

ACTIVITY BRIEF

Researching and planning chemical assays

The science at work

Quantitative chemical analysis is used to determine the purity of ingredients used to make medicines. Acceptable purities and analytical methods are provided in publications such as the British Pharmacopoeia. The ingredients of medicines are listed on the packaging. Look and you will notice that some of the ingredients have the letters 'BP' after them. This means they meet standards defined in the British Pharmacopoeia. Other publications include the European Pharmacopoeia.

Nearly all medicines are formulations. In other words they are mixtures made to a particular specification. Again, labels on the medicines tell you how much of the active ingredient is present. Quantitative chemical analysis is also used to check the composition of a medicine.

Your brief

You have to research and use quantitative chemical analysis techniques to assay the active ingredient of two medicines.

Find out about the available techniques and procedures. Then use or adapt suitable methods to carry out quantitative chemical analyses on your two chosen medicines.

Note that you will need to choose the medicines and match a method to each. Your choices will depend on:

- the medicines which are available for your use
- the quantitative chemical analyses which can be conducted safely, using the resources available to you.

Task 1 The British Pharmacopoeia

The British Pharmacopoeia is the authoritative collection of standards for UK medicines. Using *Study sheet: Investigating the British Pharmacopoeia*, find out about the pharmacopoeia and the type of information it contains.

Task 2 Looking at a typical BP assay

The British Pharmacopoeia contains assays for a vast range of medicines and their ingredients. However, you need to understand the chemistry behind the analysis in order to use the assays effectively. *Study sheet: Ibuprofen assay* guides you through a typical BP assay. It will help you to interpret the rather brief descriptions given in the BP.

Task 3 Assaying medicines containing aspirin

Compare assaying methods for aspirin in medicines. Choose a medicine containing aspirin and decide which assay you will use. Analyse the medicine, report the quantity of aspirin present and comment on how this compares with the quantity stated on the label.

Use *Practical sheet: Aspirin*.

Task 4 Assaying antacids

Many substances are used as antacid medicines. You are given a selection of BP assays. Choose an antacid medicine to analyse and decide which assay you will use. Analyse the medicine, report the quantity of active ingredient(s) present and comment on how this compares with the quantity stated on the label.

Use *Practical sheet: Antacids*.

STUDY SHEET

Investigating the British Pharmacopoeia

Introduction

From the British Pharmacopoeia website <http://www.pharmacopoeia.co.uk>:

British Pharmacopoeia (BP) - Setting standards for medicines

BP is the authoritative collection of standards for UK medicines and is an essential reference for anyone involved in pharmaceutical R&D, manufacture, testing and regulation. Produced by the British Pharmacopoeia Commission Secretariat, part of the MHRA.

Search the BP

Try using the BP to find ways of assaying medicines. All you need to do is type what you are looking for in the search engine. However, you may not find it straightforward to understand what you find.

So let's see how it works and what you need to be aware of.

Try typing the following types of medicine into the search engine:

- analgesic
- antacid
- antipyretic
- antiseptic
- laxative
- vitamin

Spend some time exploring the site. It might be a good idea to work in a group, each member taking responsibility for investigating one or two of the medicine types listed above.

Note: You may find that access is denied if you log in too often.

Some entries have this symbol alongside them:



This indicates that the entry is also part of the European Pharmacopoeia (Ph Eur)

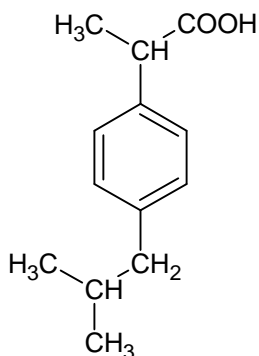
Find out about ...

- how the entries are laid out and the type of information they provide
- the difference between 'Medicinal and Pharmaceutical Substances' and 'Formulated Preparations'
- the types of analytical techniques used for assays.

In each case make a few brief notes to keep in your file or notebook.

STUDY SHEET

Ibuprofen assay



From the British Pharmacopoeia (BP) and the European Pharmacopoeia (Ph Eur):

DEFINITION

Content: 98.5 per cent to 101.0* per cent (dried substance)

Appearance: White, crystalline powder or colourless crystals

Solubility: Practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

Assay

Dissolve 0.450 g in 50 ml of *methanol R*. Add 0.4 ml of *phenolphthalein solution R1*. Titrate with *0.1 M sodium hydroxide* until a red colour is obtained. Carry out a blank titration.

1 ml of *0.1 M sodium hydroxide* is equivalent to 20.63 mg of C₁₃H₁₈O₂.

Notes

- You may wonder how there can be more than '100% content'. It allows for trace impurities that might give, in this case, an abnormally high acid content.
- ml = cm³
- M = mol dm⁻³ (or mol/dm³)
- *italicised words* are hyperlinks within the BP online database to further information.
- The IUPAC name for acetone is propanone and for methylene chloride is dichloromethane.
- The use of *R* and *R1* indicates that these chemicals are reagents.

The theory behind the analysis

Look at the structural formula for ibuprofen.

- 1 Write an equation for the reaction between ibuprofen and sodium hydroxide.
- 2 Write down the mole ratio in which ibuprofen and sodium hydroxide react.
- 3 Write down the molecular formula of ibuprofen and calculate its relative molecular mass.
- 4 Explain why '1 ml of *0.1 M sodium hydroxide* is equivalent to 20.63 mg of C₁₃H₁₈O₂'.
- 5 Explain why phenolphthalein is the preferred acid-base indicator?
- 6 Explain how the purity of a sample (as a percent by mass) would be estimated.

Practicalities

How do you know what apparatus and reagents to use?

1 Burette

- What volume of 0.1 mol dm^{-3} sodium hydroxide solution is required to react completely with 0.450 g ibuprofen?
- Why would a 50 cm^3 burette be the burette of choice?

2 Concentration of sodium hydroxide solution

In the context of the assay, 0.1 mol dm^{-3} sodium hydroxide solution really means $0.100 \text{ mol dm}^{-3}$ sodium hydroxide solution. Explain why.

You do not need to use $0.100 \text{ mol dm}^{-3}$ sodium hydroxide, but whatever you do use, you must know is concentration to three significant figures. How would you modify the assay if you were using $0.112 \text{ mol dm}^{-3}$ sodium hydroxide solution?

3 Mass of sample

It is quite difficult to weigh 0.450 g accurately. It is much easier to weigh accurately about 0.44-0.46 g. This means you weigh between 0.44 g and 0.46 g of sample to the nearest 0.001 g.

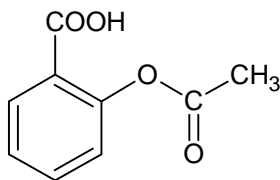
Assume that you want to get two titrations from a 50 cm^3 burette containing $0.105 \text{ mol dm}^{-3}$ sodium hydroxide solution. What mass of ibuprofen would you need for a titration of 23 cm^3 (allowing you ample solution for a second sample)? What instructions would you give in the assay?

Note: This analysis only applies to ibuprofen being added as the active ingredient to various medicines. Tablets containing ibuprofen usually have other ingredients and the method described here may not be suitable.

4 How would you carry out a 'blank titration' and what is its purpose?

PRACTICAL SHEET

Aspirin



On the next page, three methods are given for the quantitative chemical analysis of aspirin. Each works on a different principle (though two are closely related).

Begin by comparing the three assaying methods, in each case:

- researching a suitable method(s) for the quantitative analysis, including appropriate background scientific principles

Hopefully, *Study sheet: Ibuprofen assay* has prepared you for this.

- listing your information sources.

Although the assays are outlined, you need to list sources where you found out about the chemistry involved in the analytical techniques and about using the techniques correctly.

Having read through the methods, decide which aspirin product you will analyse. Now select the method you will use. For your chosen method:

- describe the practical procedures to be used

Write full instructions for the analysis by detailing the steps involved in the assay. You may decide to modify the method in some way. If so, make sure you give full details and an explanation for your modification. Check your revised method with your teacher before proceeding.

- select appropriate equipment and use it safely

Again, *Study sheet: Ibuprofen assay* should have helped you with this.

- do a risk assessment

Present your risk assessment to your teacher for approval before starting any practical work.

- carry out the analysis

- evaluate the method used.

If you work with others you can evaluate repeatability (consistency of your results when you repeat an analysis) and reproducibility (consistency of your results with those of other people).

Method 1

This assay derives from a method used in a West Country hospital pharmacy department.

Wear eye protection

Assay

Dissolve 0.5 g aspirin [HARMFUL] accurately weighed in 10 cm³ of 95% industrial denatured ethanol [HIGHLY FLAMMABLE] [HARMFUL]. Titrate this solution with 0.1 mol dm⁻³ sodium hydroxide [IRRITANT], using phenolphthalein solution [HIGHLY FLAMMABLE] as indicator.

Percentage by mass of aspirin = (1.802 x b)/a

where: a = mass of sample; b = volume of 0.1 mol dm⁻³ sodium hydroxide used

Method 2

This assay derives from the British Pharmacopoeia assay for aspirin.

Wear eye protection

Assay

In a flask with a ground-glass stopper, dissolve 1.000 g aspirin [HARMFUL] in 10 cm³ of industrial denatured alcohol [HIGHLY FLAMMABLE] [HARMFUL]. Add 50.0 cm³ of 0.5 mol dm⁻³ sodium hydroxide [CORROSIVE]. Close the flask and allow to stand for 1 h. Using 0.2 cm³ of phenolphthalein solution [HIGHLY FLAMMABLE] as indicator, titrate with 0.5 mol dm⁻³ hydrochloric acid. Carry out a blank titration.

1 cm³ of 0.5 mol dm⁻³ sodium hydroxide is equivalent to 45.04 mg of C₉H₈O₄.

Method 3

This assay derives from the British Pharmacopoeia assay for aspirin tablets.

Wear eye protection

Assay

Weigh and powder 20 tablets. To a quantity of the powder containing 0.5 g of aspirin [HARMFUL] add 30 cm³ of 0.5 mol dm⁻³ sodium hydroxide [CORROSIVE], boil gently for 10 minutes and titrate the excess of alkali with 0.5 mol dm⁻³ hydrochloric acid using phenol red solution as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of sodium hydroxide required.

Each cm³ of 0.5 mol dm⁻³ sodium hydroxide is equivalent to 45.04 mg of C₉H₈O₄.

Method 4

Spectrophotometry is used in the analysis of medicines, but the technique is not found in pharmacopoeias applied to the analysis of aspirin. However, there are a number of websites that outline possible methods. Each is based on the reaction between iron(III) chloride and phenols to give intensely coloured purple solutions.

Assay – Find possible methods by typing 'spectrophotometric aspirin analysis' into your favoured search engine on the Internet.

PRACTICAL SHEET

Antacids

There are many antacids on the market. Carry out a brief survey (either by visiting a pharmacy, e.g. at your local supermarket, or by using the Internet). Make a note of the company that manufactures them and the name and quantity of the active ingredients.

Below are a number of methods for the quantitative chemical analysis of some antacids.

Your task is to choose an antacid and match it to an appropriate assaying method.

- Research the method and explain the background scientific principles to the assay.

Hopefully, *Study sheet: Ibuprofen assay* has prepared you for this.

- List your information sources.

Although the assays are outlined, you need to list sources where you found out about the chemistry involved in the analytical techniques and about using the techniques correctly.

- Describe the practical procedures to be used.

Write full instructions for the analysis by detailing the steps involved in the assay. You may decide to modify the method in some way. If so, make sure you give full details and an explanation for your modification. Check your revised method with your teacher before proceeding.

- Select appropriate equipment and use it safely.

Again, *Study sheet: Ibuprofen assay* should have helped you with this.

- Do a risk assessment.

Present your risk assessment to your teacher for approval before starting any practical work.

- Carry out the analysis.

- Evaluate the method used.

If you work with others, you can evaluate repeatability (consistency of your results when you repeat an analysis) and reproducibility (consistency of your results with those of other people)

The assays

All the assays are based on British Pharmacopoeia assays.

Sodium hydrogencarbonate

Sodium hydrogencarbonate is also known as sodium bicarbonate (the name under which it can be found in the BP) and bicarbonate of soda. It is an 'old fashioned' remedy for indigestion and heart burn. It is also the active ingredient in medicines such as *Alka Seltzer*[®].

Assay

Dissolve 1.500 g in 50 cm³ of carbon dioxide-free distilled water. Titrate with 1 mol dm⁻³ hydrochloric acid, using 0.2 cm³ of methyl orange solution as indicator.

1 cm³ of 1 mol dm⁻³ hydrochloric acid is equivalent to 84.0 mg of sodium hydrogencarbonate, NaHCO₃.

Magnesium hydroxide mixture ('Milk of magnesia')

Milk of Magnesia[®] is a suspension of magnesium hydroxide in water. It is found in the BP under the name magnesium hydroxide mixture.

Wear eye protection

Assay

Mix 10 g with 50 cm³ of water, add 50 cm³ of 0.5 mol dm⁻³ sulfuric acid [IRRITANT] and titrate the excess acid with 1 mol dm⁻³ sodium hydroxide [CORROSIVE] using methyl orange as indicator.

1 cm³ of 0.5 mol dm⁻³ sulfuric acid is equivalent to 29.16 mg magnesium hydroxide, Mg(OH)₂.

Calcium carbonate

The active ingredient in many antacids is calcium carbonate. It is usually available in the form of tablets which contain other non-active ingredients such as binders.

Wear goggles (because of the use of very concentrated sodium hydroxide)

Assay

Dissolve 0.150 g in 25 cm³ of approximately 2 mol dm⁻³ hydrochloric acid [IRRITANT]. Boil for 2 minutes, allow to cool and dilute to 50 cm³ with distilled water. Quantitatively transfer the solution to a 500 cm³ conical flask, and dilute to 300 cm³ with distilled water. Add 6.0 cm³ of approximately 10 mol dm⁻³ sodium hydroxide solution [CORROSIVE] and about 15 mg of Murexide indicator. Titrate with 0.1 mol dm⁻³ sodium edetate until the colour changes from violet to full blue.

1 cm³ of 0.1 mol dm⁻³ sodium edetate is equivalent to 10.01 mg of calcium carbonate, CaCO₃.

Magnesium carbonate

Wear eye protection

Assay

Dissolve 0.15 g in a mixture of 20 cm³ of water and 2 cm³ of 2 mol dm⁻³ hydrochloric acid [IRRITANT]. Dilute to 300 cm³ with distilled and add 10 cm³ of ammonia buffer pH 10.0 and about 50 mg of mordant black 11 triturate. Heat to 40 °C and titrate at this temperature with 0.1 mol dm⁻³ disodium edetate until the colour changes from violet to full blue.

1 cm³ of 0.1 mol dm⁻³ disodium edetate is equivalent to 8.43 mg of magnesium carbonate, MgCO₃.

Note: 'sodium edetate' is also called 'disodium edetate' or 'EDTA disodium salt'.

Teacher notes

AQA Unit 12 The actions and development of medicines

This activity relates to the following parts of the specification:

21.2 How you will be assessed

You need to produce a portfolio of evidence which considers the actions and development of two different medicines. You need to conduct a quantitative analysis and a bioassay for each medicine.

*B. a report on the quantitative analysis of each of the **two** chosen medicines including:*

- *researching a suitable method(s) for the quantitative analysis, including appropriate background scientific principles*
- *a list of information sources*
- *describing the practical procedures to be used*
- *selecting appropriate equipment and using it safely*
- *detailing carrying out the analysis*
- *carrying out risk assessment(s)*
- *evaluating the method(s) used.*

21.3 You need to know, understand and be able to demonstrate

In order to complete the requirements of this unit you will need to know, understand and be able to demonstrate relevant knowledge of the following:

- *the different categories of medicines and their action*
- *the development of a medicine*
- *methods of analysing medicines.*

Methods of analysing medicines

You will need to:

- *research and provide details of a suitable method(s) to be used in the quantitative analysis and a suitable method(s) to be used in the bioassay. This will include details of the underlying scientific principles to be used*
- *describe in detail the practical procedures in the quantitative analysis and the practical procedures used in the bioassay including an explanation of the scientific principles involved*
- *select appropriate apparatus for both the quantitative analysis and bioassay*
- *carry out a risk assessment for the quantitative analysis and bioassay and complete the procedures in a safe manner*
- *evaluate the method used in the quantitative analysis and bioassay.*

The specifications for the unit also require the chemical analysis of two medicines. At the time of writing (March 2008) the AQA no longer required that the same two medicines be investigated for both bioassay and chemical analysis. Please refer to latest AQA guidance.

There is likely to be considerable differences in the extent to which students will be able to work autonomously on this unit. Consequently, it is likely that students will be at significantly different stages as time spent on the unit elapses. Some students will need considerable help in both the research and the practical phases of the unit.

Task 1: The British Pharmacopoeia

The purpose of this task is to give students a feel for the types of analyses used in pharmaceuticals. Information revealed by the searches may be a little confusing and students will need guidance and support.

- How the entries are laid out and the type of information they provide.

The molecular and structural formulae are usually given, together with relative molecular mass and CAS number. Entries also have identification tests, qualitative tests for impurities, assays and instructions for labelling.

- The difference between 'Medicinal and Pharmaceutical Substances' and 'Formulated Preparations'.

This is an opportunity to introduce or revise the difference between ingredients (medicinal and pharmaceutical substances) and the medicine itself (formulated preparation). The purity of ingredients must meet BP specifications and the quantities present in the formulation must meet the medicine's specification.

- The types of analytical techniques used for assays.

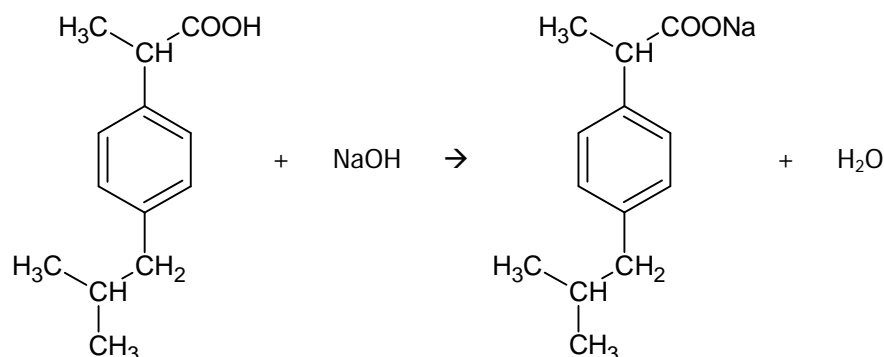
There are numerous volumetric analyses, including acid-base, redox, complexometric and potentiometric titrations. Chromatography is commonly used, but is unlikely to be a technique that students can use in school or college.

Task 2: Looking at a typical BP assay

The theory behind the analysis

- Write an equation for the reaction between ibuprofen and sodium hydroxide.

Answer



- Write down the mole ratio in which ibuprofen and sodium hydroxide react.

Answer 1:1

3 Write down the molecular formula of ibuprofen and calculate its relative molecular mass.

Answer Molecular formula = $C_{13}H_{18}O_2$; relative molecular mass = 206.3

4 Explain why '1 ml of 0.1 M sodium hydroxide is equivalent to 20.63 mg of $C_{13}H_{18}O_2$ '.

Answer 1 dm³ of 0.1 mol dm⁻³ sodium hydroxide contains 0.1 mol NaOH

Therefore, 1 cm³ of 0.1 mol dm⁻³ sodium hydroxide contains (0.1 ÷ 1000) mol NaOH

Since ibuprofen and sodium hydroxide react in a 1:1 mole ratio, 1 cm³ of 0.1 mol dm⁻³ sodium hydroxide reacts with (0.1 ÷ 1000) mol ibuprofen

1 mole of ibuprofen has a mass of 206.3 g

Therefore, (0.1 ÷ 1000) mol ibuprofen has mass of (0.1 ÷ 1000) × 206.3 g = 0.02063 g = 20.63 mg

5 Explain why phenolphthalein is the preferred acid-base indicator?

Answer This is a reaction between a weak acid and a strong alkali. The pH of the reaction at the end-point of the titration will be much higher than 7. Phenolphthalein is used because it changes colour over the pH range 8.3-10 (colourless < pH 8.3; pink > pH 10.0).

6 Explain how the purity of a sample (as a percent by mass) would be estimated.

Answer The titration allows the mass of ibuprofen in the sample to be calculated. The purity of the sample is calculated by:

$$\frac{\text{mass of ibuprofen in the sample} \times 100 \%}{\text{mass of the sample}}$$

Practicalities

1 Burette

- a What volume of 0.1 mol dm⁻³ sodium hydroxide solution is required to react completely with 0.450 g ibuprofen?

Answer 0.450 g ibuprofen contains (0.450 ÷ 206.3) mol ibuprofen = 0.002181 mol

Since ibuprofen and sodium hydroxide react in 1:1 mole ratio, 0.002181 mol NaOH is required for complete reaction.

1 cm³ of 0.1 mol dm⁻³ sodium hydroxide contains (0.1 ÷ 1000) = 0.0001 mol NaOH

Therefore, volume containing 0.002181 mol NaOH = 21.81 cm³

Therefore, volume of 0.1 mol dm⁻³ sodium hydroxide solution is required to react completely with 0.450 g ibuprofen = 21.81 cm³

- b Why would a 50 cm³ burette be the burette of choice?

Answer (i) it would enable two titrations to be carried out without the need for refilling, allowing two samples to be analysed to check repeatability, (ii) the smallest division on the burette is 0.1 cm³, and with practice the volume can be estimated to the nearest 0.05 cm³, giving a percentage uncertainty of about 0.05 in 21.81 cm³, i.e. about 0.2 %.

2 Concentration of sodium hydroxide solution

In the context of the assay, 0.1 mol dm⁻³ sodium hydroxide solution really means 0.100 mol dm⁻³ sodium hydroxide solution. Explain why.

Answer To say that '1 ml of 0.1 M sodium hydroxide is equivalent to 20.63 mg of $C_{13}H_{18}O_2$ ' implies that the concentration of the sodium hydroxide solution produces a measurement uncertainty of four significant figures, i.e. ± 0.01 mg in the calculated

mass of ibuprofen. However, other factors also affect the result, e.g. accuracy and precision of the titre volume.

You do not need to use $0.100 \text{ mol dm}^{-3}$ sodium hydroxide, but whatever you do use, you must know its concentration to three significant figures. How would you modify the assay calculation if you were using $0.112 \text{ mol dm}^{-3}$ sodium hydroxide solution?

Answer If 1 cm^3 of $0.100 \text{ mol dm}^{-3}$ sodium hydroxide is equivalent to 20.63 mg of $\text{C}_{13}\text{H}_{18}\text{O}_2$, then 1 cm^3 of $0.112 \text{ mol dm}^{-3}$ sodium hydroxide is equivalent to 23.11 mg of $\text{C}_{13}\text{H}_{18}\text{O}_2$.

3 Mass of sample

It is quite difficult to weigh 0.450 g accurately. It is much easier to weigh accurately about $0.44\text{--}0.46 \text{ g}$. This means you weigh between 0.44 g and 0.46 g of sample to the nearest 0.001 g .

Assume that you want to get two titrations from a 50 cm^3 burette containing $0.105 \text{ mol dm}^{-3}$ sodium hydroxide solution. What mass of ibuprofen would you need for a titration of 23 cm^3 (allowing you ample solution for a second sample)? What instructions would you give in the assay?

Answer
 23 cm^3 of $0.105 \text{ mol dm}^{-3}$ sodium hydroxide contains $(0.105 \div 1000) \times 23 \text{ mol NaOH}$. This would react with $(0.105 \div 1000) \times 23 \text{ mol ibuprofen} = (0.105 \div 1000) \times 23 \times 206.3 \text{ g} = 0.498 \text{ g ibuprofen}$.

Therefore, the assay might say,

Weigh accurately about 0.5 g of sample and dissolve in 50 cm^3 of methanol. Add 0.4 cm^3 of phenolphthalein solution. Titrate with $0.105 \text{ mol dm}^{-3}$ sodium hydroxide solution until a red colour is obtained. Carry out a blank titration.

1 cm^3 of $0.105 \text{ mol dm}^{-3}$ sodium hydroxide solution is equivalent to 21.66 mg of $\text{C}_{13}\text{H}_{18}\text{O}_2$.

4 How would you carry out a 'blank titration' and what is its purpose?

Answer Follow the instructions, but do not include the ibuprofen sample. The purpose is to allow for the acidity (if any) of other substances present in the titration. If the titration is, say, 0.15 cm^3 this volume should be deducted from the titration result for the sample.

General note about tasks 3 and 4

The assays are provided in the same brief concise style of the BP assays from which they derive.

Having been guided through the BP assay for ibuprofen, students should be able to tackle the planning and carrying out required by the unit specifications:

- researching the method and explaining the background scientific principles to the assay
- listing information sources

Although the assays are outlined, students need to list sources where they found out about the chemistry involved in the analytical techniques and about using the techniques correctly.

- describing the practical procedures to be used – students need to write step-by-step instructions for each analysis. They may decide to modify the method in some way. If so, you should check that the modifications are acceptable and if they are not, offer students guidance on how to proceed.

- selecting appropriate equipment and using it safely – they need to list the equipment and materials needed and be able to explain their choices
- making a risk assessment – you must check any risk assessment produced by a student and approve it or modify it if necessary before the student starts any practical work.
- carrying out the analysis – you will want to monitor their work, checking that they are using equipment and handling materials correctly and safely.
- evaluating the method used – students should carry out repeat analyses to check the repeatability of their results (repeatability being the consistency of results obtained by the same person). If they work in a group, reproducibility (consistency of results obtained by two or more people) can be evaluated.

Task 3: Assaying medicines containing aspirin

For methods 1-3 students might be encouraged to follow the same approach as they were guided through in task 2.

For methods 1-3 each analysis requires:

- balance that weighs to the nearest 0.001 g or better
- 50 cm³ burette

Method 1

Students must wear eye protection

This is a direct acid-base titration. It is not mentioned in the British Pharmacopeia, but was used in a West Country hospital to check the purity of aspirin.

Dissolve 0.5 g aspirin [HARMFUL] accurately weighed in 10 cm³ of 95% ethanol (industrial denatured alcohol) [HIGHLY FLAMMABLE] [HARMFUL]. Titrate this solution with 0.1 mol dm⁻³ sodium hydroxide [IRRITANT], using phenolphthalein solution [HIGHLY FLAMMABLE] as indicator.

Students may experience some difficulty in dissolving the aspirin unless it is finely powdered. 0.5 g of aspirin would require 27.7 cm³ of 0.1 mol dm⁻³ sodium hydroxide. In order to get two titrations from a '50 cm³ burette-full' of 0.1 mol dm⁻³ sodium hydroxide, students might decide to use slightly less aspirin. For example, 0.4 g would require 22.2 cm³ of 0.1 mol dm⁻³ sodium hydroxide.

Method 2

This is used to check the purity of aspirin that is to be incorporated into a formulation. It involves an acid-base back titration.

Students must wear eye protection

In a flask with a ground-glass stopper, dissolve 1.000 g aspirin [HARMFUL] in 10 cm³ of alcohol (industrial denatured alcohol) [HIGHLY FLAMMABLE] [HARMFUL]. Add 50.0 cm³ of 0.5 mol dm⁻³ sodium hydroxide [CORROSIVE]. Close the flask and allow to stand for 1 h. Using 0.2 cm³ of phenolphthalein solution [HIGHLY FLAMMABLE] as indicator, titrate with 0.5 mol dm⁻³ hydrochloric acid. Carry out a blank titration.

In this analysis sodium hydroxide hydrolyses the aspirin and then reacts with the 2-hydroxybenzoic acid that forms. In total, 1 mol aspirin reacts with 2 mol sodium hydroxide. 1 g of aspirin would require 22.2 cm³ of 0.5 mol dm⁻³ hydrochloric acid to neutralise the unreacted sodium hydroxide.

Students might choose to use smaller quantities, e.g. 0.2 g aspirin and 0.1 mol dm⁻³ solutions of sodium hydroxide and sulfuric acid. These present less of a hazard. They might also look at method 3 and choose to omit the ethanol and gently boil the aspirin/sodium hydroxide mixture for 10 minutes rather than leaving it to stand for 1 hour.

Method 3

This is used to check the aspirin content of aspirin tablets. It involves an acid-base back titration. Students might be asked why method 1 is not used for aspirin tablets.

Students might be given the prompt question: why are 20 tablets taken? This will highlight the importance of sampling.

Students must wear eye protection

Weigh and powder 20 tablets. To a quantity of the powder containing 0.5 g of aspirin [HARMFUL] add 30 cm³ of 0.5 mol dm⁻³ sodium hydroxide [CORROSIVE], boil gently for 10 minutes and titrate the excess of alkali with 0.5 mol dm⁻³ hydrochloric acid using phenol red solution as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of sodium hydroxide required.

This analysis uses the same chemistry as method 2.

Method 4

This method relies on the fact that aspirin can be hydrolysed using a strong alkali to give 2-hydroxybenzoic acid, which contains a phenol group. Phenols form characteristic purple coloured solutions when mixed with a neutral solution of iron(III) chloride.

Carrying out a Google search for 'spectrophotometric aspirin analysis' gives these web pages:

http://www.usi.edu/science/chemistry/mkrahlin/courses/CHEM_321/Spectrophotometric%20Aspirin.pdf

<http://services.juniata.edu/ScienceInMotion/chem/labs/ap/aspirin.doc>

<http://www.westminster.edu/acad/sim/documents/SSPECTROPHOTOMETRICANALYSISOFASPIRIN1.pdf>

http://www.chem.purdue.edu/teacher/table_of_contents/Spectronic%20Educator/VISASPIR.pdf

<http://www.hccsc.k12.in.us/huntingtonnorth/perkins/Website%20Update/Labs/Experiment%2020-The%20Analysis%20of%20Aspirin.doc>

(all last accessed on 22 April 2008)

All of the procedures give very similar methods for the analysis of aspirin based on the reaction between 2-hydroxybenzoic acid [HARMFUL] and iron(III) chloride [the solid is HARMFUL and the solution if 0.2M or greater is an IRRITANT].

However, students will require access to a spectrometer that allows absorbance at 530 nm to be measured. If this is not available, students might try a colorimeter, using a green filter.

Task 4: Assaying antacids

Many antacid medicines have more than one active ingredient. This makes them quite difficult to analyse.

For example:

- *Gaviscon Acid Breakthrough Formula*: antacid is 0.5 g of calcium carbonate
- *Gaviscon Extra Strength Tablets*: antacid is 0.16 g of aluminium hydroxide and 0.105 g of Magnesium Carbonate
- *Gaviscon Regular Strength Tablets*: antacid is 0.08 g of aluminium hydroxide and 0.02 g of magnesium carbonate
- *Tums Quik Pak*: antacid is 1 g of calcium carbonate
- *Tums Ultra 1000*: antacid is 1 g of calcium carbonate
- *Maalox Regular – Chewable*: antacid is 0.6 g of calcium carbonate
- *Maalox Regular – Liquid*: each 5 cm³ contains the antacids aluminium hydroxide (0.2 g) and magnesium hydroxide (0.2 g)
- *Roloids*: antacids are calcium carbonate (0.55 g) and magnesium hydroxide (0.11 g)
- *Phillips' Milk of Magnesia*: each 15 cm³ contains magnesium hydroxide (10.2 g)

Therefore, encourage students to select antacids with a single active ingredient.

Acid-base titrations

Sodium hydrogencarbonate

Dissolve 1.500 g in 50 cm³ of carbon dioxide-free distilled water. Titrate with 1 mol dm⁻³ hydrochloric acid, using 0.2 cm³ of methyl orange solution as indicator.

This is a straightforward acid-base titration. Boil the distilled water before use to remove carbon dioxide, but cool again before pipetting samples, or the volume will be inaccurate.

Magnesium hydroxide mixture

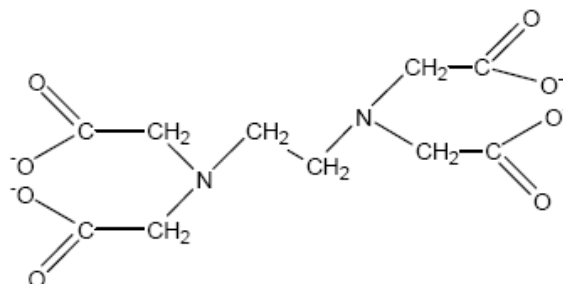
Wear eye protection

Mix 10 g with 50 cm³ of water, add 50 cm³ of 0.5 mol dm⁻³ sulfuric acid [IRRITANT] and titrate the excess acid with 1 mol dm⁻³ sodium hydroxide [CORROSIVE] using methyl orange as indicator.

This is another straightforward acid-base titration. The most challenging part is getting a suitable representative sample. *Milk of magnesia* is a suspension and, therefore, tends to settle when left to stand. The mixture must be thoroughly shaken and the sample poured quickly before the suspended magnesium hydroxide can settle.

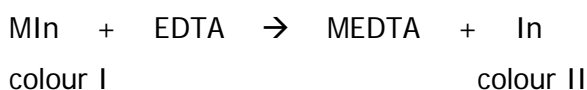
Complexometric titrations

In a complexometric titration the reaction between the analyte and the titrant involves complex formation. EDTA, ethylenediaminetetraacetic acid (disodium edetate *VS*), can be used to analyse metal ions with which it forms 1:1 complexes. EDTA is a multidentate ligand.



A ligand is an atom or group of atoms that can bind to another atom by forming coordinate (or dative) bonds. To function as a ligand, the atom must possess a pair of non-bonding electrons that it can share with the other atom prepared to accept them. In alkaline conditions, EDTA has six such atoms (four oxygen atoms and two nitrogen atoms) through which it binds to the metal ions. So EDTA is a hexadentate ligand. If two or more electron pairs of a multidentate ligand form coordinate bonds to the central atom, the resulting complex is called a chelate.

When EDTA is used in complexometric titrations, a metal ion indicator is used. A metal ion indicator changes colour when it binds to a metal ion. For the metal ion indicator to be useful in these types of titrations it must bind to the metal loosely so that the following process can take place.



Murexide is the indicator of choice in the calcium titration. The colour change is from wine red to purple when the end point is reached.

Mordant black 11 triturate (also called Eriochrome black T) is the indicator of choice in the magnesium titration. The colour change is from violet to deep blue.

Calcium carbonate

Students must wear goggles (because they are using concentrated sodium hydroxide)

Dissolve 0.150 g in 25 cm³ of approximately 2 mol dm⁻³ hydrochloric acid [IRRITANT]. Boil for 2 min, allow to cool and dilute to 50 cm³ with distilled water. Quantitatively transfer the solution to a 500 cm³ conical flask, and dilute to 300 cm³ with distilled water. Add 6.0 cm³ of approximately 10 mol dm⁻³ sodium hydroxide solution [CORROSIVE] and about 15 mg of Murexide indicator. Titrate with 0.1 mol dm⁻³ sodium edetate until the colour changes from wine red to purple.

Magnesium carbonate

Students must wear eye protection

Dissolve 0.15 g in a mixture of 20 cm³ of water and 2 cm³ of 2 mol dm⁻³ hydrochloric acid [IRRITANT]. Dilute to 300 cm³ with distilled and add 10 cm³ of ammonia buffer pH 10.0 and about 50 mg of mordant black 11 triturate. Heat to 40 °C and titrate at this temperature with 0.1 mol dm⁻³ disodium edetate until the colour changes from violet to full blue.