Drugs delivery.

Drugs delivery is about getting the drug molecules to the target site.

There are different environments and barriers that a drug might encounter on its journey to the target cell.

Example: swallowing a pill.

Drug molecule will encounter the acid pH of the stomach and the enzymes that are in the intestines to break down food.

It will then have to pass from the stomach or the intestines into the bloodstream, which has a different pH and more enzymes.

When it reaches the right cell, it will have to get through the cell membrane.

And most importantly how does it know which cells to target?

Clearly there are many areas to consider on drug delivery:

- method of delivery to get the drug to its target in one piece
- avoid it being broken down by enzymes or degraded in extremes of pH.

Liposomes

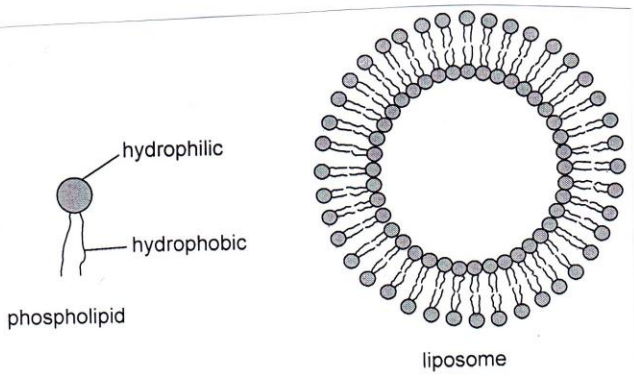
One successful method of delivery involves the use of liposomes.

These are artifical microscopic vesicles consisting of an aqueous core enclosed in one or more phospholipid layers.

A phospholipid is a molecule that is hydrophilic (water-loving) at one end and hydrophobic (water-hating) at the other end.

In water-based solutions such as bloody lipids group together to form double layers with their hydrophilic groups on the outside, forming polar interactions with the water, and their hydrophobic groups on the inside of the layer, away from the water.

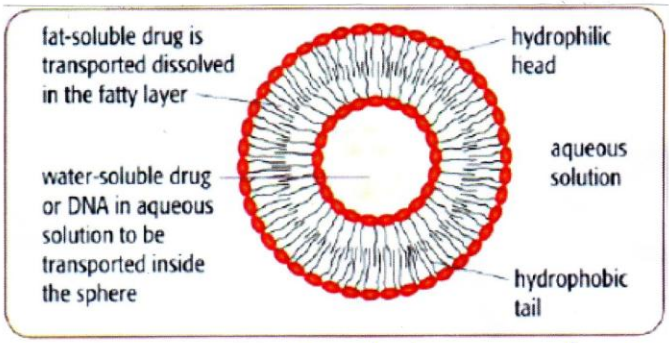
These bilayers can wrap into spherical vesicles



a phospholipid and a cross-section of a liposome

Liposomes are biodegradable and non-toxic and can be used to carry vaccines, drugs, enzymes, or other substances to target cells or organs.

They can carry both hydrophilic molecules (polar molecules that form hydrogen bonds with water and hence dissolve) and hydrophobic molecules (non-polar molecules that do not dissolve in water).



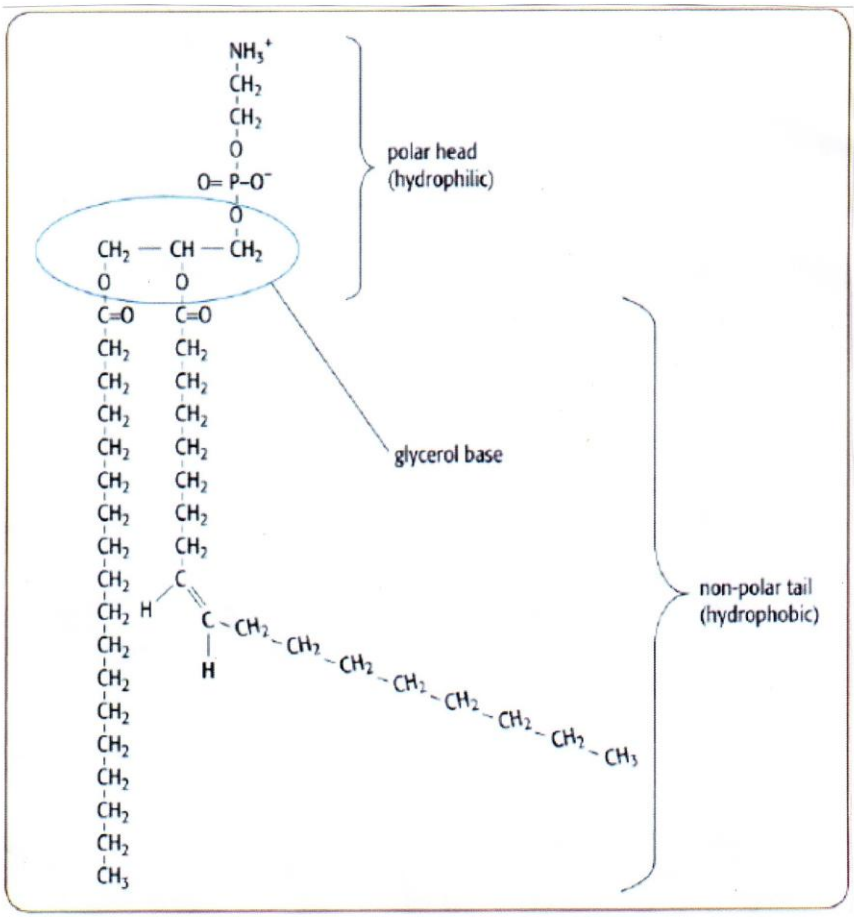
Phospholipids can be made into liposomes for carrying drugs and DNA.
They are made in a solution containing the drug or DNA to be transported to the target site.

As liposomes are made from biological molecules, they are easily degraded by the body.

By modifying the surface of liposomes biochemists have developed long-life liposomes, which do not degrade quickly and have a better chance of reaching their target.
Once the liposome reaches its target, the drug can be transferred to the target.

Exercise 1

Look at the structure of a phospholipid as below.



a. Explain why a phospholipid would decolorise bromine water.

b. Describe how water molecules would interact with the hydrophilic 'head' of the phospholipid molecule.

c. Does the structural formula represent a cis or trans isomer?
How would the other isomer differ in its shape?

d. What type of intermolecular forces would be operating between a drug that is insoluble in water and its liposome carrier?

Workings

a. it is unsaturated, containing a C=C double bond which is ready to go through electrophilic addition reaction with bromine molecule.

b. Two sites at the head of the phospholipid molecule can interact with water molecules.

- the hydrogen atoms in water, with their partial positive charge, would be attracted to the negative charged oxygen in the phosphate group.
- the oxygen atoms in water, with their partial negative charge, are attracted to the positively charged nitrogen atom in the alkyl ammonium group.

c. It is a cis isomer.
The trans isomer would have a straighter hydrocarbon 'tail'.

d. van der Waals' forces.

Gold nano cage

The latest techniques use nano-cages of gold to deliver drugs to target sites in the body.

Nanoscientists study particles between 1 and 100 nanometres (nm) in size, where $1\,nm = 1 \times 10^{-9} m$.

Researchers have found that the tiny gold particles can be selectively absorbed by tumours.

Tumours have thin, leaky blood vessels with holes large enough for the gold to pass into, unlike healthy blood vessels.

When a laser is directed at the tumour the gold nanoparticles absorb energy and are heated up.

The temperature of the tumour increases sufficiently to denature its proteins whilst surrounding tissue is barely warmed.

This destroys the tumour cells without damaging healthy cells.

There is potential to use the gold cages to carry cancer-fighting drugs to the tumour at the same time.

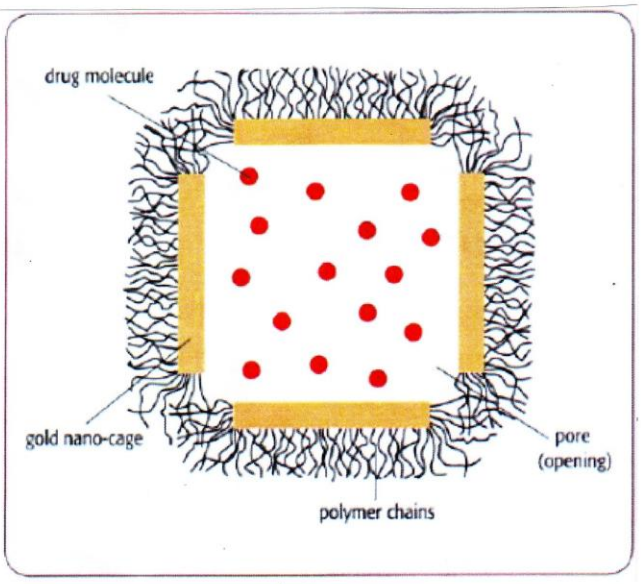
The gold nano-cages are coated by a polymer called PEG (polyethylene glycol).

This stops the body's immune system from attacking the gold particles and ejecting them from the bloodstream.

The PEG dissolves in water when it gets hot, releasing the drug from the nano-cage.

Smart (or shape-memory) polymers do the same job but they are designed to have a critical temperature at which their molecules change shape.

The polymers seal the pores in the gold nano-cage below its critical temperature.



Drug delivery by a gold nano cage.
The polymers are shown attached to the surface of the cage.
They seal the pores in the cage as it travels in the bloodstream to the tumour.
When the laser warms the gold atoms, the cage is effectively opened and the drug is released.

Once the nono-cage is warmed by the laser and it reaches its critical temperature the polymer chains straighten out and the pores are opened to release the drug.

Exercise 2.

Why can liposomes and gold nano-cages selectively deliver cancer-fighting drugs to the sites of tumours in the body?

Workings

The cells in the walls of the blood vessels in a tumour are not packed as tightly as in healthy blood vessels.

Therefore this allows the nano-particle delivery the drug can pass into a tumour but cannot get through the blood vessels of healthy organs.