# Pharmacokinetic processes: excretion

## Excretion

Excretion is the process of removing a drug and its metabolites from the body. This usually happens in the kidneys via urine produced in them.

Other possible routes include bile, saliva, sweat, tears and faeces.

Most drugs are insufficiently polar (and, therefore, water soluble) to be excreted directly. Instead they need to metabolise to produce more polar, water-soluble molecules.

**Figure 1** Must drugs are removed from blood in the kidneys.

## Excretory system

The excretory system is made up from the two kidneys, ureters, bladder and urethra, together with the branches of the two renal arteries and veins. Blood passes into the kidney's nephron (kidney tubule) where three processes can happen: [1]

- Glomerular filtration: small drug and metabolite molecules and those not bound to plasma protein are filtered from the blood. Large molecules or those bound to plasma protein are poorly excreted by glomerular filtration.
- Tubular secretion: most drugs enter the kidney tubule by tubule secretion rather than glomerular filtration. The process involves active transport against a concentration gradient and, therefore, requires energy and carriers to transport basic drugs such as dopamine and histamine, and carriers for acidic drugs such as frusemide and penicillin.
- Tubule reabsorption: Some drugs and metabolites are absorbed back into the bloodstream. This does not require energy. It is passive transport.

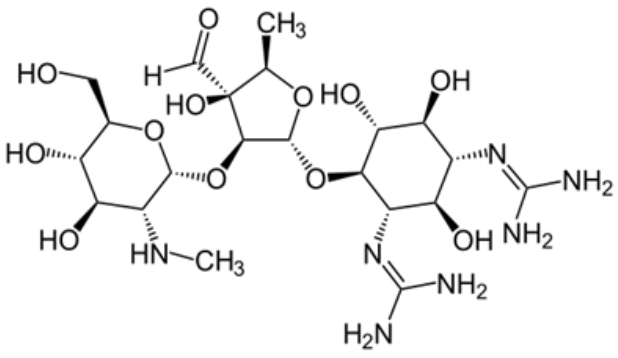

**Figure 2** Streptomycin is an antibiotic. The molecules are sufficiently polar to be excreted by the kidneys without being metabolised first.

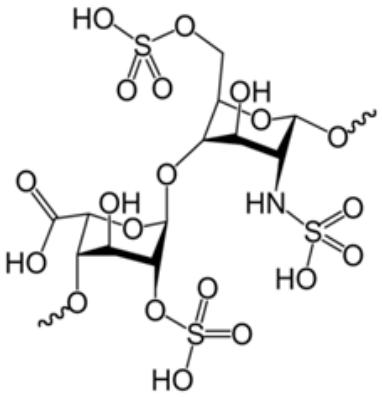

**Figure 3** Heparin, an anticoagulant drug, is too large to be excreted by glomerular filtration.

[1] See *Excretory systems* for more information about the how kidneys function

## Clearance

Clearance is the rate at which a drug is eliminated from the blood. Drugs have different clearance rates. It is important to know these in order to work out the correct doses to be given.

- Higher doses of drugs with high clearance rates may be needed as the drugs are removed from the blood rapidly by the kidneys.
- Drugs with low clearance rates mean that lower doses may be used to maintain the required drug concentration in the bloodstream.

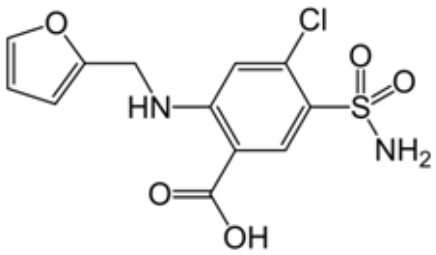


**Figure 4** Frusemide is a diuretic. It has a high clearance rate.

## Kinetics of excretion

Generally, drug excretion is a first order kinetic process. The rate at which a drug is excreted is directly proportional to its concentration in blood plasma. When administering a drug, if the times between doses are such that the drug is being replaced as quickly as it is being excreted, a constant drug concentration is maintained and a steady state is reached.

The equation for first order excretion is

rate of excretion = k[D]

where,

[D] = drug concentration in blood plasma

k = rate constant

A graph of log[D] against time is a straight line of gradient k.

Half-life ($t_{½}$) is the time it takes for the concentration of drug in blood plasma to halve. For a first order reaction it is a constant value, given by

$t_{½} = 0.693k$

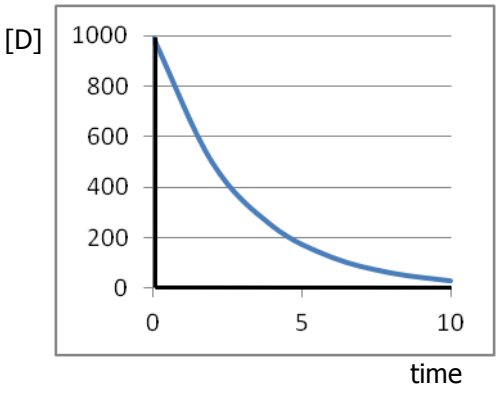


**Figure 5** Graph of drug concentration in blood plasma against excretion time.

## Finding out

Pharmacokinetic models are important for precise determination of excretion rates.

They are relatively simple mathematical models, the two most common models being:

- one-compartment and
- two-compartment.

Find out more about these models.