May 2004 – Candidate #:

Chemistry Extended Essay

Word Count: 3,842

'The qualitative and quantitative analysis of acetylsalicylic acid in aspirin tablets and of salicylic acid in Salix alba (white willow bark).'

Abstract

Acetylsalicylic acid, found in aspirin, is manmade from salicylic acid. Felix Hoffmann discovered acetylsalicylic by adding an acetyl group to salicylic acid. Acetylsalicylic acid is more palatable than salicylic acid and therefore provides greater benefits. When ingested acetylsalicylic acid combines with water to form salicylic acid. **'The qualitative and quantitative analysis of acetylsalicylic acid in aspirin tablets and of salicylic acid in Salix alba (white willow bark).'** allowed for an estimation of the quantity of Salix alba needed to be ingested for it to produce the benefits of a painkiller.

The published mass of acetylsalicylic acid present in each aspirin tablet is 300mg. To test this, back titrations were performed on several brands of aspirin. These values were compared to 300mg and with the quantities of acetylsalicylic acid found in the other brands of aspirin. Most of the brands tested contained around 300mg of acetylsalicylic acid and were therefore consistent with the published value. All of the brands had approximately the same mass of acid present.

Since aspirin is made from salicylic acid, originally extracted from Salix alba, the experiment hoped to prove the existence of salicylic acid in Salix alba bark. The willow was extracted and another back titration performed. Thin layer chromatography was also used to confirm the existence of the acid. By comparing the quantity of salicylic acid with the 300mg dose of acetylsalicylic acid found in aspirin tablets it was possible to predict the amount of willow bark that would have to be consumed to produce similar results as one aspirin tablet. The experiment showed the presence of a small amount of salicylic acid present in one gram of Salix alba. For the salicylic acid equivalent of 300mg of acetylsalicylic acid to be acquired, it would be necessary to consume 290g of bark.

Word Count: 297

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'The qualitative and quantitative analysis of acetylsalicylic acid in aspirin tablets and of salicylic acid in Salix alba (white willow bark).'

Introduction

Aspirin is over one hundred years old and used throughout the world. Felix Hoffmann invented aspirin in 1897 to treat his father's arthritis. Aspirin is an effective anti-inflammatory and can be used to treat rheumatism and arthritis. It was first sold as an anti-inflammatory and then as a painkiller, or analgesic. Aspirin helps prevent heart attacks and strokes by inhibiting the production of the blood clots that cause them. Recent studies at Boston University have shown that aspirin might also be effective in the prevention of bowel cancer. [1] Other cancers, such as turban tumour syndrome and some types of breast cancer, caused by inflammation, can also be treated with aspirin.[2] Aspirin stops the formation of prostaglandin synthase, found around injuries, which produces prostaglandins. These fatty acids cause inflammation and fevers. They also send information of injuries to the brain. By stopping the production of prostaglandin synthase, aspirin works as an anti-inflammatory and a painkiller.[3]

For decades humans have known that salicylic acid, present in Salix alba or white willow bark, relieves aches and pains. Native Americans chewed willow bark as a painkiller for centuries and Hippocrates also ground willow bark as a treatment for pains.[4] The Egyptians used willow leaves as painkillers in medicine. I plan to study pharmacy at university and find learning about traditional medicines interesting. Upon learning the history of aspirin, and taking into account that there are white willow trees around my house, I decided to try to detect any presence of salicylic acid in a sample of Salix alba bark. Before doing this I wanted to test different brands of aspirin, both soluble and insoluble, to determine how much acetylsalicylic acid was present, and if the mass remained constant throughout different brands. Finally, I decided to compare the mass of acetylsalicylic acid I calculated with the published mass. I thought that it would also be interesting to verify, if possible, the presence of salicylic acid in a sample of willow bark. When acetylsalicylic acid is ingested into the body, water is added and through a hydrolysis reaction acetylsalicylic acid is converted into salicylic acid.[5] Hoffmann synthesised acetylsalicylic by adding an acetyl group, composed of carbon, hydrogen and oxygen, to salicylic acid. Salicylic acid easily irritates the stomach and mouth but the addition of an acetyl group maintains its effectiveness as a painkiller while making it easier to ingest.[6] As acetylsalicylic acid is eventually converted into salicylic, I planned to compare the value of acetylsalicylic acid found in aspirin with the mass of salicylic acid in one gram of bark to determine the quantity of willow bark that would have to be consumed to produce the same effect as one aspirin tablet. In an attempt to answer my questions I decided to research **the qualitative and quantitative analysis of acetylsalicylic acid in aspirin tablets and of salicylic acid in Salix alba (white willow bark).**

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[1] An Aspirin a Day Keeps the Doctor at Bay; page 3
[2] Cure or Kill?; page 1
[3] Chemistry, for use with the International Baccalaureate; page 422
Chemistry for the IB Diploma; page 83
[4] Welcome to the Aspirin Foundation of America; page 1
[5] Chemistry, for use with the International Baccalaureate; page 421
[6] Aspirin Adventures; page 1

Performing a back titration is a simple method of determining the mass of acetylsalicylic acid found in different brands of aspirin. I expected to find that all of the brands would contain around the same mass of acetylsalicylic acid. I thought this because all of the brands have the same published mass of acetylsalicylic acid. I also predicted that the mass of acetylsalicylic acid I calculated would be relatively close to 300mg, the stated amount contained according to each company.

Preparation of 1.00moldm^{-3} sodium hydroxide

Before testing for the levels of acetylsalicylic acid, a 1.00moldm^{-3} sodium hydroxide solution had to be prepared. 20.00g of sodium hydroxide pellets were weighed and placed into a 500cm^3 beaker with 200cm^3 of distilled water. The solution was cooled in a water bath and placed into a fume hood in case harmful fumes were produced. The sodium hydroxide pellets were then dissolved in the distilled water. The solution was made up in a 500.0cm^3 standard flask. The assumption is made throughout that the sodium hydroxide made is exactly 1.00moldm^{-3}.

Preparation of an Approximately 0.1moldm^{-3} hydrochloric acid Solution Followed by the Standardisation of the hydrochloric acid

In order to make the 0.1moldm^{-3} hydrochloric acid, 9.00cm^3 of a concentrated (11moldm^{-3}) hydrochloric acid solution was placed into a 1000.00cm^3 standard flask and filled with distilled water.

Titrations determine the concentration of a solution through the use of a standard solution. When an acid and a base combine, salt and water are formed in a neutralisation reaction. In this case hydrochloric acid and sodium hydroxide react to produce water and sodium chloride.
$HCl_{(aq)} + NaOH_{(aq)} \rightarrow NaCl_{(aq)} + H_2O_{(l)}$

Phenolphthalein, clear in acidic solutions and pink or red in alkali solutions, was used as an indicator in the reaction. The endpoint, the point where both solutions react completely but neither are in excess, can be detected by observing this colour change. The endpoint is the point immediately before a permanent colour change.[7]
10.0cm^3 of the 1.00moldm^{-3} sodium hydroxide solution was then diluted with 90.00cm^3 of distilled water to produce a concentration of 0.10moldm^{-3}, in order to carry out a blank titration with the hydrochloric acid. 25.0cm^3 of 0.10moldm^{-3} sodium hydroxide was added to each of two conical flasks along with one drop of phenolphthalein. These solutions were titrated against hydrochloric acid (approximately 0.1molddm^{-3}), until the pink solution had just turned clear. The volume of hydrochloric acid added was recorded.

[7] Chemistry in Context; page207
Merrill Chemistry; page 616

Data Collection for the Titration Performed to Standardise the hydrochloric acid

	Number: 1	Number: 2
Final Burette reading/cm^3 ($\pm 0.05cm^3$)	23.50	23.40
Initial Burette reading/cm^3 ($\pm 0.05cm^3$)	0.00	0.00
Volume of HCl added/cm^3 ($\pm 0.05cm^3$)	23.50	23.40
Observations	Turned pale pink then colour disappeared.	Turned pale pink, then colour disappeared.

Data Analysis for the Standardisation of the hydrochloric acid

Initial calculations assumed the concentration of the hydrochloric acid to be exactly $0.100moldm^{-3}$. These results proved the presence of an inherent error which became obvious when attempting to calculate the mass of acetylsalicylic acid present in aspirin tablets. To produce more accurate results the hydrochloric acid was standardised against the sodium hydroxide with a known concentration of $0.100moldm^{-3}$. The concentration of the hydrochloric acid was found to be $0.107moldm^{-3}$.After recalculating the results, there was a significant improvement in the percentage difference in the determination of acetylsalicylic acid. (See page six)

Throughout the essay all final answers will be given to three significant figures

Calculations for determining the concentration of the hydrochloric acid:

$HCl_{(aq)} + NaOH_{(aq)} \rightarrow NaCl_{(aq)} + H_2O_{(l)}$

$v = 25.0cm^3$

$c = 0.100moldm^{-3}$

$n = c \times v$

$= 0.0250dm^3 \times 0.100moldm^{-3}$

$= \underline{2.50 \times 10^{-3}mol}$ - moles of NaOH

Hydrochloric acid and the sodium hydroxide form a 1:1 molar ratio.
Therefore: $\underline{2.50 \times 10^{-3}mol}$ - moles of hydrochloric acid

The concentration of the hydrochloric acid:

$c = n / v$

$$c = \frac{2.50 \times 10^{-3}\,mol}{(0.02345dm^3)}$$

$= \underline{0.107moldm^{-3}}$

Percentage uncertainty of the concentration of the $1.00moldm^{-3}$ sodium hydroxide:

% Uncertainty of C_{NaOH} = M_{NaOH} + V_{NaOH}

$$\% \text{ Uncertainty of } M_{NaOH} = \frac{0.005}{20.000} \times 100$$

$= \underline{0.025\%}$

$$\% \text{ Uncertainty of } V_{NaOH} = \frac{0.5}{500.0} \times 100$$

$= 0.100\%$

% Uncertainty of C_{NaOH} = 0.025 + 0.100
= **0.125%**

Percentage uncertainty of diluting the 1.00moldm^{-3} sodium hydroxide to a concentration of 0.100moldm^{-3}:

% Uncertainty of $C_{NaOH\ (0.100moldm\text{-}3)}$ = $C_{NaOH\ (1.00moldm\text{-}3)}$ + V_{NaOH} + V_{H2O}

% Uncertainty of $C_{NaOH\ (1.00moldm\text{-}3)}$ = 0.125%

% Uncertainty of V_{NaOH} = $\frac{0.06}{10.00}$ x100
= 0.600%

% Uncertainty of V_{H2O} = $\frac{0.04}{100.00}$ x 100
= 0.040%

% Uncertainty of $C_{NaOH\ (0.100moldm\text{-}3)}$ = 0.125 + 0.600 + 0.040
= **0.765%**

Percentage uncertainty of the concentration of the 0.107moldm^{-3} hydrochloric acid:

% Uncertainty C_{HCl} = V_{NaOH} + V_{HCl} +C_{NaOH}

% Uncertainty V_{NaOH} = $\frac{0.06}{25.00}$ x 100
= 0.24%

% Uncertainty V_{HCl} = $\frac{0.05}{23.45}$ x 100
= 0.213%

% Uncertainty of $C_{NaOH(1.00moldm\text{-}3)}$ = 0.125%

% Uncertainty C_{HCl} = 0.24 + 0.213 + 0.125
= **0.578%**

Acetylsalicylic acid Determination

Back titrations are performed when reactions occur too slowly for standard titrations to be used. As acetylsalicylic acid is insoluble an excess amount of a sodium hydroxide with a known concentration was added. A reaction then took place between the acid and the base, leaving the excess base to be titrated against a known concentration of hydrochloric acid. The mass of the insoluble acid can then be calculated.[8] The reaction between acetylsalicylic acid and sodium hydroxide is as follows.

$CH_3COOC_6H_4COOH_{(s)} + 2NaOH_{(aq)} \rightarrow CH_3COONa_{(aq)} + HOC_6H_4COONa_{(aq)} + H_2O_{(l)}$

To test the accuracy of the procedure, five tests were performed using weighed samples of acetylsalicylic acid. 0.100g, 0.200g, 0.300g, 0.400g and 0.500g of pure acetylsalicylic acid were weighed and placed into separate conical flasks. 25.00cm^3 of 1.00moldm^{-3} sodium hydroxide was added to each flask, followed by 25.00cm^3 of distilled water. The conical flasks were covered, to prevent evaporation, and left to simmer gently on a hotplate for ten minutes. Afterwards the solutions were left to cool in a water bath. Each solution was transferred into a 250.00cm^3 standard flask with washings and the flasks were made up with distilled water. 25.00cm^3 of each solution

[8] Chemistry, for use with the International Baccalaureate; page 41

was pipetted into three conical flasks and the solutions were titrated against a $0.107moldm^{-3}$ hydrochloric acid solution using phenolphthalein until just before the pink colour turned completely clear. The volumes of hydrochloric acid used were recorded. Titrations were carried out for all of the masses of acetylsalicylic acid.

Data Collection for acetylsalicylic acid Determination

Each different mass of acetylsalicylic acid was titrated three times, once roughly and then twice more, the mean volume of hydrochloric acid is the mean of the two more accurate titrations.

Mass (g) of acetylsalicylic acid (± 0.005)	**Mean Volume (cm^3) of $0.107moldm^{-3}$ HCl Added (± 0.05)**
0.100	22.20
0.200	21.55
0.300	20.20
0.400	18.93
0.500	17.95

Data Analysis- calculations for determining the mass of acetylsalicylic acid through the volume of hydrochloric acid added.

$CH_3COOC_6H_4COOH_{(s)} + 2NaOH_{(aq)} \rightarrow CH_3COONa_{(aq)} + HOC_6H_4COONa_{(aq)} + H_2O_{(l)}$

$v = 25.00cm^3$

$c = 1.00moldm^{-3}$

$n = c \times v$

$= 1.00moldm^{-3} \times 0.0250dm^3$

$= \underline{0.025}$ – initial volume of NaOH added

Example of calculations: The solution containing 0.100g acetylsalicylic acid to which $22.20cm^3$ of hydrochloric acid was added.

$HCl_{(aq)} + NaOH_{(aq)} \rightarrow NaCl_{(aq)} + H_2O_{(l)}$

$n = c \times v$

$n = 0.107 \times \frac{22.20}{1000}$

$= \underline{2.3754 \times 10^{-3}}$

This equals the moles of NaOH used to neutralise the HCl, as this is a 1:1 ratio.
Therefore Moles of NaOH = 2.3754×10^{-3}

The moles of NaOH is then multiplied by 10, as the $25.00cm^3$ of $1.0moldm^{-3}$ NaOH was then diluted when made up into a $250.0cm^3$ standard flask.

Moles of NaOH = $(2.3754 \times 10^{-3}) \times 10$

$= \underline{2.3754 \times 10^{-2}}$ – number of moles of NaOH neutralised by HCl

n used to neutralise $CH_3COOC_6H_4COOH$

= # n of NaOH initially – # n of NaOH neutralised by HCl

$= 2.5 \times 10^{-2} - 2.3754 \times 10^{-2}$

$= \underline{1.246 \times 10^{-3}}$ – Moles of NaOH used to neutralise the acetylsalicylic acid

Moles of $CH_3COOC_6H_4COOH$ present in the solution

$= \frac{1.246 \times 10^{-3}}{2}$ (As NaOH and $CH_3COOC_6H_4COOH$ form a 1:2 molar ratio.)

$= 6.23 \times 10^{-4}$ – moles of $CH_3COOC_6H_4COOH$

Mass of acetylsalicylic acid present:

mass = n x MM

mass = 6.23×10^{-4} x [9(12) + 8(1) + 4(16)]

$= 6.23 \times 10^{-4} \times 180$

$= 0.112g$

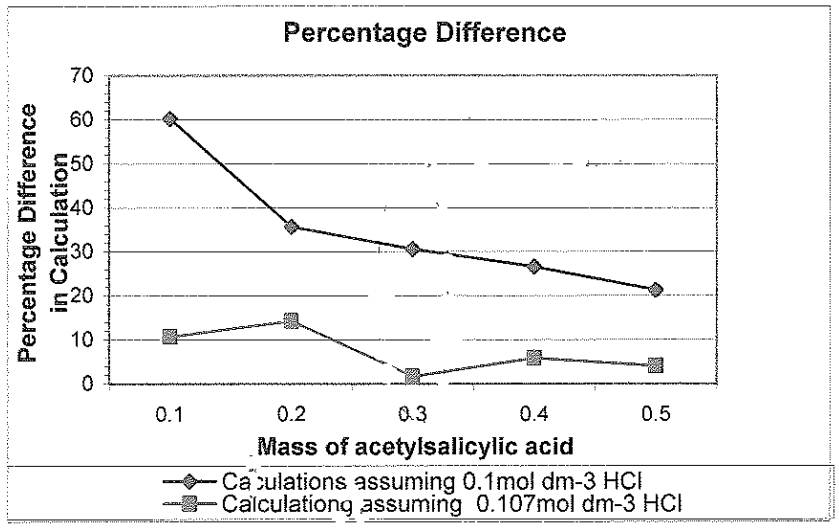
$$\text{Percentage Difference} = \frac{|\text{Actual - Theoretical}|}{\text{Actual}} \times 100$$

$$\% \text{ Difference} = \frac{|0.112g - 0.100g|}{0.112g} \times 100$$

$= 10.7$

This table (below) shows the calculations of each standard sample of acetylsalicylic acid based on the volume of hydrochloric acid that was added to the solution during the titration.

Mass (g) of acetylsalicylic acid used (± 0.005)	Mass (g) of acetylsalicylic acid calculated assuming 0.1moldm^{-3} HCl	Mass (g) of acetylsalicylic acid calculated using 0.107 moldm^{-3} HCl	% Difference when assuming 0.1 moldm^{-3} HCl	% Difference when assuming 0.107 moldm^{-3} HCl
0.100	0.252	0.112	60.3	10.7
0.200	0.311	0.175	35.7	14.3
0.300	0.432	0.305	30.6	1.64
0.400	0.545	0.425	26.6	5.88
0.500	0.635	0.521	21.3	4.03



From the graph above you can tell that the percentage errors decreases significantly when calculations are made using the calculated concentration of the hydrochloric acid, 0.107moldm^{-3}, instead of assuming the concentration is exactly 0.1moldm^{-3}.

Percentage Uncertainty of the mass of acetylsalicylic acid calculated

$= V_{NaOH} + C_{NaOH} + V_{HCl} + C_{HCl} + M_{acid\ added}$

% Uncertainty of $V_{NaOH} = \frac{0.06}{25.00} \times 100$

$= 0.24\%$

% Uncertainty of $C_{NaOH} = 0.125\%$

% Uncertainty of $V_{HCl} = \frac{0.05}{22.20} \times 100$

$= 0.23\%$

% Uncertainty of $M_{acid\ added} = \frac{0.005}{0.100} \times 100$

$= 5.00\%$

% Uncertainty of calculated mass of acetylsalicylic acid:

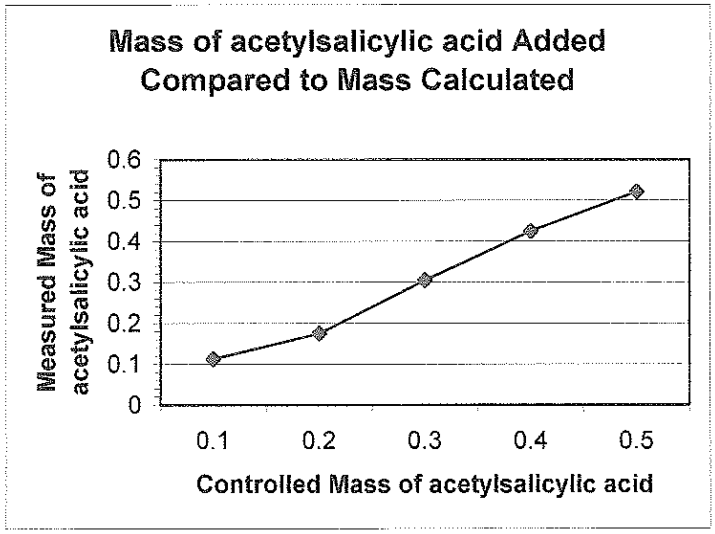
$= 0.24 + 0.125 + 0.23 + 5.000$

$= \mathbf{5.60\%}$

The table below shows, for each mass of acetylsalicylic acid used, the percentage difference between the known value and the calculated value and the percentage uncertainty of the apparatus.

Mass (g) of Acetylsalicylic Acid Used (± 0.005)	% Difference Calculated	% Uncertainty of Mass Acetylsalicylic Calculated
0.100	10.7	5.60
0.200	14.3	3.10
0.300	1.64	2.28
0.400	5.88	1.88
0.500	4.03	1.64

As a result of most of the percentage differences being greater than the percentage uncertainties, there must be both random and systematic errors in the experiment.



The above graph shows a small variation in the determination of the mass of acetylsalicylic acid. This shows that the experiment includes inherent errors.

Procedure for the Determination of the Mass of acetylsalicylic acid Present in Different Brands of Aspirin Tablets

The method for the determination of the mass of acetylsalicylic acid present in the aspirin tablets is carried out the same as the procedure for acetylsalicylic acid determination. Instead of weighing the specific masses of acetylsalicylic acid, 1.3g to 1.7g of the aspirin tablets were weighed. The mass of one aspirin tablet and the total mass of the aspirin tablets used in each sample were recorded. Then the procedure was carried out as before.

After initial tests of each different brand, modifications were made to see if they would effect the results. In most of the solutions the aspirin tablets did not dissolve completely and left a precipitate, solid matter separate from the solution. This precipitate is composed mostly of maize starch, used in the tablets as a filler. Methods consulted suggested the use of ethanol to dissolve the tablets.[9] For safety reasons, the only ethanol available at school contained purple dye. If this ethanol had been used the endpoint of the titration would have been hard to recognise, as it is dependent on the identification of phenolphthalein's colour change, which could not have been detected through the interference of purple dye. Instead of ethanol, 20.00cm^3 of methanol was added to the second test of the Boots soluble aspirin. The second samples of Disprin and Boots Aspirin were heated in a water bath to insure the high temperatures of the hotplate did not cause the breakdown of the molecules. At the same time the third samples of Boots Aspirin and Boots Soluble were used as controls, meaning all four samples were made under the same conditions.

Data Collection for the Different Brands of Aspirin

Aspirin Brand	Mean Volume (cm^3) of $0.107moldm^{-3}$ HCl Added (± 0.05)
Safeway	9.80
Safeway #2	9.90
Aspirin 16	9.50
Aspirin 16 #2	9.58
Disprin	13.20
Disprin #2	13.48
Boots Soluble	11.18
Boots Soluble #2	11.10
Boots Soluble #3	11.30
Boots Aspirin	10.53
Boots Aspirin #2	10.25
Boots Aspirin #3	10.30

See appendix[1] for more data regarding acetylsalicylic acid determination is aspirin.

[9]Determination of Aspirin using Back Titration; page 7
Volumetric Determination of Acetylsalicylic Acid in Aspirin; page 2

Data Analysis for the Different Brands of Aspirin

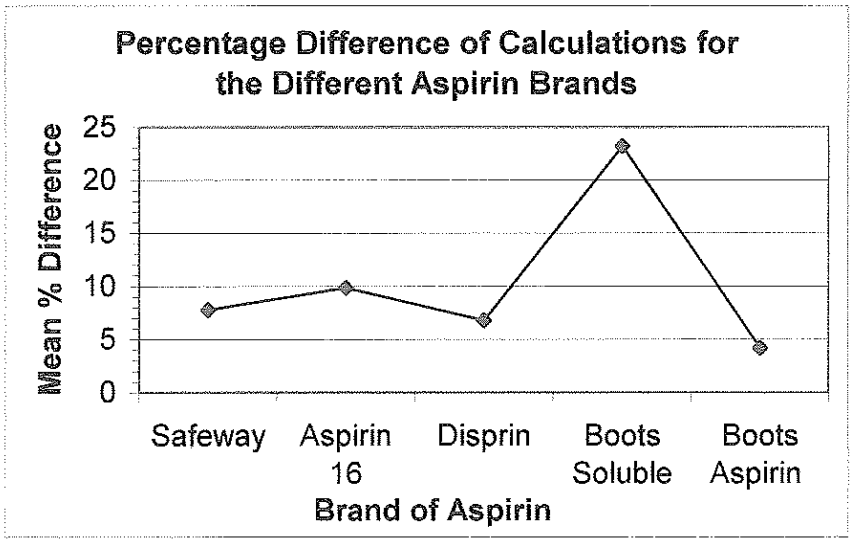
Calculations for determining the mass of acetylsalicylic acid in aspirin tablets are the same as those demonstrated for calculating the mass of acetylsalicylic acid in the samples with already known masses. The only difference is that to calculate the mass of acetylsalicylic acid per tablet it is necessary to divide the overall mass of acetylsalicylic acid by the number of tablets.

This table shows the mass of acetylsalicylic acid calculated for each sample, the percentage difference between the theoretical mass, 300mg, and the calculated mass, the percentage uncertainty and any comments regarding modification of the procedure.

Aspirin Brand	Mass of acetylsalicylic acid calculated (mg)	% Difference between calculated mass and 300mg	% Uncertainty of Mass acetylsalicylic acid Calculated	Comments
Safeway	326.6	8.14	1.21	
Safeway #2	324.2	7.46	1.21	
Aspirin 16	333.8	10.13	1.25	
Aspirin 16 # 2	332.0	9.63	1.25	
Disprin	326.3	8.06	1.08	
Disprin #2	317.5	5.51	1.06	Heated in a water bath
Boots Soluble	391.3	23.33	1.09	
Boots Soluble #2	393.7	23.80	1.09	With methanol
Boots Soluble #3	387.3	22.54	1.08	Control*
Boots Aspirin	309.1	2.94	1.22	
Boots Aspirin #2	315.7	4.97	1.23	Heated in a water bath
Boots Aspirin #3	314.5	4.61	1.23	Control*

*The controls were exposed to the same conditions as those heated in the water bath however; they were heated straight from the hotplate like the other samples.

All of the percentage uncertainties were smaller than then the percentage differences therefore showing that systematic errors must be present in the experiment as well as random errors.



As can be seen above the samples produced results that were relatively close to 300mg. The percentage difference of the individual solutions ranged from 2.94 to 23.8. Since all of the percentage differences calculated are larger than the percentage uncertainties systematic errors are present. The graph above shows that the percentage difference is irregular throughout the different tests. This means that there must also be a high level of random errors. Boots Soluble aspirin was the only brand that constantly produced percentage differences greater than twenty percent. This increase in percentage difference can be understood when taking into account that Boots Soluble aspirin not only contains acetylsalicylic acid and maize starch but citric acid, calcium carbonate, lactose and sodium saccharin. Citric acid and calcium carbonate make the tablets fizz and the acid allows the tablets to dissolve in the stomach. Maize starch is used as a filler. Lactose and sodium saccharin make the tablets palatable and act as sweeteners. Titrations are only able to detect the overall mass of acid present therefore the mass of acid calculated assumes that the only acid present is acetylsalicylic acid. The greater mass of acid present in Boots Soluble aspirin, assumed to be acetylsalicylic acid, is therefore accounted for by the presence of citric acid. By taking into account the presence of citric acid in Boots Soluble aspirin, all of the aspirin tablets contain values of acetylsalicylic acid that are around 300mg. The experiment proves that all of the aspirin brands contain around the same mass of acetylsalicylic acid. The main limitation of this method is that it cannot compensate for different acids being present in the tablets. An alternative method, such as the use of thin layer chromatography, would have to be used in order for different acids to be taken into account.

Method for Extraction of salicylic acid From Salix alba Bark

10.000g of willow bark was weighed and cut into small pieces using scissors. In order to extract the salicylic acid, the pieces of willow bark were placed in a 100.00cm^3 solvent of methanol, acetic acid and water (90:2:8). This solution was left for a few days in the refrigerator (approximately 4°C). The solution was filtered through Whatman number 1 filter paper while under vacuum in a Buchner flask. The willow extract was then extracted further with 40.00cm^3 of the same solvent. The solution was then left in a fume cupboard to evaporate, as the school does not own an evaporator. When the solution had evaporated to 25.00cm^3 the extract was added to a separating funnel with 20.00cm^3 of ethyl acetate. The solution was swirled and then left to settle. The bottom layer of the solution was removed and the upper layer was returned to a beaker and left to evaporate. When the solution had evaporated, 10.00cm^3 of methanol was added and the mixture was swirled until all of the extract was dissolved in the methanol.[10]

To quantitatively determine the mass of salicylic acid present in the willow another back titration was performed. After adding phenolphthalein to the extracted willow and methanol solution, 2.00cm^3 of the solution was added to 10.00cm^3 of 0.100$moldm^{-3}$ sodium hydroxide, and the solution turned red. This solution was titrated against 0.107$moldm^{-3}$ hydrochloric acid until the solution changed back to its original brown colour.

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[10] Photochemical Methods; page 33-39
Willows; e-mail from Steve Woodward

Salicylic acid is present in willow bark, but the acid detected in this titration could have been due to acetic acid being used in the solvent. A blank titration was carried out to determine the origin of the acid. A sample without willow bark was made with methanol, acetic acid and water (90:2:8) solvent. A sample was also made containing 5.000g of willow bark and a solvent containing methanol and water (45:5). All extractions were carried out as described above.

The qualitative determination of salicylic acid was carried out using thin layer chromatography (TLC). Chromatography is used to separate mixtures in order to determine their components. Thin layer chromatography gives a better separation of mixtures compared to paper chromatography. Each substance detected with chromatography has two phases a stationary phase and a mobile phase. The mobile phase will pass the stationary phase and components are therefore separated by the amount of time spent in each phase. An R_f value can be calculated in order to identify the salicylic acid.[11]

In addition to the two willow extracts, two other solutions were made. One contained pure acetylsalicylic acid and the other pure salicylic acid. For each solution 0.100g of the acid was dissolved in 10.00cm^3 of methanol. Two drops from each of the solutions were placed onto two TLC plates and allowed time to dry. The first plate contained the solutions containing acetylsalicylic acid, salicylic acid and the willow extract with the acetic acid solvent. The second plate contained both the acetylsalicylic acid, salicylic acid and the willow with the solvent not containing acetic acid. The plates were placed into a dichloromethane-methanol (94:5 v/v) solvent, with a cover to prevent evaporation, until the solvent reached approximately 1-2 cm from the top of the plate. After the plates had dried they were placed under a UV light at 254nm. A comparison was made between the chromatography of the acetylsalicylic acid, salicylic acid and willow solutions.

Since willow bark naturally contains various quantities of water, the dry mass percent of the willow was needed to produce accurate results. First a crucible was heated at 100°C for an hour, cooled in a dessicator and weighed. Then approximately 2g of willow was placed into the crucible and weighed. At 100-102°C the crucible and willow were heated for 48 hours. The crucible and willow was then reweighed.

Data Collection for Determination of salicylic acid in Salix alba

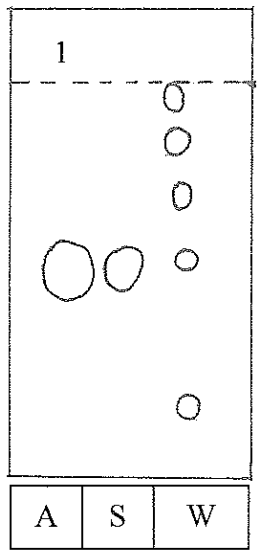
The quantitative determination of salicylic acid:

	Test 1-willow and solvent	**Test 2**- no willow in acetic acid solvent
Final Burette reading/cm^3 (±0.05)	39.10	43.65
Initial Burette reading/cm^3 (±0.05)	32.75	35.15
Volume of HCl added/cm^3 (±0.05)	6.35	8.50
Observations	Originally brown-yellow, turned red with NaOH, was then titrated and returned to original brown colour.	The clear solution changed pink after the addition of NaOH. Turning colourless after adding HCl.

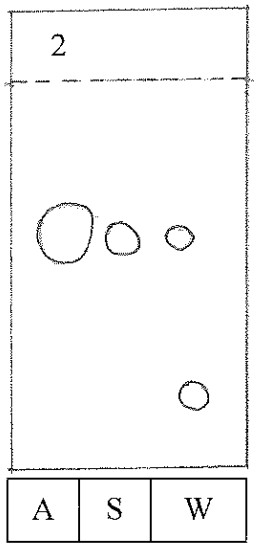
[11] Chemistry, for use with the International Baccalaureate; page 672

The qualitative determination of salicylic acid:

TLC Data Collection



A - acetylsalicylic acid
S - salicylic acid
W - willow extract with acetic acid



A - acetylsalicylic acid
S - salicylic acid
W- willow extract without acetic acid

Dry mass percent:

Sample	**Wet Weight** (±0.005)	**Dry Weight** (±0.005)
1	2.620	1.070
2	2.160	0.860
3	2.280	0.900

Data Analysis for the Determination of salicylic acid From Salix alba

Calculations for Test 1 (quantitative analysis):

$10.00cm^3$ of $0.100moldm^{-3}$ NaOH present in excess
Moles = $0.100moldm^{-3}$ x $0.01dm^3$ = 1×10^{-3}

Moles of HCl: $n = c \times v$

$$n = 0.107 \times \frac{6.35}{1000}$$

Moles of HCl = 6.7945×10^{-4}
Therefore: Moles of NaOH = 6.7945×10^{-4}

$HOC_6H_4COOH_{(s)} + NaOH_{(aq)} \rightarrow HOC_6H_4COONa_{(aq)} + H_2O_{(l)}$
Initial added – moles neutralised by HCl
$1 \times 10^{-3} - 6.7945 \times 10^{-4}$
= 3.2055×10^{-4} – Moles of NaOH used to neutralise the salicylic acid

3.2055×10^{-4} – moles of HOC_6H_4COOH

Mass = $3.2055 \times 10^{-4} \times 138$
= 0.044236g of salicylic acid present
= 4.42mg

Test Number	Mass of salicylic acid Detected (mg)
1	4.42
2	1.25

4.42 – 1.25 = 3.17mg – mass of salicylic acid found in 10.000g of wet Salix alba taking into account acetic acid solvent.

Dry Mass:
Percent Dry Matter = $\frac{\text{weight of sample after drying}}{\text{weight of sample before drying}} \times 100$
Sample One = $\frac{1.07}{2.62} \times 100$
= 40.84%

Sample	% Dry Matter
1	40.84
2	39.81
3	39.47

Average percentage dry matter equals 40.04%

Of the 10.00g of wet willow used in the sample only 4.004g was dry willow mass.
4.004g = 3.17mg
$\frac{4.004\text{ g}}{4.004} = \frac{3.17}{4.004}$
1g = 0.792mg
Therefore each gram of Salix alba contains 0.792mg of salicylic acid.

The equation below shows that the combination of salicylic acid and acetic anhydride produces acetylsalicylic acid.
$2\ HOC_6H_4COOH + (CH_3CO)_2O \rightarrow 2CH_3COOC_6H_4COOH + H_2O$

MM = 138	MM = 180
mass = ?	mass = 300mg
	moles= $\frac{300}{180}$
moles = 1.6667	= 1.6667

mass = 1.6667 x 138
= 230mg

If one aspirin tablet contains 300mg of acetylsalicylic acid, it would have been produced from 230mg of salicylic acid. In order for 230mg of salicylic acid to be consumed around 290g of willow bark would have to be chewed or ingested. It is impractical to expect to gain the same amount of salicylic acid from willow bark as you would of acetylsalicylic acid from one aspirin tablet.

Calculations for TLC (qualitative analysis):

R_f of salicylic acid = $\frac{\text{Distance moved by component}}{\text{Distance moved by solvent}}$

$= \frac{3.60\text{cm}}{6.60\text{cm}}$

$= 0.545$

Conclusion and Evaluation

This lab proved the existence of salicylic acid in Salix alba. However, there was only a small mass present in one gram of bark. In order to reach the equivalent of 300mg of acetylsalicylic acid, 290g of willow bark would need to be consumed. The aspirin tablets tested had calculated values of acetylsalicylic acid close to 300mg. This shows that all of the brands basically have the same mass of acid present, and the mass is around the expected mass.

One problem with the procedure is the assumption that the sodium hydroxide used is exactly 1.00moldm^{-3}. The sodium hydroxide should have been standardised using a hydrochloric acid solution with a known concentration. Another limitation is that the concentration of the hydrochloric acid was calculated by diluting a sample of 1.00moldm^{-3} sodium hydroxide into 0.1moldm^{-3}. This means that all of the calculations, based on the assumption that the hydrochloric acid has a concentration of 0.107moldm^{-3}, are slightly inaccurate as there is a 0.765 percentage error in the dilution of the sodium hydroxide. Practically this limitation cannot be helped. Attempting to standardise the hydrochloric acid by using 0.1moldm^{-3} sodium hydroxide would unnecessarily waste a large volume of hydrochloric acid.

When testing the aspirin tablets, the solutions that were titrated were often yellow-brown. One limitation of titrations is that the solutions must be colourless or the colour might interfere with the perception of the colour change.[12] After titrating the solutions, they returned to their original colour. This meant their original colour had to be taken into consideration during the titration. This is a weakness of the experiment that cannot be helped. If the hydrochloric acid was in the flask and the sodium hydroxide was added through a burette it would probably be more difficult to detect the endpoint. As colour change to light pink would be difficult to see through the yellow-brown colour. Another common weakness of titrations is that end points are subject to interpretation. People's perception of colours vary, this means that different endpoints would be reached based on the person. To rectify this, titrations could be performed using a pH meter instead of only relying on indicators.

It was also difficult to ensure that the solutions only simmered on the hotplate instead of boiling. To render this problem a hotplate with a wider range of temperatures could be used or alternatively a Bunsen burner. After heating the solutions containing the different brands of aspirin precipitate was formed in the mixture. Most of the precipitate was not added into the solution when titrating. It is possible that if the precipitate had been able to dissolve in the solution it could have diluted the acetylsalicylic acid and therefore the results would have been closer to the predicted

[12] Merrill Chemistry; page 616

values. Methanol was used in an attempt to dissolve the precipitate but unfortunately was unsuccessful. Ethanol might have been a better dissolvent but as stated before, it was only available with a dye.

While most of the results were fairly accurate the Boots Soluble tablets continually obtained over a twenty percent percentage difference. This was due to the fact that citric acid is added to soluble tablets to make the tablets soluble and allow them to dissolve in the stomach. Titrations cannot differentiate between different types of acid. As a result the high percentage difference for Boots soluble can be accounted for by the presence of citric acid. TLC could have been used to distinguish between the two acids and then quantity the amount present.

Throughout the experiment, data analysis showed that the percentage difference of the mass of acetylsalicylic calculated was usually greater than the percentage uncertainty. Therefore simply repeating the procedure would not have produced more accurate results, as both systematic and random errors were present. The application of the aforementioned modifications could produce more accurate results. For the determination of acetylsalicylic acid, calculations demonstrate a trend in that both the percentage difference and the percentage uncertainties decrease when a greater quantity of acetylsalicylic acid is being used. As the 300mg of acetylsalicylic acid in an aspirin tablet is a relatively small amount, the error in this experiment is greater than if larger amounts of the acetylsalicylic acid were being looked for. In Salix alba an even smaller amount of salicylic acid was trying to be determine. This means that if percentage errors had been able to be calculated they probably would have been high.

Given more time the lab could be extended so it could quantify the mass of salicylic acid in the willow bark using thin layer chromatography. A known quantity of willow extract could be applied to a TLC plate and using dichloromethane-methanol as a solvent, the identified salicylic acid ($R_f = 0.545$) could be extracted and an acid-base titration could then quantify the salicylic acid in the willow extract. The use of TLC plates to quantify the salicylic acid would most likely produce more accurate results than the method performed in this lab. It would also be interesting to determine if salicylic acid is only present in Salix alba or if is was found in other types of willow bark. To test this different types of willow could be extracted using the same method.

Word Count: 3,842

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Appendix:

Appendix[1]

Aspirin Brand	Amount of aspirin used (g) (±0.005g)	Mass of one aspirin tablet (g) (± 0.005g)	Number of Tablets
Safeway	1.510	0.370	4
Aspirin 16	1.380	0.340	4
Disprin	1.500	0.500	3
Soluble Boots	1.820	0.610	3
Boots Aspirin	1.320	0.330	4
Safeway #2	1.480	0.370	4
Boots Soluble #2	1.820	0.610	3
Aspirin 16 #2	1.370	0.350	4
Disprin #2	1.530	0.520	3
Boots Aspirin #2	1.320	0.330	4
Boots Soluble # 3	1.820	0.590	3
Boots Aspirin #3	1.320	0.330	4