Pharmacokinetic processes: liberation

Drug delivery systems

Drug delivery systems (also called dosage forms) are necessary to enable the effective, safe and reliable use of medicinal drugs.

Most drugs are formulated into tablets or other forms of medicine. A formulation is a mixture, made to a specific recipe, of the active medicinal drug and one or more inactive substances. These inactive substances are called excipients.

There are a number of reasons for using these inactive substances. They can be used, for example, to

- increase the ease with which an active drug is absorbed by the body;

- 'dilute' very powerful drugs to enable convenient and accurate doses to be measured out;

- control the release of the active drug over a period of time, e.g. controlled-release tablets.

Where, when and for how long

A drug delivery system must ensure that the medicinal drug is available at the site of action:

- in suitable quantity (drug concentration), which depends on
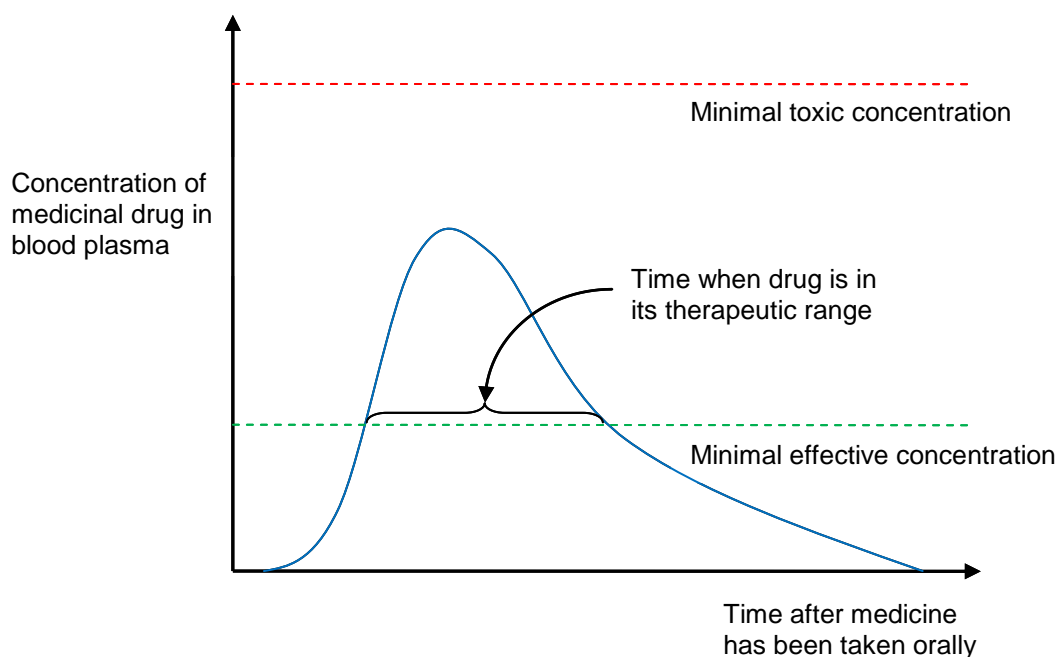
- when it is needed and for as long as it is needed.

Figure 1 The aim is to deliver the correct concentration of a medicinal drug to where it is needed for as long as it is needed. It should be above the minimal effective concentration and below the minimal toxic concentration. This is its therapeutic range.

As well as the delivery system used, the required drug concentration depends on the frequency of dosing, the drug clearance rates and the route of administration.

Releasing the active drug

Liberation describes the way that a drug is released from its administered form.

There are various release types:

- immediate: the medicine is formulated to release the medicinal drug without delay;

- delayed: the medicine is formulated to release medicinal drug sometime after it is taken (usually orally);

- extended: the medicine is formulated to make the drug available over an extended period, allowing a reduction in dosing frequency compared with immediate or delayed-release medicines.

For oral administration important liberation processes include the disintegration of tablets or the dissolving of soluble coatings of tablets and capsules.

- Dispersible aspirin

  Dispersible aspirin tablets typically contain several excipients: dried maize starch powder, sodium lauryl sulfate, lactose, sodium saccharin, anhydrous citric acid, calcium carbonate, povidone, isopropyl alcohol and lactose (starch basic granules).

  Two of these ingredients react with one another in water:

  citric acid + calcium carbonate → calcium citrate + carbon dioxide + water
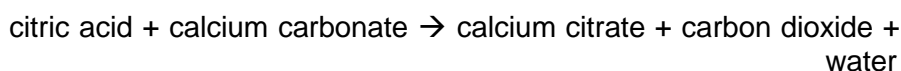
  The effervescence as carbon dioxide gas is released helps break up the tablets, releasing small particles of aspirin. The smaller the particles, the more quickly they dissolve and are absorbed.

Figure 2 Dispersible aspirin tablets break up in water because carbon dioxide is released.

- Paracetamol capsules

  Paracetamol capsules consist of a white powder held in a hard gelatine shell.

  The white power is paracetamol mixed with the excipients pre-gelatinised maize starch, magnesium stearate and sodium lauryl sulfate.

  The capsule shell is made from the excipients titanium dioxide, erythrosine, quinoline yellow, patent blue, gelatine, methyl parahydroxybenzoate and propyl parahydroxybenzoate.

  The gelatine shell dissolves slowly, meaning that it can pass through the stomach to regions of higher pH before the bulk of the paracetamol is liberated.

  The gelatine shell is an example of an enteric coating. Enetric coatings are often used to encapsulate drugs that are sensitive to conditions in the stomach.

Figure 3 Some people find capsules easier to swallow than tablets.

Finding out

For a medicinal drug, how are (a) minimal effective concentration, (b) minimal toxic concentration determined?

When might delayed release be preferable to immediate release?