Dissolution of paracetamol tablets

Student worksheet

Health and safety note

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

Principle

The rate at which drugs taken orally dissolve in the stomach and other regions of the gastrointestinal tract is an important factor in determining how quickly a drug can be absorbed into the bloodstream and carried to where it needs to act.

Rate of dissolution can be measured using the paddle method. This experiment is based on a method published in *The International Pharmacopoeia Fourth Edition*.

Equipment and materials

For the dissolution

- 1 dm^3 beaker
- 1 cm^3 pipette (or plastic syringe)
- 1 dm^3 measuring cylinder
- Paddle stirrer
- 500 mg paracetamol tablet – Harmful
- Stopwatch
- For extension work (optional):
  - o paracetamol capsule – Harmful
  - o dispersible paracetamol – Harmful
  - o various buffer solutions to mimic pH found in different regions of the gastrointestinal tract

For the colorimetric analysis

- Calibration graph for the colorimetric determination of paracetamol (see *Colorimetric analysis of paracetamol*)
- Colorimeter and suitable filter
- 5 cm^3 pipette & pipette filler
- 100 cm^3 volumetric flasks
- 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

Method

1. Use a measuring cylinder to measure 600 cm^3 of deionised water into a 1 dm^3 beaker. Place a mechanical stirrer in the beaker so that its paddle or fins are well below the surface of the water. Switch the stirrer on and stir the water gently. Record the temperature of the water.

2. 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.

3. Drop a paracetamol tablet into the water (try to avoid splashing by holding it near to the water surface before dropping). Start the stopwatch and immediately withdraw a 1 cm^3 sample and put it into a 100 cm^3 volumetric flask and make up to volume with deionised water. Label the flask 'zero time'.

4. Withdraw further 1 cm^3 samples every minute for 10 minutes and dilute them as described in step 3. Label them '1 min' to '10 min'.

For 'zero time' and each of the other diluted samples:

5. Pipette 5 cm^3 of the solution into a 100 cm^3 volumetric flask. 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.

6. Then add 1 cm^3 of 5 mol dm^{-3} hydrochloric acid. Make up to the mark with deionised water.

7. After 20 minutes measure the absorbance and use it to calculate the concentration of paracetamol.

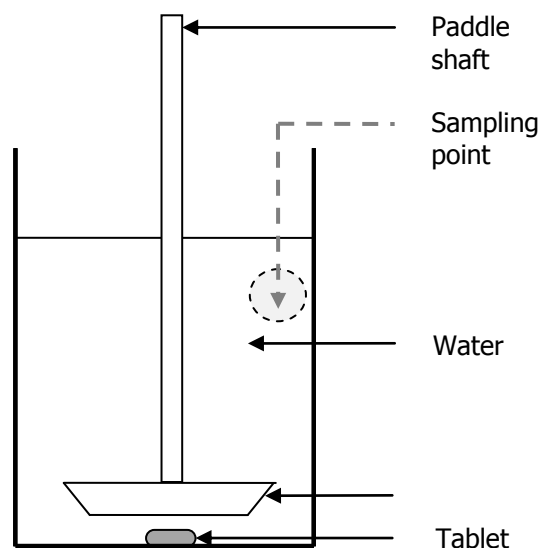8. Now calculate the concentration of paracetamol in the sample taken.

Figure Experimental set up.

Possible extension ideas

Compare the rates of dissolution of various paracetamol formulations, such as capsules and dispersible ('soluble') paracetamol.

Repeat the experiment using buffer solutions that reflect pH values found in the gastrointestinal tract instead of water.

Processing data

1. Plot a graph of the concentration of paracetamol in solution against the time the sample was taken. Describe the shape of the graph obtained.

2. Depending on what, if any, of the extension ideas were tried, comment on:

   a) differences in rates of dissolution of different paracetamol formulations;
   b) the effect of pH on the rate of dissolution (bearing in mind how the pH of fluids in the gastrointestinal tract varies).