

Aspirin Purity by pH Titration

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Purpose of this Exercise: To determine the purity of your synthesized aspirin sample by acid-base titration, and to compare the results with those from pure salicylic acid, acetylsalicylic acid, and with commercial aspirin tablets.

Background Information

Aspirin (originally a legally restricted brand name owned by Bayer for its brand of acetylsalicylic acid, but now a generic term) has been in use as an analgesic (pain-killer) and antipyretic (fever-reducer) for over a century. During most of that time, little was known about its mode of action in the body, although this has become better understood in recent years. It has also been realized that, in addition to its mild short-term analgesic effect, aspirin has some potent long-range benefits, including reducing the probability of users' suffering heart attacks and colon cancer.

Chewing willow twigs was a traditional folk remedy in many parts of Europe for headache and other minor pains. In the nineteenth century, chemists isolated salicylic acid from willow twigs and showed that it was the effective ingredient. The name derives from the Latin name *Salix*, the genus of willow trees. Pure salicylic acid, however, is very damaging to the stomach, and the acetyl derivative was prepared in order to reduce this undesirable side effect. Acetylsalicylic acid has become the most extensively used pharmaceutical product in the world.

On standing for prolonged periods of time in a humid atmosphere, aspirin tablets develop a vinegary smell that you may have noticed. This is due to the *hydrolysis* of acetylsalicylic acid (ASA) to form salicylic acid (SA). A hydrolysis is a reaction with water to break one or more bonds. In this case, the acetyl group comes off as acetic acid, which causes the vinegary smell.

This is a reversal of the synthesis process you carried out previously in this course.

In this exercise, we will determine by acid-base titration the amounts of ASA and SA in your synthesized sample of aspirin. [Incomplete reaction or inadequate washing of the product are likely to have left the ASA contaminated with some SA.] The same titration process can be used to determine ASA content in commercial aspirin tablets. Commercial tablets usually contain inert binders such as starch, so it is not possible to determine the ratio of SA and ASA by titration alone unless the binder is removed. We can, however, determine the overall percent of active ingredient.

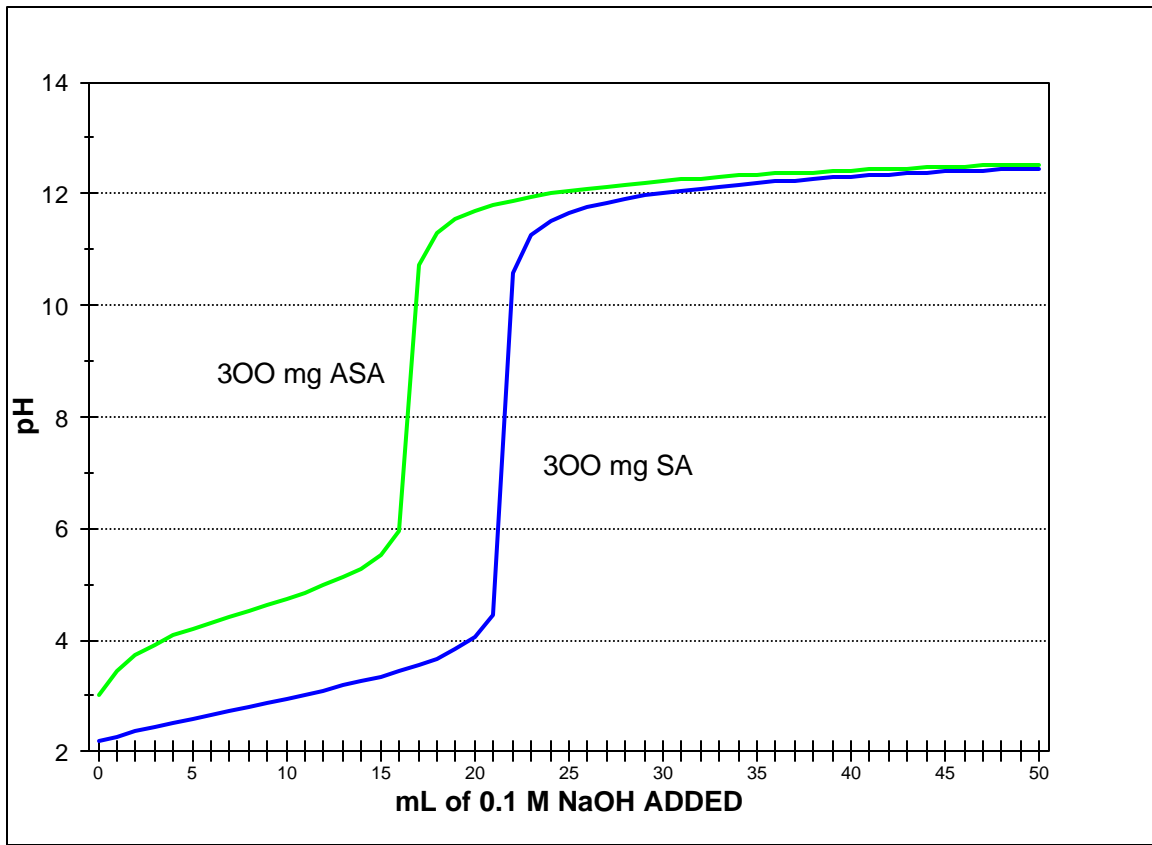
We will make use of the effective molar mass of the synthesized samples to assay their content, but we will also take note of the overall *titration curve* (see below) for confirmation of our conclusions. This can be done for both the synthesized sample and the tablets.

Some data on SA and ASA relevant to this exercise are the following:

<u>Compound</u>	<u>Salicylic Acid (SA)</u>	<u>Acetylsalicylic Acid (ASA)</u>
Formula	$C_7H_6O_3$	$C_9H_8O_4$
Molar Mass	138.12	180.15
K_a	1.08×10^{-3}	2.72×10^{-5}
pK_a	2.99	4.57
Solubility (g/100 mL)	0.18	0.25

SA and ASA have significantly different molar masses. If we titrate the same weight of the two acids with base, it will take more base to reach the endpoint with salicylic acid, since there will be more mmoles of acid in the sample due to its lower molar mass. A mixture will require an intermediate amount of base. We can use this fact to assay the sample.

It can also be seen from the data above that SA is a stronger acid. The K_a of a weak acid is the equilibrium constant for the reaction in which the acid dissociates in water. A smaller value indicates less dissociation and therefore a weaker acid. SA is about 40 times stronger than ASA, and we can detect this if we look at titration curves of the two acids. A titration curve is a plot of the pH of a solution of the acid as a function of the amount of base added. The stronger acid will produce a more acidic solution (lower pH) in the lower region of the curve prior to complete neutralization. The figure below illustrates calculated titration curves for 300 mg of pure SA and 300 mg of pure ASA with 0.1 M NaOH. Remember that the pH at the point of half-neutralization is equal to the pK_a of the acid.



Procedures

CAUTION Sodium hydroxide solutions are very caustic and can cause prolonged and painful injuries to skin or eyes. Avoid all contact with these solutions. If accidents occur, flood the affected area with water for several minutes. Wear safety glasses at all times while in the laboratory.

Part 1. Indicator Titration

1. Be sure to read SUPL-006 carefully before coming to lab. Part 1 of this exercise will be done *in pairs, but each student must do a phenolphthalein titration of his/her synthesized aspirin.*
2. *Accurately* (on the analytical balance) weigh out ~0.2 g samples of SA, ASA, and each of your synthesized aspirin samples. You don't have to do all the weighings at once, but label containers clearly so you won't get confused.
3. Dissolve each sample in 10 mL of 95% ethanol stirring vigorously. When the sample is completely dissolved, add 90 mL of distilled water, and stir the solution again.
4. Add two or three drops of phenolphthalein indicator to each solution and titrate with the standardized sodium hydroxide solution provided. (The concentration is about 0.05 M. Record the *precise value* in your notebook and on the data sheet.) Determine the endpoint carefully by looking for formation of a persistent light pink color. Repeat as necessary to assure an accurate and reproducible result.
5. Calculate the effective molar mass (EMM) of each sample, using the data sheet as a guide. The EMM is the mass of sample in mg which produces one mmole of H⁺ ions upon titration. For a pure compound with one acid group per molecule, this should be the actual molar mass of the compound. For a mixture, this will be a weighted average of the molar masses of the acid components.
6. If the sample consists only of ASA and SA, then the percent composition can be derived from the EMM according to the relationships:

$$\%SA = 100 (180.15 - EMM) / (180.15 - 138.12) = 2.379 (180.15 - EMM)$$

$$\%ASA = 100 (EMM - 138.12) / (180.15 - 138.12) = 2.379 (EMM - 138.12)$$

Calculate the % composition of your sample.

Note that the relationship between percent composition and EMM applies to mixtures containing **only** SA and ASA! **If the measured EMM is greater than 180.15 or less than 138.12, the above formulas do not apply. Simply report that the EMM was out of the possible range and assume the sample consists of 100% SA or ASA, whichever is appropriate.**

If your EMM for pure SA or pure ASA differs from the expected value by more than 10%, you should repeat that titration before proceeding to the next part.

Part 2. pH Titration.

Part 2 will be done **individually** sharing pH meters. Please work efficiently and cooperatively. Before beginning this part, using data from Part 1, calculate how much of your synthesized aspirin will be required to consume 25 ± 3 mL of the sodium hydroxide.

7. Weigh another sample of your synthesized aspirin in accordance with the calculation above on the analytical balance. Dissolve the sample in 10 mL of 95% ethanol. When the sample is completely dissolved, add 90 mL of distilled water as in Part 1. Be sure that the solution is homogeneous, and that it is at room temperature.

(a) Calculate the volume of NaOH which will be required to titrate the actual weight of your sample and enter it in your notebook and on the data sheet.

(b) Using the pH meter, determine the pH of the solution.

(c) Add about 2 mL of NaOH solution from your buret, read the buret, and again determine the pH. Record in your notebook a table showing buret reading, total volume of base added, and pH.

(d) Repeatedly measure the pH after adding incremental amounts of standard NaOH solution from your buret. Two mL increments will be adequate at first, but decrease the size of the increments as you approach the endpoint. You should be able to calculate from your work in Part I the volume of NaOH solution required to reach the endpoint. As you approach it, the pH begins to change more quickly. You should then reduce the amount of NaOH solution added between pH readings. **In the vicinity of the endpoint (within ± 1 mL), you should take readings after every drop.** A suggested format for data collection is on the back of Data Sheet 1. This will insure that you plot pH against the actual volume delivered.

(e) After the endpoint has been passed by about 1 mL, continue adding base, **up to an additional 10 mL**, in one mL, and then, two mL increments, taking pH readings in order to define the upper portion of the titration curve.

(f) Plot the data on graph paper, using Fig. 1 as a guide, and turn in your graph with the data sheet. Indicate the endpoint on your graph explicitly. Write on your graph the EMM calculated from your endpoint, and the percent composition of your sample.

Part 3. Analysis of commercial aspirin tablet

8. A commercial aspirin tablet usually contains 325 mg (0.325 g) of acetylsalicylic acid. This is an appropriate amount to titrate. If your tablet is a different size, adjust the amounts by using, for example four 80 mg tablets. Weigh a tablet (or tablets, as appropriate) and crush it completely, dissolve it in 10 mL of 95% ethanol by stirring vigorously. Because of the binders in normal aspirin

tables, this solution may not turn clear . When the tablet appears to be dissolved, add 90 mL of distilled water, and titrate the resulting solution either with phenolphthalein indicator or with the pH meter, as in Part 2. Assuming that all of the acid in the tablet is acetylsalicylic acid, calculate the amount present. If you obtained a titration curve, is the curve consistent with that of pure acetylsalicylic acid?

NOTE:

In choosing tablets to bring in for this exercise, you should investigate the composition of the tablets carefully. There are some elements of common sense that need to be considered.

- 1.) The tablets must contain aspirin. Tablets with aspirin substitutes such as acetaminophen, ibuprofen or naproxen will not give meaningful results in this exercise. Such tablets are sold under a wide variety of trade names. **You must read the label.**
- 2.) **Buffered** aspirin tablets will not give meaningful results. Why?

You are encouraged to prepare a table in your notebook like the one on the back of the datasheet for collection of the pH titration data before coming to class.

SUSB-012 Data Sheet

Name	Section	Date
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Partner's Name _____

Part 1

	<u>Run 1</u> Pure ASA	<u>Run2</u> Pure SA	<u>Run 3</u> Synth. Asp.
Conc. of NaOH solution		_____M	
Mass of vial + sample	_____mg	_____mg	_____mg
Mass of vial - sample	_____mg	_____mg	_____mg
Mass of sample	_____mg	_____mg	_____mg
Final buret reading	_____mL	_____mL	_____mL
Initial buret reading	_____mL	_____mL	_____mL
Volume of NaOH used	_____mL	_____mL	_____mL
mmoles of NaOH used	_____mmol	_____mmol	_____mmol
mmoles acid	_____mmol	_____mmol	_____mmol
EMM = mg/mmol	_____	_____	_____
% Salicylic Acid			_____%
% Acetylsalicylic Acid			_____%

Part 2: Please attach your titration curve(s) to this data sheet.

Weight of your sample _____ mg Calculated Volume of NaOH _____ mL

Part 3

Mass of aspirin tablet: _____g

Vol. of NaOH solution: _____mL

Mmoles of NaOH used: _____mmol

Mmoles of ASA present: _____mmol

Mass of ASA present: _____g

% ASA by weight _____%

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* The net volume added is the buret reading minus the **initial** buret reading.

SUSB-012 Pre-Laboratory Assignment

Name

Section

Date

1. A student, Iva Heddake, weighs an aspirin tablet and finds that it weighs 385 mg. She crushes it, dissolves it, and titrates it with 0.0500 M. NaOH solution. The volume required to reach the endpoint is 29.97 mL. How much ASA is in the tablet, and what is its % by weight of the tablet? [You can't use the EMM formula for this problem. Why not?]
2. Another student, Peter Principle, boils the water in which he is attempting to dissolve his aspirin tablet, which weighs 392 mg, for several minutes. His titration with 0.050 M. NaOH solution requires 44.37 mL. What is the apparent % ASA in the tablet? [Again, don't attempt to use the EMM formula.] Is there a problem here? If so, what is likely to have happened?
3. Titration of a 324 mg sample of Joe Bftsplk's synthesized aspirin with 0.100 M. NaOH solution required 20.30 mL. What is the EMM of the sample, and what is the % ASA?
4. A buffered aspirin sample containing 325 mg of aspirin and 360 mg of calcium carbonate is dissolved in 100 mL of water and the solution is permitted to stand for an extended period. What reaction(s) is (are) likely to occur? How much 0.05 M NaOH will be required to titrate the resulting solution to a phenolphthalein end point? Why?

