

## 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 and pure acetylsalicylic acid.

### 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.

On standing for prolonged periods of time in a humid atmosphere, aspirin tablets develop a vinegary smell that you may have noticed. This was the basis for one of the tests you performed to verify that your synthesis produced aspirin. It 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 by which you made the aspirin.

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.

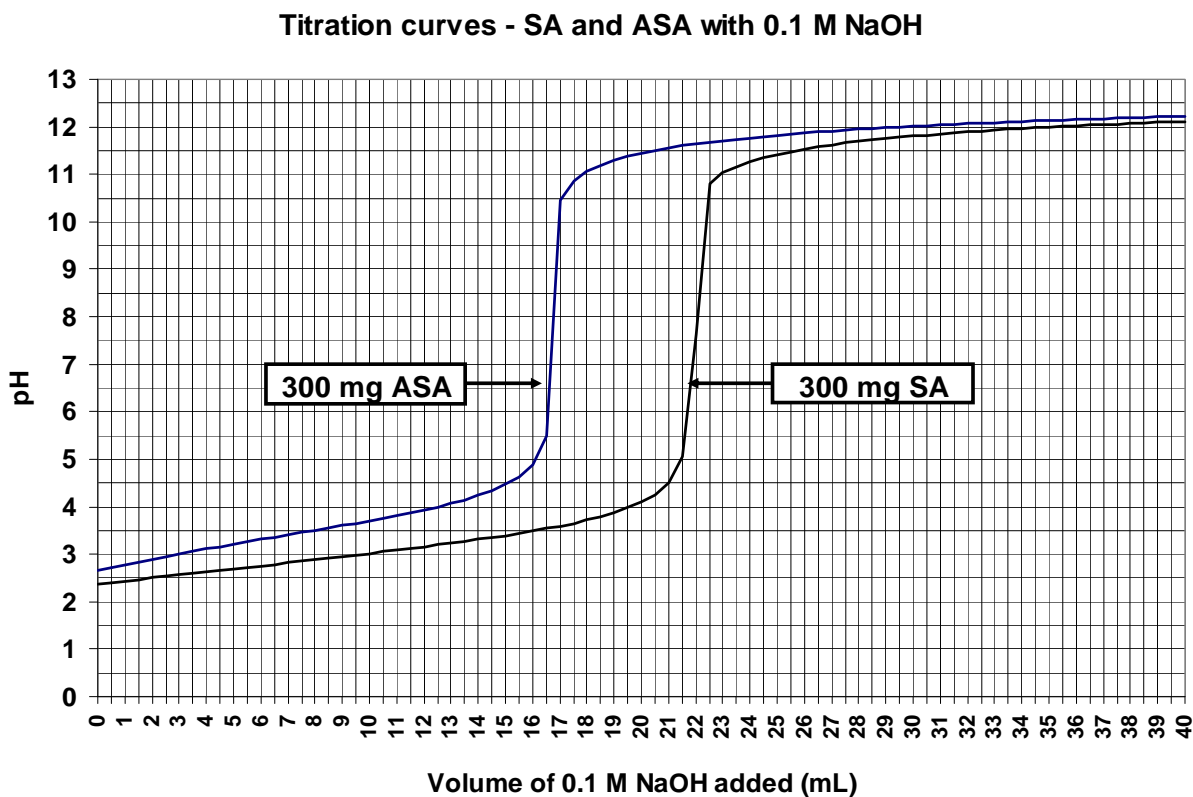
Some data on SA and ASA relevant to this exercise are the following:

Compound	Salicylic Acid (SA)	Acetylsalicylic Acid (ASA)
Formula	$C_7H_6O_3$	$C_9H_8O_4$
Molar Mass	138.12	180.15
$K_a$	$1.08 \times 10^{-3}$	$3.16 \times 10^{-4}$
$pK_a$	2.99	3.50
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 using a 250 mL Erlenmeyer flask. **After 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<sup>+</sup> 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 (which you will derive in the pre-lab exercise).

$$\begin{aligned}\%SA &= 100 ( 180.15 - \text{EMM} ) / ( 180.15 - 138.12 ) = 2.379 ( 180.15 - \text{EMM} ) \\ \%ASA &= 100 ( \text{EMM} - 138.12 ) / ( 180.15 - 138.12 ) = 2.379 ( \text{EMM} - 138.12 )\end{aligned}$$

Calculate the % composition of your sample. **Using the values of the molar masses (EMMs) of SA and ASA that you have determined for the pure substances in the above formulas will minimize any systematic errors you may have made in the titrations.**

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  $25 \pm 3$  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 in a 250 mL **beaker**. After 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  $\pm 1$  mL), and only in that region, you should take readings after every drop or two.** A suggested format for recording the data collection in your notebook is on the back of Data Sheet 1. This will insure that you plot pH against the actual volume delivered. There is no need to transcribe the data on to this data sheet.

(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. Be sure to use the criteria described in SUSB-004 (which is available on the web at:

<http://www.ic.sunysb.edu/Class/che133/susb/supl004.pdf>)

in drawing your graph.

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\* Remember to use the values of the molar masses of SA and ASA that you have determined from the titrations in the formulas utilizing EMM.

## SUSB-012 Data Sheet

Notebook Grade: \_\_\_\_\_

Safety Grade: \_\_\_\_\_

\_\_\_\_\_  
 Name Section Date

\_\_\_\_\_  
 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	_____ g	_____ g	_____ g
Mass of vial - sample	_____ g	_____ g	_____ g
Mass of sample	_____ g	_____ g	_____ g
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



## Pre-Laboratory Questions – SUSB-012

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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. 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?
4. Titration of an **X** mg sample of synthesized aspirin with 0.100 M. NaOH solution required 20.30 mL. What is the EMM of the sample, and what is the % ASA? Calculate **X** by adding one-half of the last two digits of your USB ID in mg to 300 mg.

