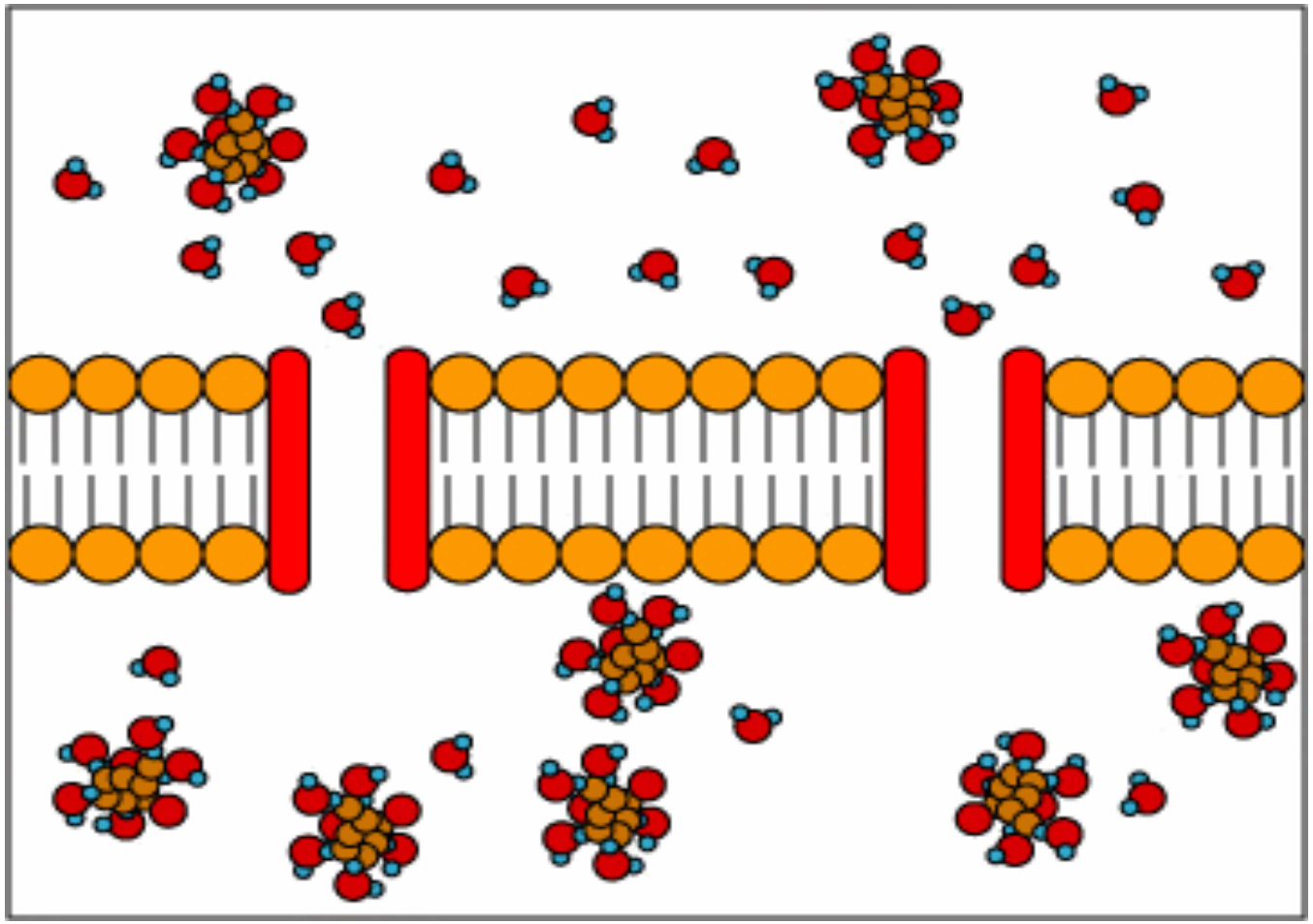
4- Pore (convective) transport:

- A certain type of protein called transport protein may form an open channel across the lipid membrane of the cell.
- Very small molecules, such as urea, water and sugars are able to rapidly cross the cell membrane through these pores.

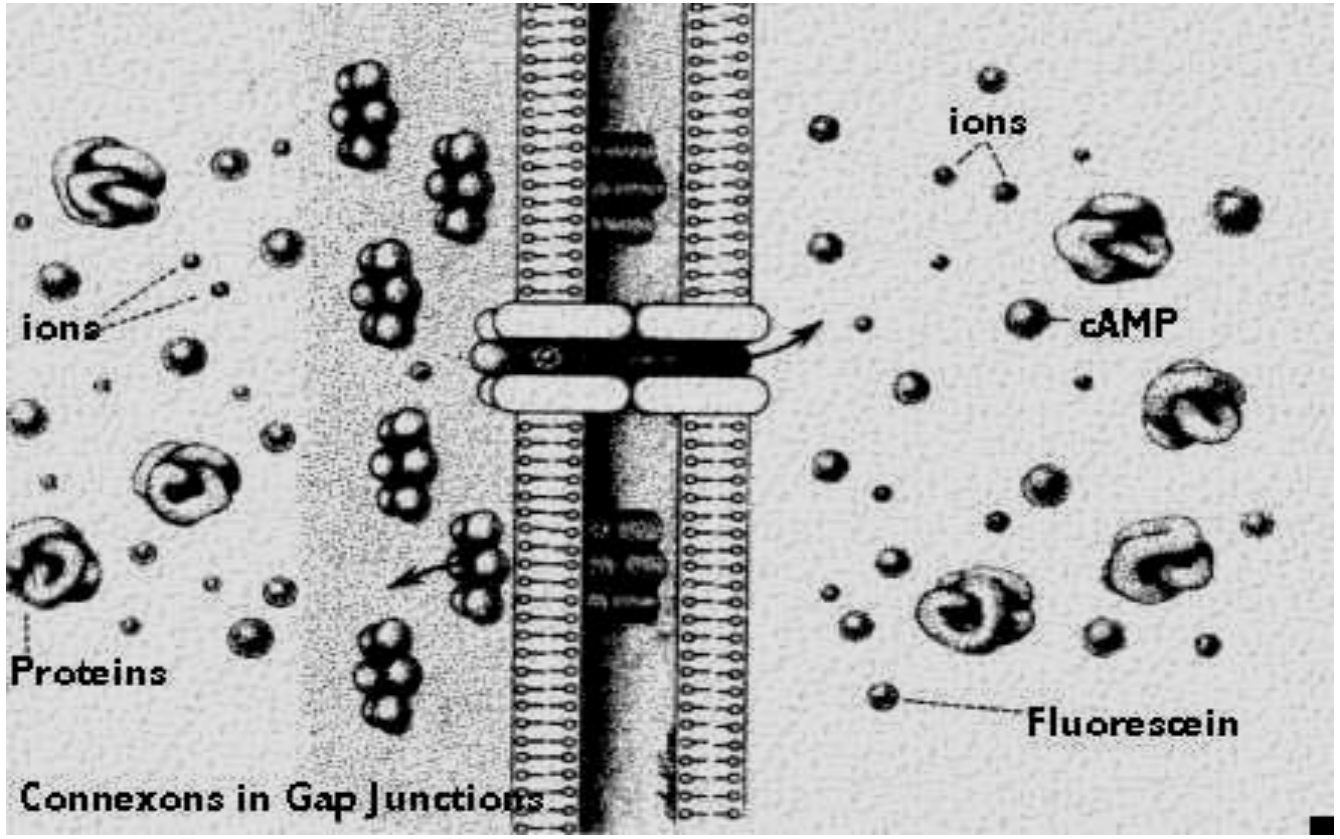
5- Ion pair formation:

- Strong electrolyte drugs are highly ionized or charged molecules, such as quaternary nitrogen compounds.
- These drugs penetrate membranes poorly. When linked up with an oppositely charged ion, an ion pair is formed in which the overall charge of the pair is neutral. This neutral complex diffuses more easily across the membrane.
- e.g. the formation of an ion pair for propranolol (basic drug) with oleic acid.

Transport of Substances Across a Membrane by Channel Proteins



2-Transport across the membranes



Mechanism of ion pair transport of drugs