Rate of permeation of paracetamol through cellulose tubing

Student worksheet

Health and safety note

Wear eye protection. 5 mol dm^{-3} hydrochloric acid is an irritant.

Principle

The ease with which a drug can move through a cell membrane is measured by the drug's permeability. One way that pharmacologists measure rates of permeation is by using artificial membranes and a technique called parallel artificial membrane permeability assay (PAMPA). However, it can only measure passive transport. Another technique measures permeation through a monolayer of real cells. This measures both passive and active transport. The caco-2 assay is an example.

Cellulose tubing is a partially permeable membrane. It may be used to model passive transport through cell membranes. Passive diffusion through membranes is driven by concentration differences and does not require an input of energy.

Equipment and materials

For the permeation

- 15 cm length of cellulose tubing knotted at one end (twist twice, fold over and tie with cotton thread)
- Sawn-off plastic syringe barrel to support the cellulose tubing (Figure 1)
- Elastic band
- 400 cm^3 beaker
- 1 cm^3 pipette (or plastic syringe)
- Paddle stirrer
- 0.05 mol dm^{-3} paracetamol in buffer solution

For the colorimetric analysis

- Calibration graph for the colorimetric determination of paracetamol (see *Colorimetric analysis of paracetamol*)
- Colorimeter and suitable filter
- Boiling tubes (x7)
- 0.02 mol dm^{-3} iron(III) chloride solution
- 0.002 mol dm^{-3} potassium hexacyanoferrate(III) solution
- 5 mol dm^{-3} hydrochloric acid − Irritant
- 5 cm^3 graduated pipette (or plastic syringe) (x3)

Method

1. Measure 350 cm^3 of buffer solution into a 400 cm^3 beaker. Place a paddle stirrer in the beaker.
2. Tie a knot in the end of the cellulose tubing. Soak the tubing in water and use an elastic band to fasten it to the sawn-off syringe barrel (figure 1).
3. Measure 5 cm^3 of 0.05 mol dm^{-3} paracetamol in buffer solution into the tubing.
4. Clamp the sawn-off end of the plastic syringe so that the level of the

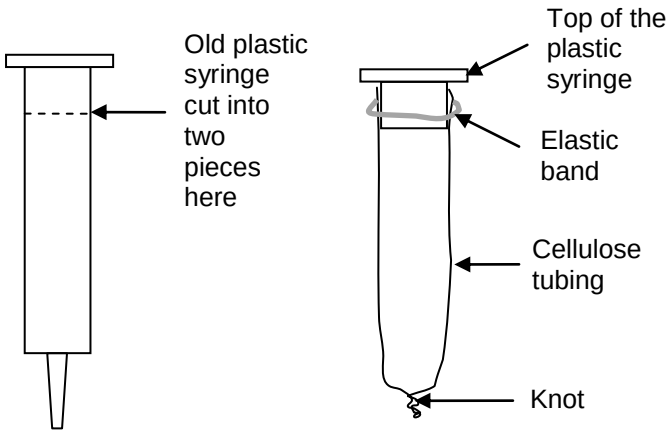

Figure 1 Preparing the cellulose tubing for permeability experiments.

paracetamol solution in the cellulose tubing is level with the buffer solution in the beaker (figure 2). Start the paddle stirrer.

5. Choose a spot about 4 cm below the water surface and about 2 cm from the side of the beaker from which to withdraw samples.
6. Start the stopwatch and immediately withdraw a 1 cm^3 sample and put into a boiling tube. Label the tube 'zero time'.
7. Withdraw further 1 cm^3 samples every 5 minutes for 30 minutes. Label them '5 min' to '30 min'.

For 'zero time' and the other six diluted samples:

8. Add 2 cm^3 of 0.02 mol dm^{-3} iron(III) chloride solution and 4 cm^3 of 0.002 mol dm^{-3} potassium hexacyanoferrate(III) solution. Leave for 10 minutes. Then add 1 cm^3 of 5 mol dm^{-3} hydrochloric acid.

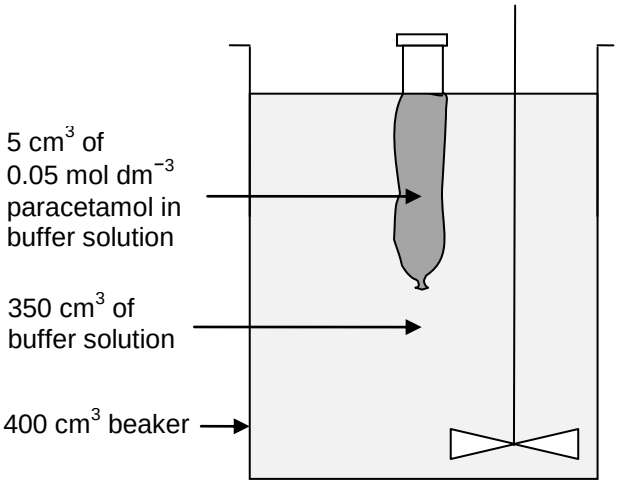

Figure 2 Experimental set up for permeation study.

9. After 20 minutes measure the absorbance and use it to calculate the concentration of paracetamol. From this value calculate the concentration of paracetamol in the original sample.

Processing the data

If the experiment was left long enough and samples taken, the graph would be similar to that shown in figure 3.

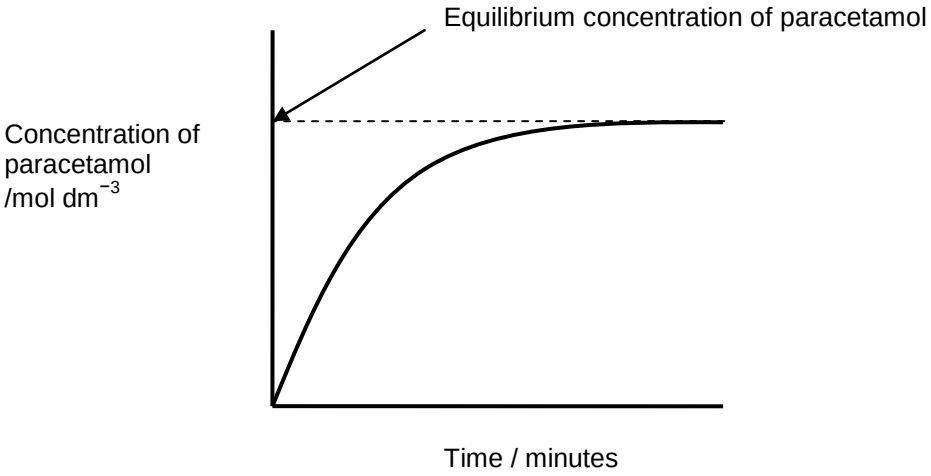

Figure 3 Equilibrium is reached when the concentration of paracetamol is the same inside the cellulose tubing as it is outside the tubing.

However, permeation is quite slow and it is likely that you will obtain a straight line graph (possibly a slight curve). This is still useful though, as it can be used to measure the initial rate of permeation, when the concentration of paracetamol is 0.05 mol dm^{-3}.

Therefore,

1. plot a graph of concentration of paracetamol against time;
2. calculate the gradient of the straight line or the gradient (figure 4).

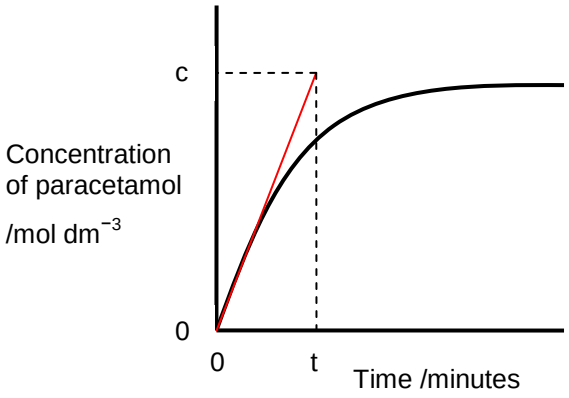

Figure 4 Initial rate of permeation $= \frac{c}{t}$ mol dm^{-3} min^{-1}

Possible extension ideas

The experiment could be repeated using different initial concentrations of paracetamol in the same buffer and, in each case, determining the initial rate of permeation. Plot a graph of initial rate of permeation against initial concentration of paracetamol. From this decide whether the permeation process is:

- zero order;
- first order;
- second order.

Further extension ideas are:

Investigate the effect of pH on permeation rate by using a number of buffer solutions.

Investigate the effect of temperature on rate of permeation could be investigated.

Compare the rate of permeation of paracetamol with that of aspirin and other compounds.