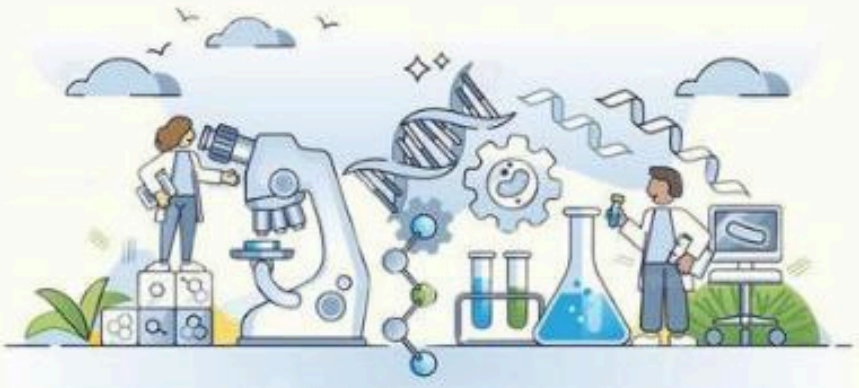
تفريغ بيوفارما



اسم الموضوع:

Drug Absorption part-1

إعداد الصيدلاني/ـة:

ليان شاهر

Soul Academy

لجان الدفعات

Drug absorption

Absorption

Main factors affecting oral absorption:

I Physiological factors.

II Physical-chemical factors.

III Formulation factors.

I Physiological factors affecting oral absorption:

1- Membrane physiology.

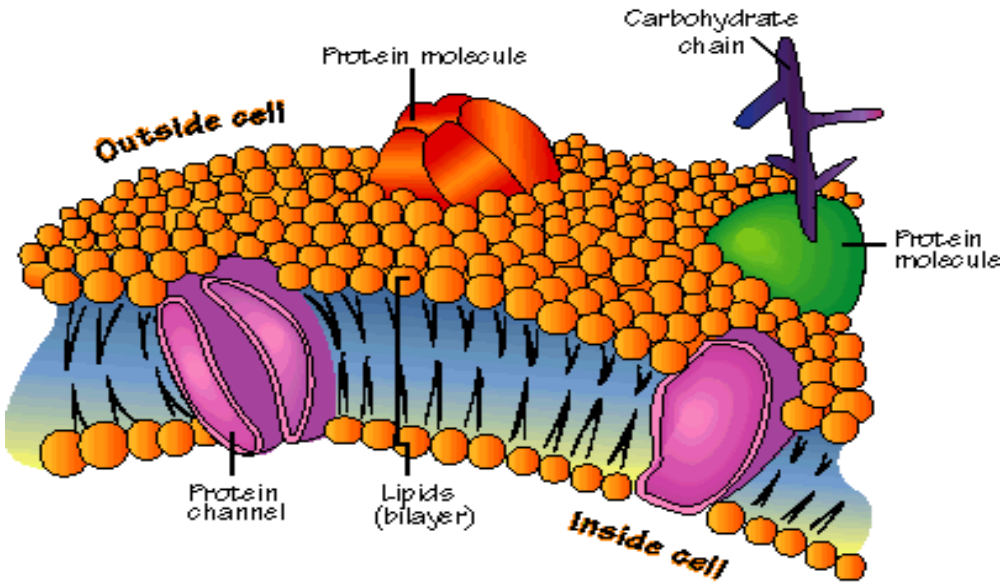
2- Passage of drugs across membranes.

3- Gastrointestinal physiology.

- Characteristics of GIT physiology and drug absorption
- Gastric emptying time and motility
- Effect of food on drug absorption

Physiological factors influencing bioavailability

1- Membrane physiology:



* هسا هون لازم نعرف انو الادوية , الدهنية اللي بتكون (lipid in nature) بتخترق ال membrane بسهولة لكن ادوية ال hydrophilic صعب تخترقه الا اذا حجمها صغير و عن طريق aqueous channels موجودة بـ membrane

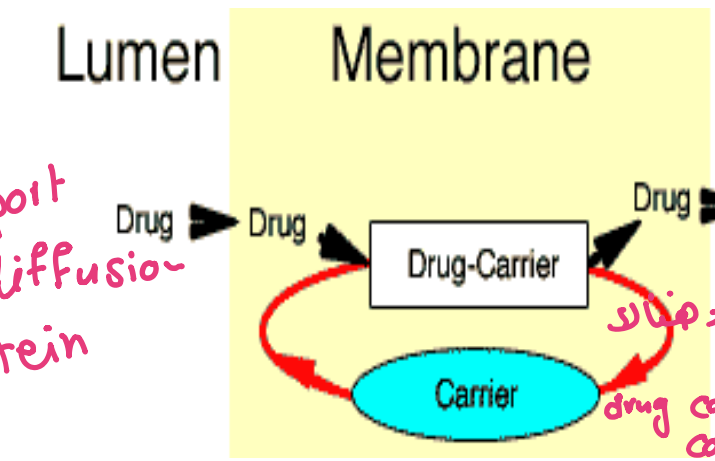
1- Membrane physiology

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

2-Passage of drugs across membranes

Transport across the membranes:

1- Carrier mediated:



هساهون عنا ٣ أنواع :

① active transport
② facilitated diffusion
③ P- glycoprotein

شرح لهاي الـ آلية

① الدوا موجود بـ G-Lumen زي الامعاء مثلاً

② بروح الدوا لـ epithelial cell في الامعاء وبرتبط بـ carrier موجود هناك

③ ارتباط الدواء بالناقل بكون drug carrier complex

④ الناقل بحمل الدوا للدم وهناك بصير release يعني (بفك الـ complex) والدوا بدخل للدم.

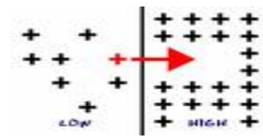
يعني بادخصار الدوا برتبط مع بروتين اللي هو ناقل وبدخل للدم.

2-Transport across the membranes

A- Active transport:

- A few lipid-insoluble drugs (e.g.5-flurouracil, L-dopa) that resemble 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).



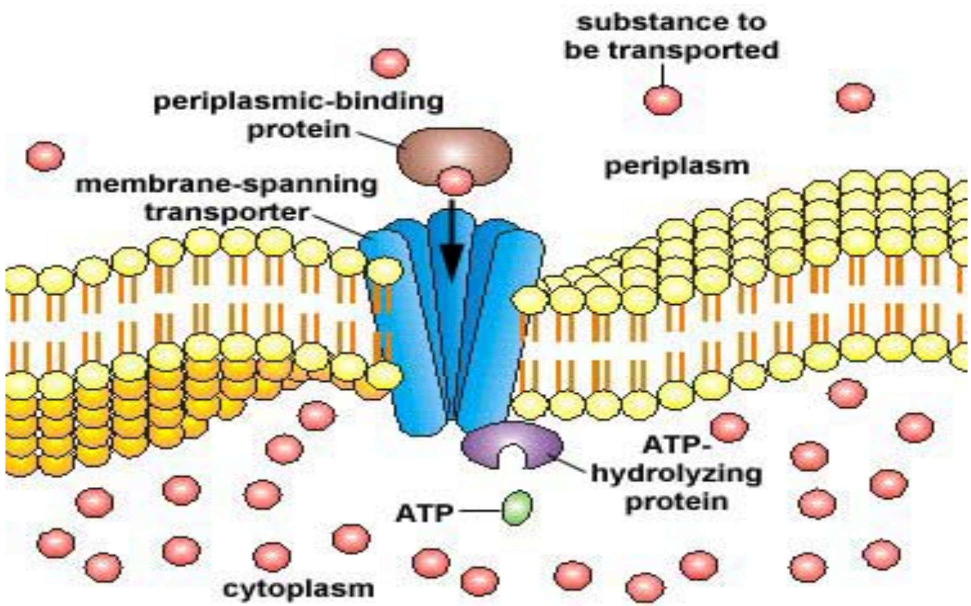
- It is an energy-consuming system.

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

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

2-Transport across the membranes

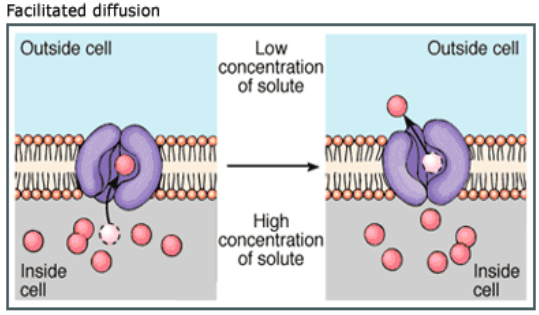
آخر معلومة فيه
اذا كان التركيز قليل
عادي بيصير واذا
كان عالي بيصير بيكون
الاستهلاك احسن
وهاي بس للـ Active
باقي الانواع عكس هيك



2-Transport across the membranes

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.



2-Transport across the membranes

هاي عبارة عن طريقة عكسية بتطرد
ما بتدخل مثل (anti cancer + antibacterial)
بكون عندي مقاومة لهدا وعين ....
اذا كانة شغال بيطل يشتغل بطلع ٢ ليات
بحيث بس يدخل واحد
ليطردو لبرا .

C- P-glycoprotein:

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

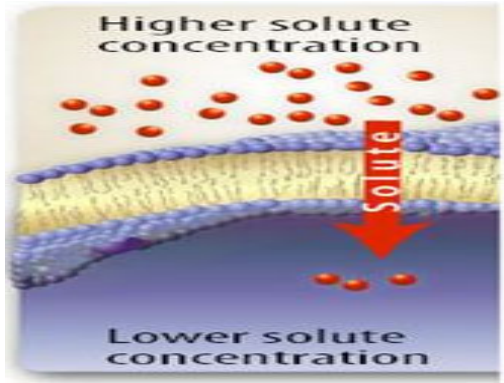
- Act as reverse pump generally inhibiting absorption.

- This is an active, ATP-dependent process.

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

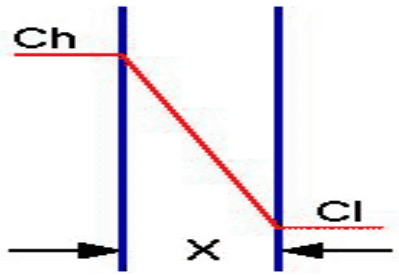


Diagram of Passive Transport with a Concentration Gradient

-The

be

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

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.

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.

(Ch -Cl): concentration difference.

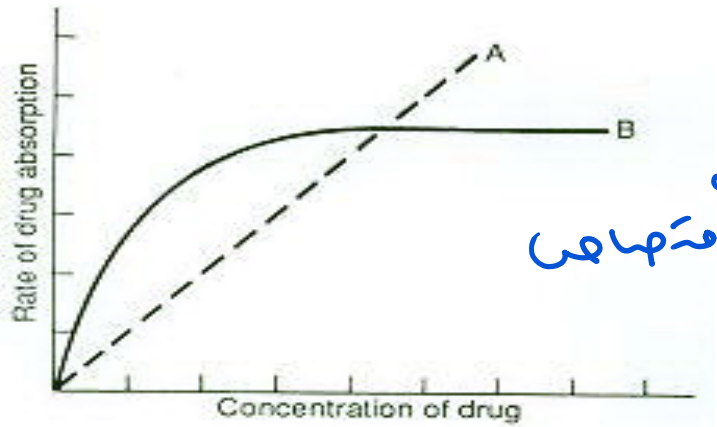
The drug concentration in blood or plasma will be quite low compared with the concentration in the GI tract. It is this concentration gradient which allows the rapid complete absorption of many drug substances.

- Normally Cl << Ch then

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

constant, ka

2-Transport across the membranes



كل ما كان التركيز
اعلى كان ال
diffusion اكثر

ال surface area
كثير بتلعب دور بالامتصاص

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

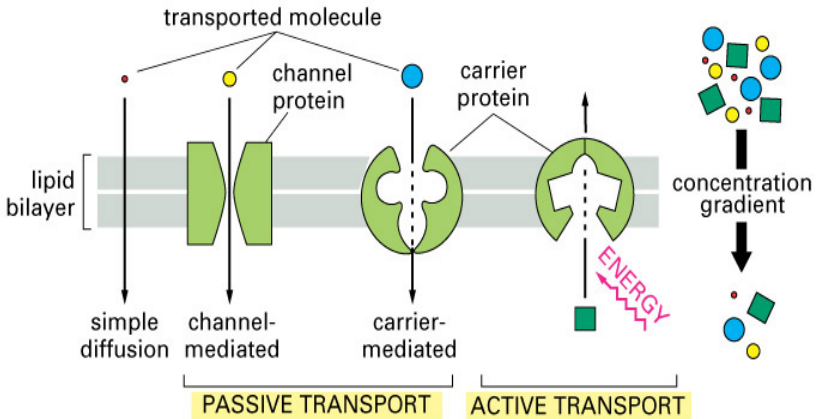


Illustration of Different Transport Mechanisms

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.

liquid + fluid ← **Pinocytosis:** refers to the engulfment of small molecules or fluid.

food word ← **Phagocytosis:** refers to the engulfment of larger particles or macromolecules.

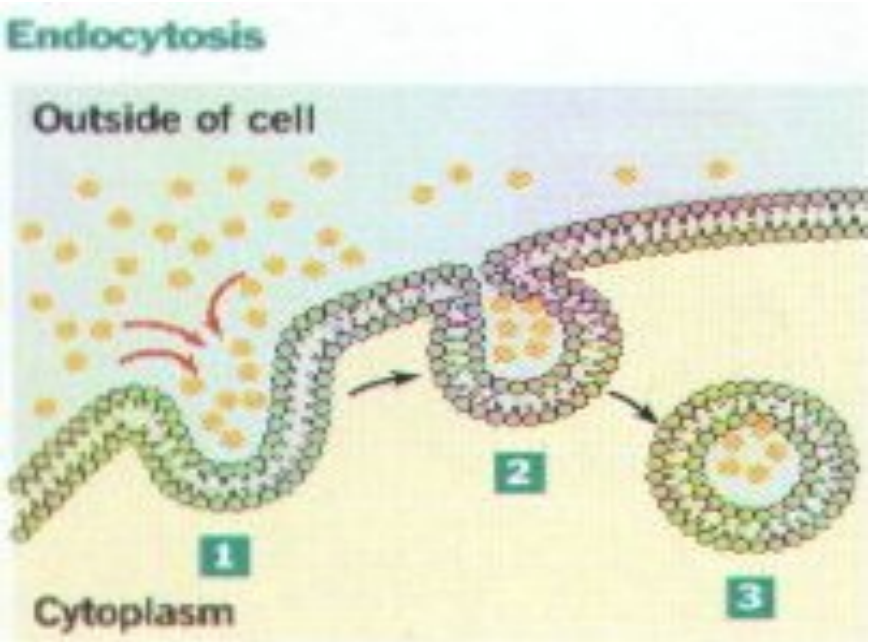
eating + drinking

- 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.

Example

- 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:

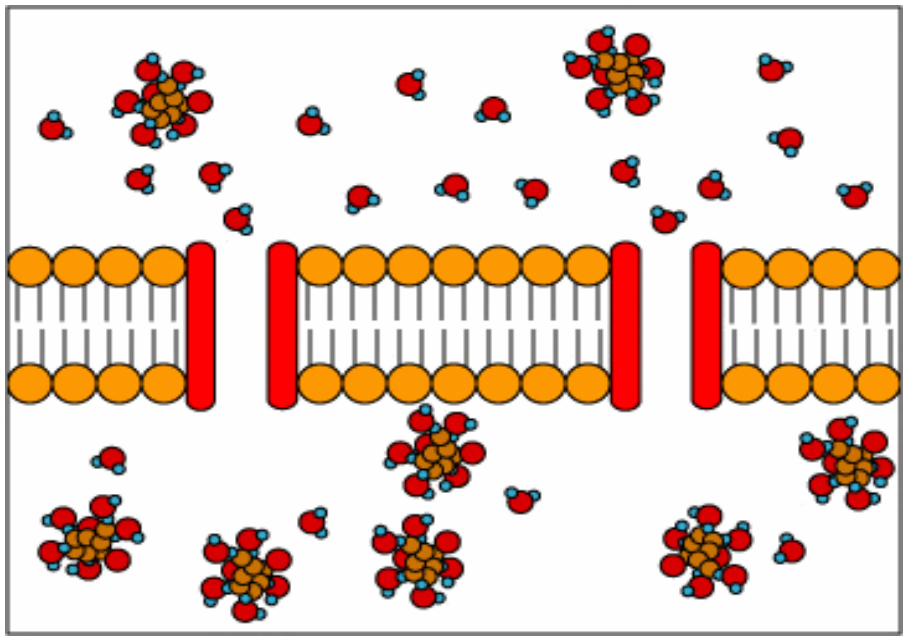
- A certain type of protein called transport protein may form an open channel across the lipid membrane of the cell.
- Very small molecules, such as urea, water and sugars are able to rapidly cross the cell membrane through these pores.

5- Ion pair formation:

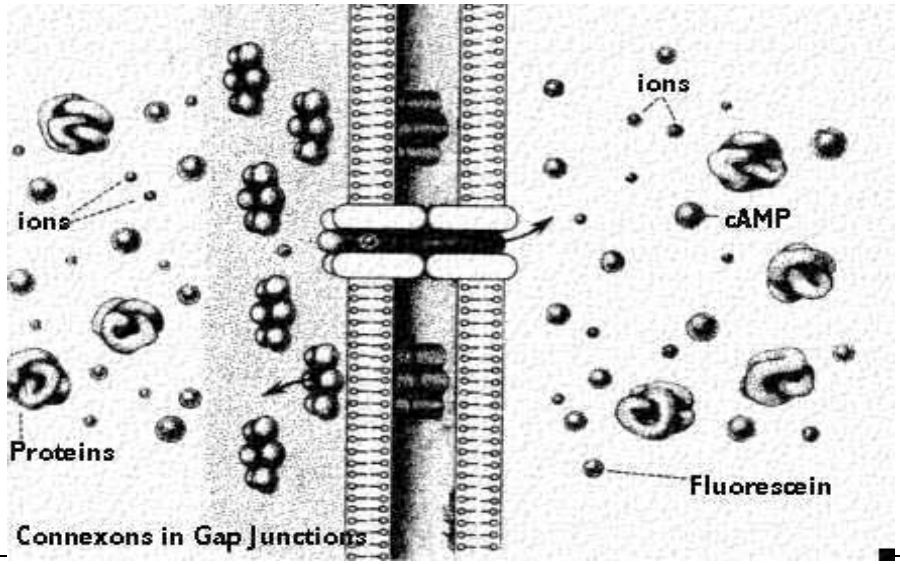
- Strong electrolyte drugs are highly ionized or charged molecules, such as quaternary nitrogen compounds.
- These drugs penetrate membranes poorly. When linked up with an oppositely charged ion, an ion pair is formed in which the overall charge of the pair is neutral. This neutral complex diffuses more 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

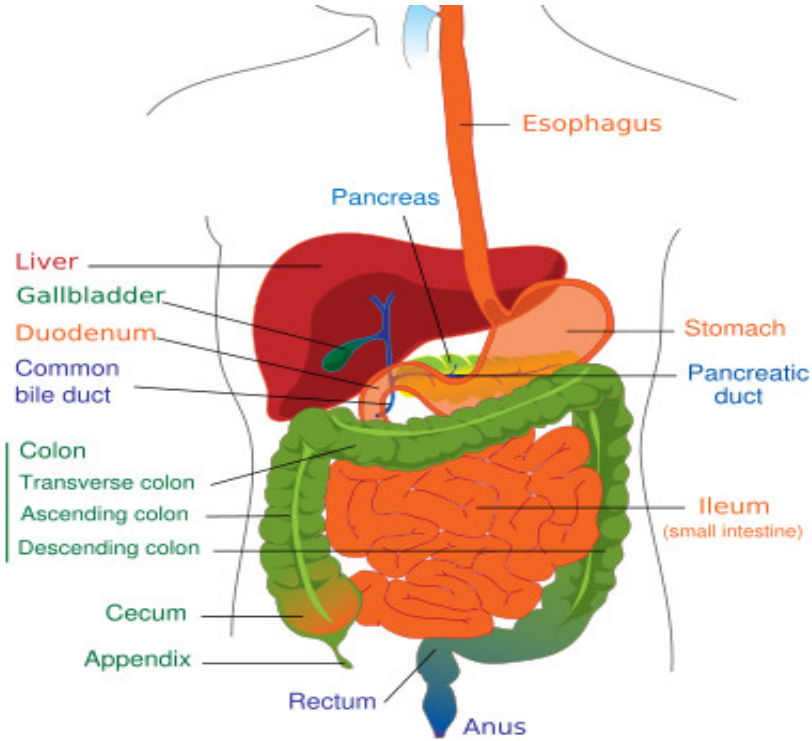
3- Gastrointestinal (GI) Physiology

- The gastrointestinal tract is a muscular tube approximately 6 m in length with varying diameters.

- It stretches from the mouth to the anus and consists of four main anatomical areas: the oesophagus, the stomach, the small intestine and the large intestine or colon.

- The majority of the gastrointestinal epithelium is covered by a layer of mucous. This is a viscoelastic translucent aqueous gel that is secreted through out the GIT, acting as a protective layer and a mechanical barrier.

Gastrointestinal (GI) Physiology



Gastrointestinal (GI) Physiology

I. Characteristics of GI physiology and Drug Absorption:

Organs	pH	Membrane	Blood Supply	Surface Area	Transit Time	By-pass liver
Buccal	approx 6	thin	Good, fast absorption with low dose	small	Short unless controlled	yes
Oesophagus	5-6	Very thick no absorption	-	small	short, typically a few seconds, except for some coated tablets	-

آكثر مكان thin عشان هيك بكون الامتصاص سريع جدا لانو مساحتها قليلة وبكون الها اعلى blood supply

I. Characteristics of GI physiology and Drug Absorption

Organs	pH	Membrane	Blood Supply	Surface Area	Transit Time	By-pass liver
Stomach	1.7-3.5	normal	good	small	30 min (liquid) - 120 min (solid food)	no
Duodenum	5 - 7	normal	good	Very large	very short,	no

I. Characteristics of GI physiology and Drug Absorption

Organs	pH	Membrane	Blood Supply	Surface Area	Transit Time	By-pass liver
Small Intestine	6 – 7.5	normal	good	Very large	About 3 hours	no
Large intestine الامتصاص للwater	6.8 - 7	-	good	Not very large	long, up to 24 hours	Lower colon, rectum yes

(1) الأكثر حامضية بتكون بالمعدة

يعطيكم العافية

اذا في اي غلط او اي اشي مو فاهمينو ابعثولي!!