

Comparison of the active ingredient and purity of two different commercial Aspirin tablets

## COSHH ASSESSMENT

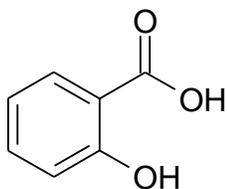
<b>Chemicals- Hazardous in quantities used in experiment</b>	
Salicylic acid	<b>IRRITANT</b> if inhaled or comes in contact with eyes or skin.
Ethanol	<b>HIGHLY FLAMMABLE</b>
Ferric chloride	<b>CORROSIVE</b> causes burns to eyes/skin. <b>HARMFUL</b> if swallowed
Iodide reagent	<b>HARMFUL</b> if swallowed
Hydrochloric acid	<b>CORROSIVE</b> . Causes severe burns to skin/eyes. Extremely harmful vapour. Dispense in fume cupboard. <b>WEAR GLOVES</b> .
Acetone	<b>HIGHLY FLAMMABLE</b> . Can cause serious damage if splashed into eyes. Degreases skin, possibly causing dermatitis. Vapour narcotic in high concentrations. Evacuate laboratory if spillage exceeds 80 cm <sup>3</sup>
Sodium nitrite	<b>TOXIC</b> by ingestion, large doses causing nausea, vomiting, cyanosis, collapse and coma. Small doses cause a fall in blood pressure, headache and visual disturbances. <b>IRRITATING</b> to eyes.
Alkaline β-naphthol	<b>CORROSIVE</b> . Causes burns to skin and eyes. If ingested causes severe internal irritation and damage.
Methanol	<b>HIGHLY FLAMMABLE</b> . <b>TOXIC</b> by ingestion. Damaging if splashed into eyes. High concentrations of vapour may cause dizziness, stupor, cramps and digestive disturbance. Lower levels may cause headache and nausea. Chronic effects-damages the central nervous system, particularly the optic nerve and internal organs. Evacuate laboratory if spillage exceeds 80 cm <sup>3</sup>
Brady's reagent	<b>TOXIC</b> by ingestion, inhalation and skin contact. <b>IRRITATING</b> to eyes and skin. Danger of cumulative effects.
Chloroform	<b>VERY TOXIC</b> by inhalation and ingestion. <b>IRRITATING</b> to the eyes and skin and has been found to cause cancer in laboratory animals. May cause adverse mutagenic or teratogenic effects. Evacuate laboratory if spillage exceeds 10 cm <sup>3</sup>
Acetyl chloride	<b>HIGHLY FLAMMABLE</b> . Causes severe burns. Vapour is extremely irritating to eyes and mucous membranes. If ingested causes severe internal irritation and damage.
<b>First aid for above chemicals</b>	
Eyes	Irrigate thoroughly with water for at least 10 minutes. <b>OBTAIN MEDICAL ATTENTION.</b>
Lungs	Remove from exposure, rest and keep warm. In severe cases <b>OBTAIN MEDICAL ATTENTION.</b>
Skin	Wash off thoroughly with water. Remove contaminated clothing and wash before re-use. In severe cases <b>OBTAIN MEDICAL ATTENTION.</b>
Mouth	Wash out mouth thoroughly with water and give plenty of water to drink. <b>OBTAIN MEDICAL ATTENTION.</b>

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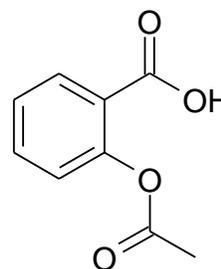
### Background

Salicylic acid is an effective medicine for reducing pain, fever and swelling. Many plants have been found to produce salicylic acid naturally, such as the willow tree, which was recognised over 2000 years ago as a valuable source of medicine. Salicylic acid is found mainly in the leaves and bark of the willow tree. Despite its analgesic properties, salicylic acid is also an extremely irritating substance that burns the sensitive linings of the mouth, throat, oesophagus and stomach. These unwanted side effects can be attributable to the carboxylic acid ( $-\text{CO}_2\text{H}$ ) and phenol ( $\text{PhOH}$ ) groups, both of which are acidic. A way to remediate these undesirable properties without rendering the medicine ineffective is to derivatise the phenolic hydroxyl group ( $-\text{OH}$ ) with an acetyl group ( $-\text{COCH}_3$ ), yielding acetyl salicylate. This is the active ingredient found in commercial 'Aspirin', but it does not occur naturally. Acetyl salicylate contains just one acidic functional group, and passes through most of the digestive system of the body without causing burns. For the majority of commercial samples of Aspirin, the contents are labelled as Aspirin, lactose, starch and talc.

**Salicylic acid**



**acetyl salicylate (Aspirin)**



## **Aims and objectives of current investigation**

The aims of the investigation are to determine the amount and identity of the active ingredient in Aspirin tablets, and to compare the results of different commercial sources. Over a series of sessions, you will:

- Design two experimental procedures to extract the active component(s) from samples of Aspirin.
- Quantify the amount and % composition of the active component(s) within the Aspirin samples.
- Identify the structures of the active component(s) by performing analytical tests on the extracts.
- Compare your results with literature data for the expected product(s) and assess the purity / composition of the active ingredient(s) (e.g. How accurate are the claims on the packaging?).
- Evaluate the different experimental procedures.

The style of these laboratory sessions may be somewhat different to that which you have experienced before. For example, in the first session, you will be discussing some aspects of experimental design before implementing an agreed procedure. The results of this first experiment will then be discussed and used to plan for a second, possibly improved method to be carried out in the next session. The investigation will also give you the opportunity to use some laboratory skills/techniques for which you should already have had some previous experience (e.g. functional group tests, melting points, IR, GC).

This problem-based approach should enable you to develop your laboratory skills and your understanding of the underlying chemistry.

## Session 1

The aim for Session 1 is to isolate the active ingredient from two commercial Aspirin tablets, compare the yields obtained from each source, and identify the nature of the extracted chemical(s). When designing your method, you should consider the following:

- The experimental procedure: it should be simple, rapid (no longer than 1 hour) and must address the aim of the session.
- Some/all of the glassware and solvents available to you
- The type of simple chemical tests that you could perform on your extract to determine its composition.
- The collation of relevant data. You will need to record results and observations in order to evaluate the success of the procedure.

Discuss the aims of the experiment and suggest some methods that should enable you to achieve these aims. You will have **20 minutes** to do this.

**Note:** When designing an experimental procedure, it is helpful to consider the following:

- Glassware/equipment that is available to you
- Experimental order
- Time
- Safety
- Solvents available to you
- The desired outcome(s)
- Data/information to be recorded

## **Method to carry out a simple extraction of acetyl salicylate from Aspirin**

Use 2 tablets of each Aspirin sample provided.

Aspirin tablets contain starch as a binder. The active component of Aspirin is soluble in hot ethanol, but the starch is not. Weigh the 2 tablets accurately to 3 decimal places then finely crush them to a powder on a piece of hard filter paper using a spatula. Transfer the powder to a 50 cm<sup>3</sup> conical flask, add 20 cm<sup>3</sup> of ethanol and heat the mixture until it boils on a hot plate. At this point, filter the hot mixture through fluted filter paper into a *pre-weighed* 100 cm<sup>3</sup> beaker and then evaporate the filtrate to dryness. Use a hotplate to remove most, but not all of the solvent. Remove the final 10-20% of the ethanol on a steam bath. Allow the beaker to cool. Re-weigh the beaker containing your extract and determine the yield. Perform some simple chemical tests on your extract to investigate the suitability of the extraction procedure.

### **Chemical tests:**

Carry out chemical tests (a) and (b) on the following (record all observations):

- Both extracts
- An Aspirin tablet (finely crushed) which has not been extracted.
- An authentic sample of salicylic acid.
- The discarded fluted filter paper and the residue in the conical flask.

Note: Quantities of compounds / reagents described for these qualitative tests are guidelines only.

#### (a) Ferric Chloride Test for a free phenolic (–OH) group:

The addition of ferric chloride to salicylic acid produces a specific colour following a reaction with aqueous ferric  $[\text{Fe}(\text{H}_2\text{O})_6]^{3+}$  ions. The oxygen atoms of the carboxylic acid group (–CO<sub>2</sub>H) and the phenol group (–OH) concomitantly form a complex with  $[\text{Fe}(\text{H}_2\text{O})_6]^{3+}$ . This complex has an intense violet colour. With acetyl salicylate, the (–OH) group of salicylic acid has been replaced by a (–O–COCH<sub>3</sub>) group, which prevents the formation of the violet-coloured complex .

Add 3 drops of ferric chloride solution to 0.2 g of a crushed Aspirin tablet in about 2 cm<sup>3</sup> of water. If you observe a violet colouration, this indicates the presence of the free phenol –OH group. Repeat the test using 0.1 g of salicylic acid and 0.1 g of your extracted samples. Note any differences between the intensities of the violet colour and consider the significance of these differences.

(b) Test for starch

Add 1-2 drops of Iodine-KI reagent to a small amount of your sample. Samples containing starch will produce a blue-black colour. If starch is not present, the colour will remain orange/yellow. What would the presence of starch in your extract indicate about the selectivity of the extraction? What impact might this have on the % extraction calculations ?

**Session 1 Post-laboratory Exercise**

Complete the accompanying tables and consider the outcomes of the tests along with your responses to the following statements (choose 'agree', 'disagree' or 'cannot be sure'). Give a brief justification for your answer in each case.

1. Weighing the extract reveals its chemical composition.
2. If the mass of the extract is equal to the original mass of the tablets, the extraction can be described as 100% efficient.
3. An efficient extraction yields 100% of the active ingredient.
4. Expressing the yield of extract as a % of the original mass of tablet gives the extraction efficiency of the active ingredient.
5. The mass of active ingredient in each tablet is exactly the same.
6. Expressing the yield of extract as a % of the mass of the active ingredient given on the packaging could give an incorrect low value.
7. Expressing the yield of extract as a % of the mass of the active ingredient given on the packaging could give an incorrect high value.
8. It is unlikely that the extraction procedure would have caused degradation of acetyl salicylate.





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### Session 2 pre-laboratory exercise

Following the Session 1 discussion, it is unclear whether all of the active ingredient was obtained using the simple extraction method (i.e. whether the method was *quantitative*) and if the extract only contained the active ingredient (i.e. whether the method was *selective*). In addition, since the chemical test (ferric chloride) gives a positive result for salicylic acid, but a negative result for acetyl salicylate, this method is of limited value and does not provide conclusive proof of the presence of acetyl salicylate. More subtly, the test does not establish whether any significant transformation of acetyl salicylate to salicylic acid might have taken place during the extraction. With these points in mind, carry out the following tasks before the beginning of Session 2:

1. Research an alternative method for extracting the active ingredient from Aspirin tablets, focussing on extraction efficiency and possible degradation during extraction. How should this second method be an improvement on the first?
2. Suggest a titrimetric method for determining the amount of acetyl salicylate in an extract obtained from an Aspirin tablet. What features of the method make it suitable for direct analysis of acetyl salicylate (i.e. what makes it *fit for purpose?*).

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