

تفريغ يوفارما



اسم الموضوع:
Drug Absorption part-1
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لجان الرِّفعات

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.

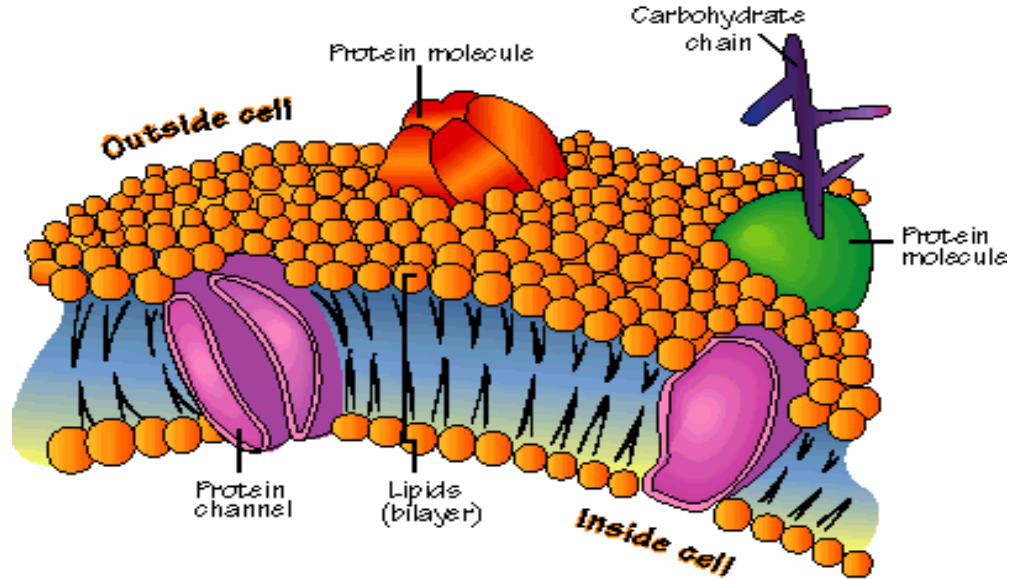
2- Passage of drugs across membranes.

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:



* هسه هون لازم نعرف انو الادوية ، لدهنية الي بتكون (Lipid in nature) بدخترق
اد (membrane) بسهولة لكن ادوية اد hydrophilic صعب تخترقه الا اذا حجمها
صغيري و عن طريق aqueous channels موجودة ب membrane

1- Membrane physiology

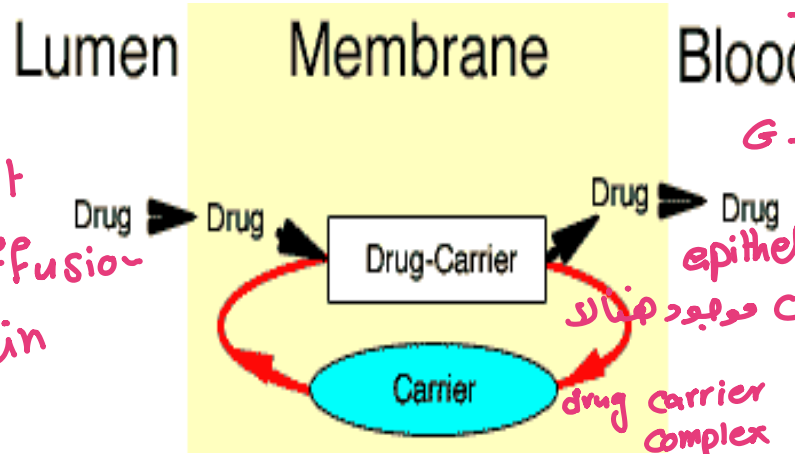
- The cell membrane is the barrier that separates the inside of the cell from the outside.
- The cell membrane is made up of phospholipids, proteins, and other macromolecules.
- The phospholipids make up a bilayer. It contains hydrophilic and hydrophobic molecules.
- The proteins in the cell membrane 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:

- ← هسه هون عنا
٣ أنواع :
- ① active transport
 - ② facilitated diffusion
 - ③ p-glycoprotein



- شرح لهاي الآلية
- ① الدواء موجود في Lumen - G
 - ② تركيزه الاعلى من الخلية
 - ③ يدخل الدواء الى الخلية عبر carrier موجود هناك
 - ④ ارتباط الدواء بالناقل يكون drug carrier complex
 - ⑤ الناقل يحمل الدواء الى الدم وهناك يخلو release يعني (يفك) (complex) والدواء يدخل للدم.

يعني بادخلة الدواء يرتبط مع بروتين الى هو ناقل ويدخل للدم.

2-Transport across the membranes

A- Active transport:

- A few lipid-insoluble drugs (e.g. 5-fluorouracil, 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.

لأنه ما زاد التركيز زاد امتهانها و لكن لحد معين
يظهر بعدها عند قابل للامتهانها أكثر
لأنه الناقل عددها محدود

مثال ممكن المكتوب الكبتوه

vancyclovan drug → anti piral drug
الواثر polar عالية → المزاج النارى + ulcer (المخو)
ف ببربطه مع valine عشان يمر من carrier

شرح لـ 5-Fluorouracil

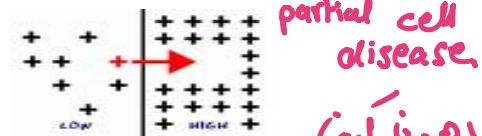
هو عبارة عن anti cancer فيه uracil drug

عبارة عن neocotide فهو فعال في anti cancer
يقدر الجسم بتمتصه فلذلك هاي الخاقل

شرح لـ L-dopa

فيه tyrosine وهو عبارة عن عاقله بتركيز

عليها OH في para position
و OH في بيتا ويستخدم



هيا هونا كيف

بدهو للدوم ولها
highly polar

بالعادة بكونه الناقل

من هيكور او 9.9

او neoclitide

في شان هيل بجمع دوا

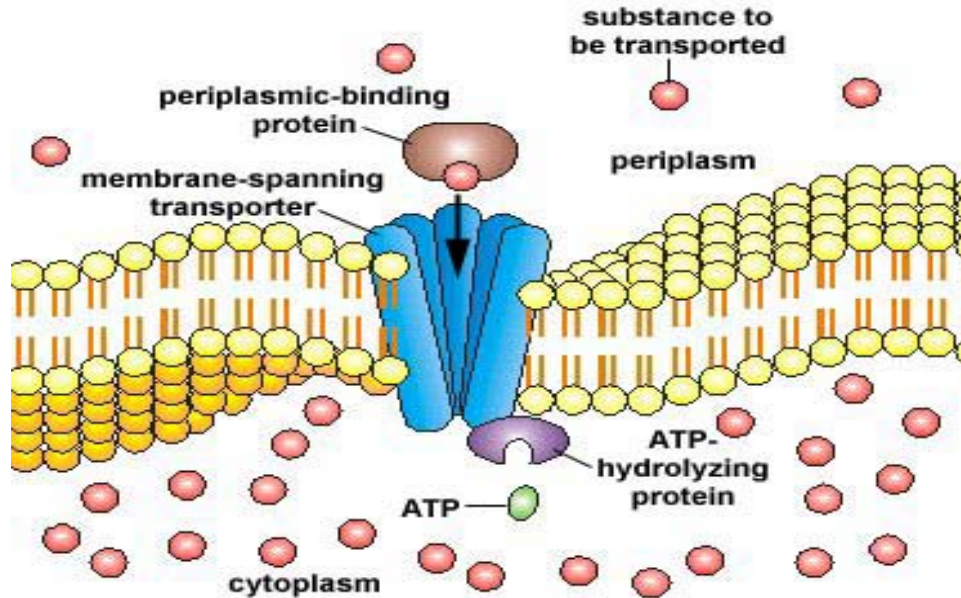
بشهو عشان نسهفند

بالتالي بدهم منافضه

carrier

حبة حناج ATP

2-Transport across the membranes



آخر معلومة فئة
اذا كان تركيز مكي
عادي بعد صودا
كان عالي بدهن يكون
الانه هاجد احسن
وهي بيعد Active
بافى انواع عكس صودا

اذا كان المركب قليل
ما يحتاجه
↑
لا يوجد
عدد واحد
عندهم
اذا كان
عند كمية
كبيرة
الحجم
الحاج
يحتاجه
لأنه لا يوجد
حاجته

2-Transport across the membranes

بكونه هيدروفيل المركب polar
والنواقل polar لأنهم لا
nonpolar فهو ما يحتاجه داخل الخلية.

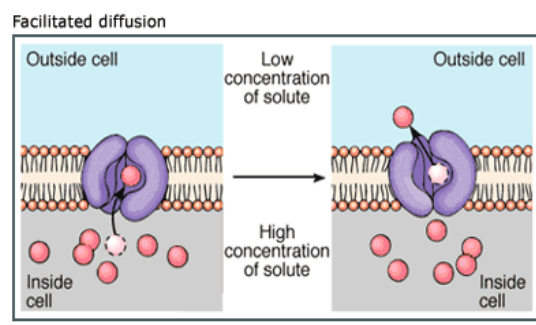
B- Facilitated diffusion:

ما يحتاجه ATP

- 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.

كيف يحتاجه الجسم
العدة بغيره يرتبط
فيديو عن ناقلات
carrier
وما يبدو ATP

يكون عكسي



2-Transport across the membranes

هذه عبارة عن طريقة عكسية بطرد
ما يتدخل مثل (anti cancer + antibacter)

يكون عندي مقاومة لها وعين ...

إذا كان شغل يبطل يشتغل بطلع ٣ ليات
بحيث يبقى في خلايا
ليطرد 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.

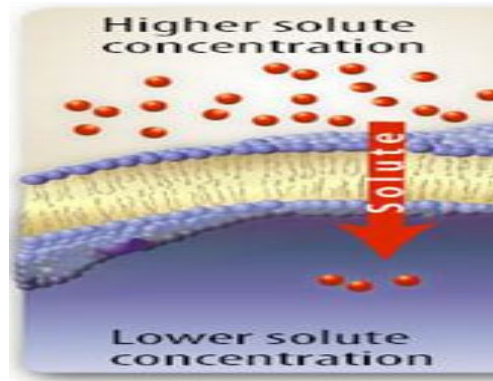
أول شيء يدرس solubility و polarity

و solvent التي يندوب والسبه التي ذائبة وهما القابل بدرسها قبل ما جرب اي دوا

2-Transport across the membranes

2- Passive diffusion: ما يحتاج ATP

- 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. من الأعلى للأقل
- 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.



هون الشيء بحكنا هون (لازم يكون فرق التركيز كبير)
من المعدة لدم الدم من قتل

مع فهم الاديّة
التي موجودة عندي
بالسوق يكون هون
امتصاصها

فرق التركيز
صغري
خلي ار
molecule
تنتقل

2-Transport across the membrane

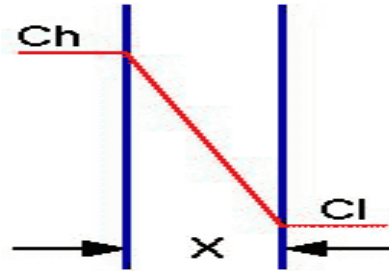


Diagram of Passive Transport with a Concentration Gradient

-The Rate of diffusion = $\frac{d\dot{M}}{dt} = -\frac{D \bullet A \bullet (Ch - Cl)}{x}$

خزق. لتركيز
خزق. لوقت

2-Transport across the membranes

- The parameters of this equation are:-

الها عبقة ب molecule ففو
Hydrophilic ولا Lyophobic
كل مكان Lyophobic اعلى كان diffusion اعلى

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.

كل مكان ب size اعلى كان ب diffusion اعلى والعكس صحيح .

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.

كل ما زادت
area ب
زادت الامتصاص
لأنها وسعت المساحة

بعض اللزوجة بتلعب دور مهم له و ارح يضيق
المخار و هي الامتصاص

2-Transport across the membranes

هل سمالة، وهو مثلا الافعه او المصه او الغفلات

يتمتع للدوا يترك اولاً

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.

الفرق بالتركيز بين Lumen + plasma

(Ch - Cl): concentration difference.

كل ما كان الفرق أكبر كان diffusion أسرع

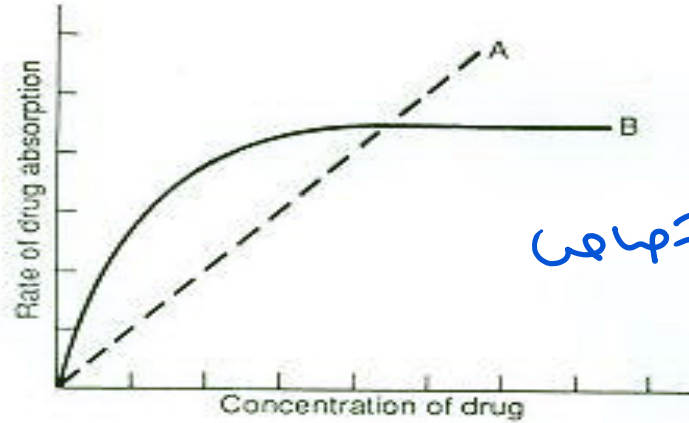
The drug concentration in blood or plasma will be quite low compared with the concentration in the GI tract. It is this concentration gradient which allows the rapid complete absorption of many drug substances.

- Normally $Cl \ll Ch$ then

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

constant, k_a

2-Transport across the membranes



Surface area اور
کثیر بہ تعداد ذرات

کے مابین، تفریق
ایک کان،
diffusion اکثر

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

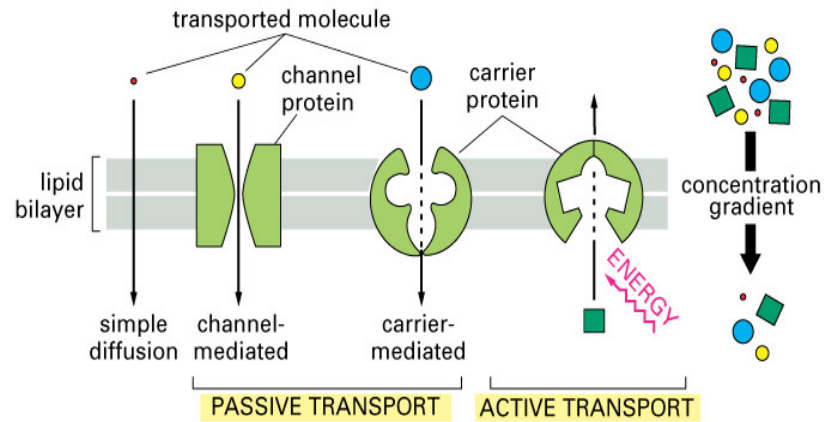


Illustration of Different Transport Mechanisms

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.

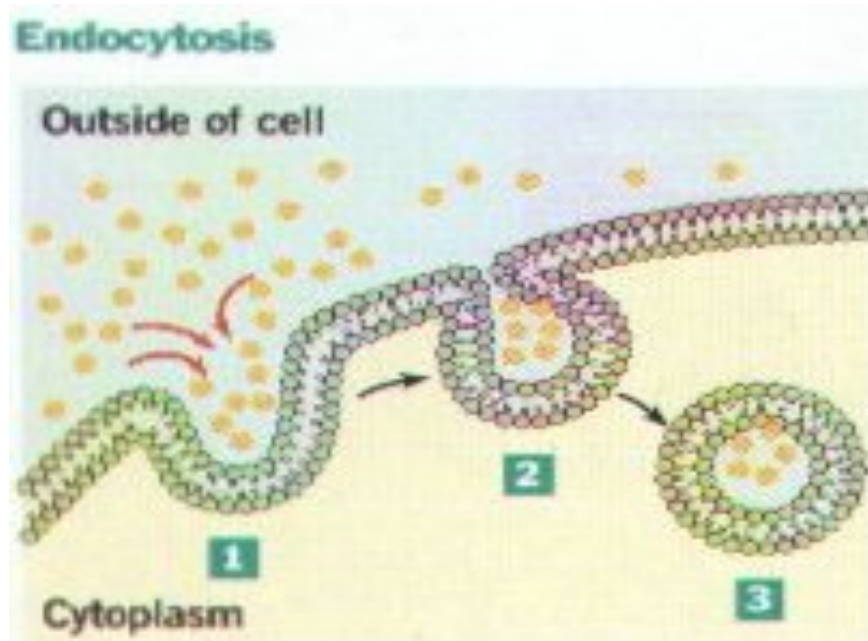
Food + drink ← **Phagocytosis:** refers to the engulfment of larger particles or macromolecules.
eating + drinking

- 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.

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

Example

2-Transport across the membranes



2-Transport across the membranes

بروتينات مسحة للادوية بالمرور من خلالها

ليتر فينت

جرفتها water
and very small
molecules
+ urea

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.

لو ما جرق
و بمللوي مثال
ها
Polar
charge
big
فاجرق

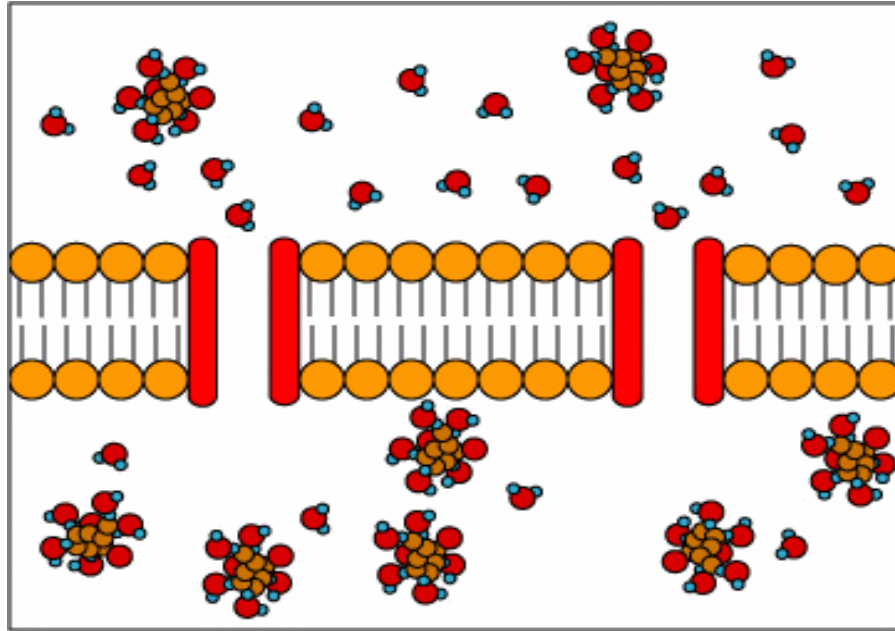
يسبقم للاصط
وبوقف التوتر
الشقيقة

charge (+)

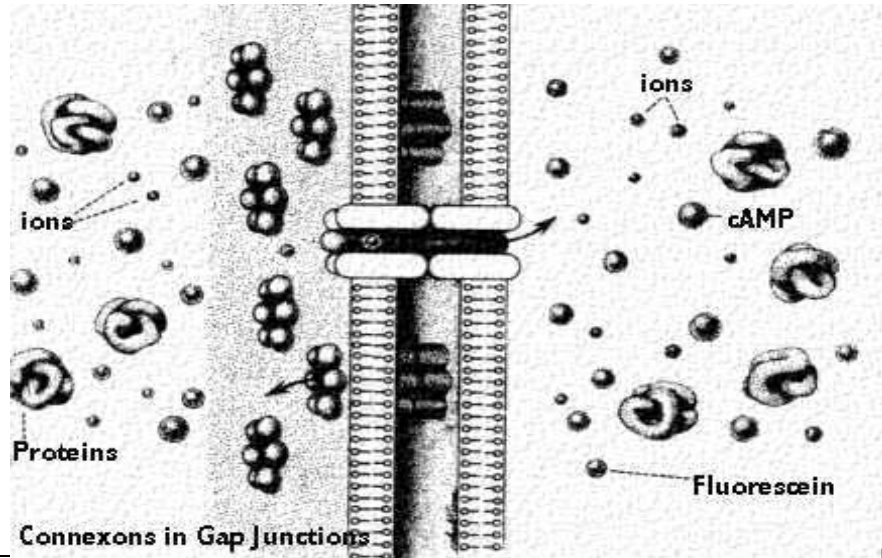
و جعل sharing له الشحنة مع
له ا بزوج الشحنة بهي
سجل الامه صا

* بعض الادوية اذا بوجتها مع الال يقل امه صاها
ولكن هاذ اذا بوجتو مع دية اكل دية
بزيده صاها

Transport of Substances Across a Membrane by Channel Proteins



2-Transport across the membranes



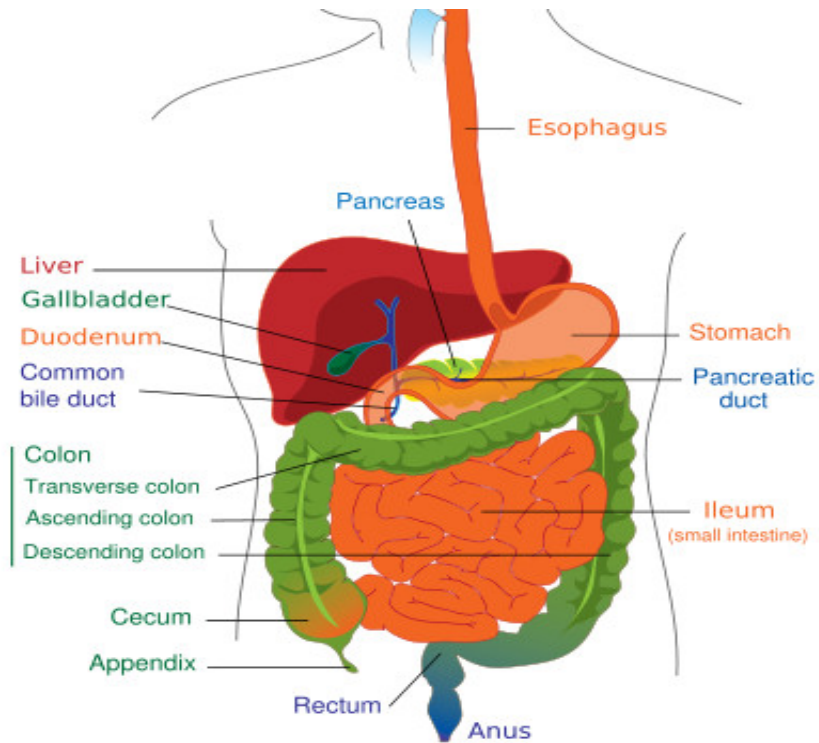
Mechanism of ion pair transport of drugs

3- Gastrointestinal (GI) Physiology

- The gastrointestinal tract is a muscular tube approximately ^{الطول} 6 m in length with varying diameters.
- It stretches from the ^{يبدأ} mouth to the ^{ينتهي} 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.

والتركيبه
تباين
بمختلف

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 الشفة	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	-

الزفكان
Thin
عشان صير
بكون الامعاء
سريع هذا
لانه سائلها
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	6.8 - 7	-	good	Not very large	long, up to 24 hours	Lower colon, rectum yes

الدم فيها
water

١) أكثر حمضية بكون بالمعدة

يعطىكم العافية

إذا في أي غلط أو أي شيء مو فاهمينو ابعتوني