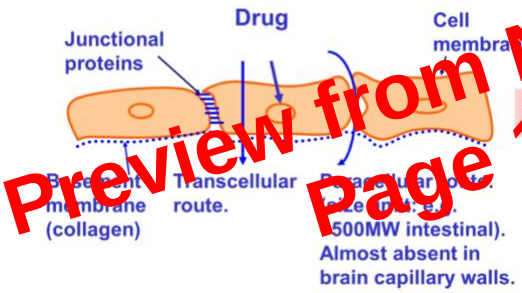
This has a high surface area which gives a good opportunity for things to pass into and out of a membrane. Paracellular has a lower bioavailability in terms of its pathway.

- Tight junctions have a net negative charge. Having a preference for transporting positive molecules. Although this is still size dependent.

Epithelial cells are found in all major cavities of the body.

- The epithelia form structures in the lungs which allow for interactions with the air.
- Line most organs, including the stomach.
- Found in glands where there is secretion of chemicals which aid the properties of a certain tissue type.
- Can specialise to act as sensory receptors. They form taste buds, line the nose and are found within the ear and the eye.
- Female reproductive organs are lined with ciliated epithelial cells.
- The skin and capillary beds are also made of epithelium.



Epithilia – not found in all epithelial cells. Main use is for protection as they act as a boundary between two different things. Act is a sensory aspect as well as for transport and absorption.

Epithelial cells line the entire vascular system and control the passage of materials, as well as the transit of white blood cells into and out of the blood stream.

Connective tissue – supports and binds other tissues together.

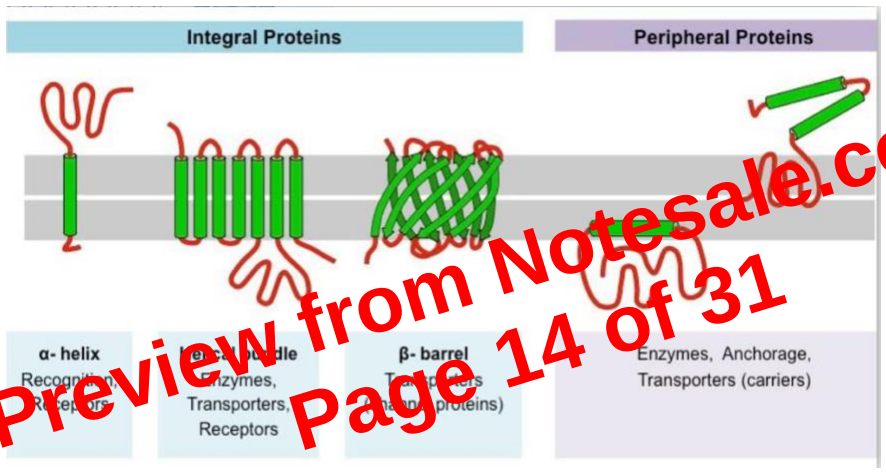
- Help to secure cells around the extracellular matrix and support cells to protect them.
- Often also produce chemicals and blood cells that help to support the proliferation of other cell types.

- Proteins are also found within the membrane to allow for specific functions and interactions.

Diagram:

Membrane proteins

- These are the different types of proteins found within a cell. Some create an ion channel. These allow the membrane to understand what is being taken in or given out.



Cardiovascular system

- Highlights that when a drug enters the blood stream it is transported to all different systems within the body.

- Blood from the heart goes to lungs and then to all other organs. This system underpins all of the movement of blood.

The main component of blood is water, followed by ions, amino acids, proteins and cells (red blood cells etc). So, when the blood is centrifuged the red blood cells are at the bottom, with white blood cells above and liquid plasma at the top. Blood plasma is what suspends white blood cells. Serum on the other hand does not contain cells.

Blood vessels

e.g. Aspirin is a weak acid so will pick a hydrogen ion allowing it to be in its neutral state and therefore be able to pass through the lipid membrane.

Weak bases – best absorbed in the intestine. The protonated from is ionised.
e.g. Morphine needs to be in a basic solution so does not uptake a proton to become ionised

To calculate need to know if a weak base or acid.

<u>Calculation steps</u>

Log [HB/H+] = pKa – pH

10^{ans} = [HB/H] (antilogging)

3.2/1 = HB+/B

So, for every 3.2 of HB+, there is 1 of B (75% cannot cross the membrane and 25% can)

- Unionised passes through the membranes. Cell membrane are impermeable to polar molecules.

Different compartments of the body have different pH's

Changing the property of urine can either help or prevent the movement of a drug from the blood. By keeping within the blood a drug is less likely to be detected in a urine sample.

- To enhance renal excretion of a weak base, urine can be made more acidic
- Basifying the urine helps for renal excretion of a weak acid (add sodium bicarbonate). Alkaline using allows for a greater fraction of the drug to be protonated and therefore neutral, allowing them to pass through membranes.

- A weak acid will be absorbed better in the stomach with a high pH as due to la Chatelier's principle acidity will be increased protonating the molecule. Allowing it to be neutral and lipid soluble. A unionised drug is easily absorbed.

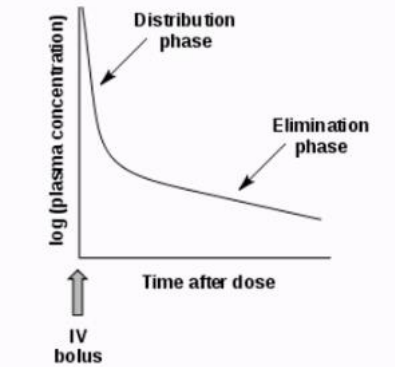
  (For excretion of this drug want to make ionised, by basifying the urine)

- Collect data, choose a model which best fits and then fit model to data.

If taking data points, using an animal for example, must take readings at different time points. This would also need to be repeated with a group of animals to ensure that the results are reliable.

- If a mathematical model can be fitted it prevents needing to analyse all data points. Provides a good estimation of data.

Also considers equilibrium over time. Some drug is directly excreted, and some allows for an equilibrium to occur.



- equilibrium causes the rate of change to slow.

Terminology:

- Compartment – a theoretical volume for the chemical to be distributed within.
- Steady-state – no net change in concentration. Has reached equilibrium.
- Bolus dose – instantaneous input into the compartment One injection into the body.

Rate equations

- Explain how drugs move between compartments. Rate of change as the drug starts to move.

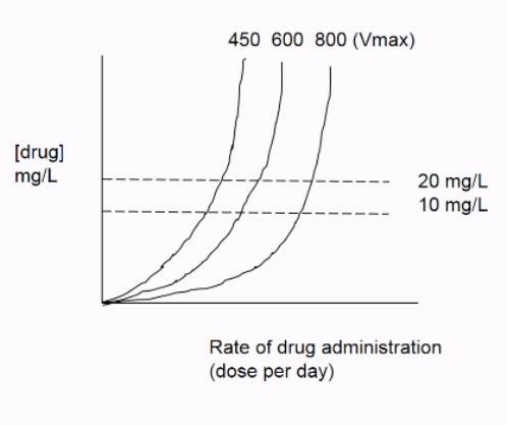
Zero-order process is when the rate constant does not depend on the chemical concentration.
Rate = K x Co

First-order process is when the rate is proportional to the concentration of one of the chemicals.
Rate = K x C1

Second order process is when the rate is proportional to the concentration of both chemicals.
Rate = K x C1 x C2

Saturable process is when the interaction of two chemicals. The enzyme is constant. This is when the limit is reached and the graph plateaus.

Saturation of drug metabolism:

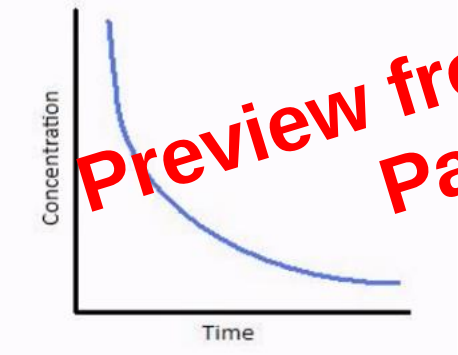


- How the drug is acting upon to be decomposed and therefore excreted.

Drug clearance/excretion.

Most drugs are eliminated from the body through the urine. Air also contributes to the distribution of a drug through the lungs. So, the drug can also be eliminated through the breath.
Drug from the plasma enters the Nephron where from this it is excreted within the urine.

Drug clearance = ([drug] in urine x Rate of urine production) / [drug] in plasma



- When t1/2 is the same each time this shows first order.

How to calculate Kel experimentally

- Plot a graph of ln[plasma] vs time
- Slope gives -Kel

This is not that easy as drugs do not only exist in the plasma, they are also metabolised there due to enzymes. The metabolite is then what is found within the urine.

Enzyme limited kinetics

- t/12 is no longer equal which shows a zero-order reaction.